The History of Tropical Medicine.

1923.

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same beneficent rule appeared the great Arabian physicians Rhazes, Haly Abbas, and Avicenna.

Arabian medicine was carried into Spain by the Moors, and flourished exceedingly under the generous sympathy of the Cordova Caliphs, producing workers like Albucasis and Avenzour.

Even Egypt had its 'Hall of Wisdom' erected by Hakim Biamrillah in 1005, under the protection of the Cairene Caliphs.

During this period medical instruction was given to scholars in the large hospitals and in the dispensaries, which were numerous.

The features of Arabic medicine which are especially interesting to us are the references to tropical diseases, and these are sufficiently numerous because the Arabic physicians were brought into contact with strangers from various parts of the world who had been attracted to Arabic countries by the wisdom of the Caliphs with regard to learning and liberty. As these strangers often brought with them strange herbs and drugs, so Arabic medicine abounds with references to new remedies for disease.

Associated with Arabic medicine is the appearance of many Jewish medical works, and so much so that it appears to us that this should be held to be *the second period of Jewish medicine*. The reason for this development is because the Caliphs allowed the Jews to live and work in freedom at a time when Christianity as a whole was persecuting them.

The decline of Arabian medicine came in the thirteenth century, with the fall of Cordova in A.D. 1236 and with the Mongol invasion of Bagdad in A.D. 1258, and though it lived for long in Spain, still, its day was over and its scholars were passing to the *School of Salerno*, from which were to come those piercing rays of medical knowledge which were to illuminate the closing years of the Middle Ages.

Before, however, passing on to the consideration of mediæval medicine we will make brief reference to a few of the Arabic works on medicine, which included not merely dictionaries and translations, but original works on general medicine, pharmacopœias, works dealing with natural history, and veterinary matters.

Abû Zakarîya Yûḥannâ ben Mâsawayh or Mesua, was the son of a Christian apothecary in the hospital of Gundeshâpûr. He was appointed by the Caliph Hârûnu-'r-Rashîd to translate Greek works, of which he did many, but he also wrote original treatises—e.g., one upon 'the Curiosities of Medicine.' He died in A.D. 857, and some of his books, as far as we know, were the first medical works to be printed in movable type in 1471. He seems to have been the first to write a medical treatise in tabular form in his 'Kitâbu-'l-Mushajjar,' which comprised treatises on the general rules of medical art and on the diseases of regions and organs, including four books on the diseases of the skin.

Abû Bakr Muḥammad ben Zakarîya-'r-Râzî, or Rhazes, was born at Ray in 'Iraq-i-'Ajam, but did not commence the study of medicine until he was thirty-two years of age, when he was taught at Bagdad by 'Alî ben Rabban at-Tabarî. He was first Director of the Ray Hospital and later of the Bagdad. He died about A.D. 923.

His works are numerous, and we may mention 'Kitâbu-'l Manşûrî' System of Medicine, which is divided into ten chapters. It includes anat diagnosis, ailments and drugs, preservation of health, cosmetics and th of pityriasis, advice to travellers, surgery, poisons, regional diseases, fevers, and also the qualities necessary for a physician, and remarks on quacks and impostors. He gave the earliest accounts of smallpox and measles, which earned for him lasting fame.

A System of Midwifery—'Kitâb u-Tadbîr-al-Habâlâ'—was written in the fourth century by a physician *Abu-'l-'Abbas Aḥmad ben Muhammad ben Yaḥya-'l-Baladî*. This book included the management of pregnancy and the diseases of the fœtus and the infant, as well as the rearing of the child.

Khalaf ben 'Abbâs-az-Zahrawî, or Albucasis, was born at Az-zahrâ, near Cordova, and died probably about A.D. 1013. His great work is 'Kitâbu-'T-Tasrîf,' which is an encyclopædia chiefly valued for its surgical portion, which was translated into Latin in the twelfth century, and for long remained the standard surgery of Europe.

Ophthalmic surgery was considered by *'Alî ben 'Îsâ al-Kuḥḥâl*, or Jesu Haly

Abû 'Alî al-Husayn ben 'Abdullah ben Sînâ, or Avicenna, often called Ash-Shaykh (the Reverend) or Ar-Ra'is (the Chief), was born at Ashainah, in Bukhârâ, in A.D. 980. He was physician to the Sultan of Bukhârâ, but later he retired to Jurjan, where he wrote his celebrated 'Kitâbu'L-Qânûn,' or Book of the Canon. He died in A.D. 1037. His great work is essentially medical, as the surgical portion is poorer than that of Albucasis, and is in many places a treatise on tropical medicine

Hibatullâh ben Zayd ben Hasan ben Ya'qûb ben Ismâ'îl ben Jamî' al Isrâ'îlî, or Ibn Jami Isrâ'îlî was brought up in Old Cairo, and was considered to be the greatest of the Egyptian physicians. He was physician to the celebrated Al-Malik u'n Nâsir Salâh u'd Dîn (Saladin), for whom he made his *Theriac*. He died in A.D. 1198.

The last of the great Arabian physicians, *Dâ'ûd ben 'Umar al-Anṭâkî*, wrote an encyclopædia of medicine, and after living for a [illegible] time in Cairo went to reside in Mecca, where he died in A.D. 1599

Medieval Medicine. Following Garrison, we may date medieval medicine from the time that the *School of Salerno* established its influence in Europe. As to the origin of this epoch-making school, we know nothing, but we do know that it was here that Arabic translations of Greek medical works were turned into the Latin language by scholars from Spain, and we also know that the knowledge so obtained led to great practical results, in that *universities* were founded, the great movement of building *hospitals* was begun, both of which were founded and aided by Church and State alike. Salerno laid the foundations of these advances in medical teaching and care of the sick, and thus prepared the way for modern medicine, especially as it encouraged individual medical talent.

Foundations of Modern Medicine.

The revival of learning was only made possible by the destruction of feudalism, and this was brought about, as Garrison and others have pointed out, by the discovery of gunpowder. To this great act of freedom must be linked the discovery of printing by means of movable type, and the sack of Mainz in 1462, which disseminated the art of printing all over Europe and thus enabled knowledge to be easily preserved and widely distributed.

While these events were stirring the general public, medical men were confronted with new diseases from the East, which came in epidemic form, and these terrible outbreaks compelled them to observe and to record their observations; and, indeed, it is during this period that Girolamo Fracastoro, studying syphilis and typhus, started modern epidemiology by formulating the theory of contagion.

The subject of infection has been recently studied in a most able manner by C. and D. Singer, who have shown that to primitive peoples infection and contagion are in the general order of things, and not to be questioned, but that Hippocrates had no idea as to the spread of epidemic disease by infection. They point out that it was Thucydides (471-391 B.C.), while studying the 'plague of Athens,' who first established spread of disease by contact, and Aretæus the Cappadocian who added conveyance of infection from a distance, facts recognized by some of the Arabians like Haly Abbas, while the School of Salerno clearly stated that disease could be spread by contact, air, and fomites; and Remacle Fuchs (1510-1587) was not merely clear on these points, but wrote about the 'seminaria,' or seeds of disease. All these were, however, merely the precursors of Fracastoro (1478-1553), whose doctrine of disease seeds or germs, foreshadowed in his 'Syphilis' in 1530, is clearly stated in his 'De contagionibus et contagiosis morbis et eorum curatione' in 1546, in which he details different types of infection, by contact alone, by contact and fomites, by contact, fomites, and from a distance. He considers infection to be nothing else than *the passage of a putrefaction from one body to another*. He distinguishes infections from poisons because the former possess seeds which can reproduce their like in a second body. In addition, he was the first to recognize typhus fever and the specific characters of fevers.

These factors—viz., new methods of warfare changing society, new methods of spreading knowledge and apparently new epidemics—were the forces which in our opinion laid the foundations of modern medicine.

The Discovery of the Tropics.—It will be noted that in early times medicine was relatively highly developed in Egypt and India, while it was very primitive in the Temperate Zone, but the question as to the supremacy of East over West was settled by the Battle of Salamis, and thenceforth the general tendency was that learning advanced in the West and languished in the East. But the West knew that there was an East: the question was how to get there. A few travellers lived to return and tell the tale of the overland journeys to the East, and these were sufficient to indicate that the overland route was unsuited for traffic on a large scale, though trade came through gradually.

The problem of finding a way to the East was solved by the Portuguese, who in 1415 established contact with the Atlantic Islands, in 1444 with the West Coast of Africa, and later with the Congo and Angola. In 1486 they reached the Great Fish River, and in the last decade of the fifteenth century the route to India viâ the Cape was made known.

While this was going on in the East, Colombus was tracing a route to America across the Atlantic in 1492, and in 1519 Magellan passed through the Straits to which his name has been given, and showed the route to the East, while still later the complete voyage round the world was carried out successfully.

China and Tibet, however, remained unknown until the seventeenth century and Central Africa until the nineteenth century.

Early Tropical Medicine.—The work of the last section being carried out in ships with more or less numerous crews, it was customary for these vessels to be provided with a surgeon, or, at all events, with a person with some knowledge of medicine and some powers of observation. Later, when intelligent people settled in tropical regions they made records of their experiences, and in this way a curious literature sprang up, partly geographical, partly zoological, partly botanical, partly medical, and partly ethnographical. It is in this literature that we find some of the earliest references to disease in the tropics. The literature itself is sufficiently indicated in the list of works given at the end of this chapter; but being so mixed in its nature, it produced but little effect, and was left almost unnoticed until after the rise of modern tropical medicine.

Foundations of Modern Tropical Medicine.

The discoveries of new lands made as indicated above by voyages, were in due course extended by land exploration, and later by settlements founded by Europeans and their families, and as these grew in number and in size, so the number of medical practitioners also increased.

These medical men studied the diseases of the European settlers and of the natives of the regions in which they resided, and recorded their results in numerous publications, as is indicated in the list of works given at the end of this chapter.

These works naturally reflected the teaching which the author had received in Europe prior to his tropical career, and, therefore, as knowledge in Europe progressed, so information with regard to tropical diseases was amplified.

The factor which was most potent in the foundation of modern tropical medicine was the steady evolution and perfection of the compound microscope. It was this instrument which enabled *Laveran* to discover the malarial parasite, and *Manson* to find the periodicity of the *Microfilaria nocturna*.

These investigators may well be called the *pioneer founders* of modern tropical medicine, and that foundation was secured by the world-wide interest in tropical disease aroused by *Ross's discovery* of the spread of malaria by the mosquito. From the date of these discoveries *modern tropical medicine*, in our opinion, begins, because they opened up the possibility of finding the cause, the treatment, the method of spread, and the prevention of a tropical disease, and, moreover, for some reason or another, subsequent work on these lines has apparently been much more successful in the tropics than elsewhere.

Thus modern tropical medicine was essentially based upon the microscopical diagnosis of the disease, and differed thereby from earlier tropical medicine, which was entirely clinical; yet, in our opinion, clinical and microscopical diagnosis should go hand in hand, and the practitioner should never so depart from the essential of all medical knowledge, the thorough bedside examination of the patient by clinical methods, as to commit the error of entirely trusting to the microscopical diagnosis. If he trusts entirely to the clinical diagnosis errors must occur; if he leans absolutely upon laboratory examinations, which are often negative, he will again find himself in difficulties. The real foundation of modern tropical medicine is the blending together of clinical work with scientific research, thus making a living progressive science of medicine, in which causation, treatment, and prophylaxis of known diseases are associated with State-aided research into the unknown. We will now briefly look at the history of these various points.

Causation of Diseases.—One of the most marked features of modern tropical medicine is the success which has attended attempts to find the causal agent of the various diseases; and to trace the rather romantic history of these discoveries, it is necessary to subdivide the subject into Helminthology, Protozoology, Mycology, Bacteriology, Serums and Vaccines, Entomology, Toxicology, Climatology, and Dietetics.

Helminthology.—We have already noted that the Ebers Papyrus mentioned the presence of worms in the intestines; that Moses not merely knew the guinea-worm, but how to extract it by winding it round a stick; and we have further drawn attention to Agatharchides' description of this worm in 170 B.C. and to the reference to broad and round worms by Paul of Ægina and may, therefore, pass on to more recent work.

Trematodes were first recognized by Jehan de Brie in the form of the liver fluke of sheep, which was afterwards described in 1547 by Gabucinez. This initial work was extended later by Leeuwenhoek (1675), Swammerdam (1752), Rosenhof (1758), Muller (1777), Zeder (1800), who called them 'sucking worms,' and Rudolphi who gave the name Trematode, from τρηματώδης, meaning pierced by holes. Quite recently these worms have been the subject of two great discoveries, which may be briefly summarized.

In 1874 the trematode *Clonorchis sinensis* (= *C. endemicus*) was discovered by McConnell in the liver of a Chinaman, but the method of infection was not known until Kobayashi worked this out in 1912, 1915, and 1917, showing that the encysted stage could be found in twelve varieties of fish, and that kittens produced the adult trematode when fed upon infected fish, and finally that the first intermediate host is a mollusc—*i.e.*, a species of Melania.

In 1851 Bilharz discovered the trematode *Schistosoma hæmatobium* in the portal vein of an Egyptian. Since 1907 Sambon has shown that under this name was concealed, as suggested by Manson, a second parasite, which he called *Schistosoma mansoni*. In 1915 Leiper not merely confirmed the existence of these two distinct parasites, but traced their life-histories through the molluscs to the adult form in mammals. This is indeed a great and valuable discovery, and by no means the first by which this distinguished helminthologist has benefited mankind.

With regard to the Cestoda and Nemathelminthes space does not permit of a history at this point, as this will be given later; but with regard to the latter group Sir Patrick Manson's researches into filariasis were epoch-making.

The detailed history of *Filaria bancrofti* will be given later, and it will suffice to state here that the microfilaria was discovered by Demarquay in 1863, and that Manson discovered its development in the mosquito in the years 1877-1879, while in 1882 he laid stress upon the nocturnal periodicity of the microfilaria, a fact entirely disbelieved when first reported.

The great importance of the discovery of the development of this worm in a mosquito is that it paved the way for Ross's discovery of the spread of malaria by a similar agency.

It is quite impossible here to give even a reasonable list of the workers on this important branch of causation, but references to their discoveries will be found later in this book.

Protozoology. Protozoa were recognized by Leeuwenhoek in 1675, and the first life-history of a protozoon (a vorticella) was worked out by Trembley in 1744-1747.

Among the protozoa parasitic in human beings, one of the first to be discovered was *Balantidium coli*, found by Malmsten of Stockholm in the year 1856, and now known to be often associated with a chronic catarrh and ulceration of the large bowel. *Lamblia intestinalis*, discovered by Lambl in 1859, and *Trichomonas hominis*, found by Davaine in 1854, are considered by many authors (Ebstein, etc.) to be the cause of certain cases of diarrhœa.

In 1875 an ameba was found by Lösch in St. Petersburg, in a peasant who suffered from an ulcerative inflammation of the large intestine, and Sonsino in Cairo also described the finding of large numbers of amebæ in the intestinal mucus of a child who had died of dysentery. Other observers, however (e.g., Grassi, Celli, and Cunningham) found amebæ in persons whose health had undergone no change. Kruse and Pasquale first suggested that there might be two species of amebæ, one pathogenic, the other harmless. Later Schaudinn showed that there were two kinds of amebæ affecting man, viz., *Entamœba coli*, which was non-pathogenic; and *Entamœba histolytica*, described by himself, which was the cause of a certain kind of dysentery (amebic dysentery) and of the abscess of the liver which at times followed it.

The discovery which has had the greatest influence on tropical medicine was that of the parasite of malarial fever by Laveran on November 6, 1880. True, this had to some extent been foreshadowed by Merkel in 1847, and Virchow in 1848, both of whom saw, and the latter figured, protoplasmic masses and pigment. Still, the entire credit for this great discovery is due to Laveran, for the others failed to recognize the parasitic nature of the forms they saw. The development of our knowledge concerning this parasite is due to the valuable researches of Golgi, Marchiafava, Celli, Bignami, and many others. Of great importance was Golgi's discovery of the plurality of species of the malarial parasite. Laveran's discovery and the work of his successors left, however, a great gap in the history of the parasite. They described lucidly its life-history in the human being, but could not explain how man became infected.

Sir Patrick Manson, reasoning on his work on the mosquito and filaria, suggested that there might be a stage of the development of the parasite in the mosquito. Working on Manson's theory, Ross, at that time in the Indian Medical Service, after years of patient hard work, was able to trace the full development of a bird's parasite in Culex, and partially that of the human parasite in the Anopheles, and thus made not merely a great discovery, but one which ought to be in time of lasting benefit to mankind. The full development of the human parasite was found out by Grassi, who also showed that only Anopheles are capable of transmitting the parasite. Ross and Grassi's most important discoveries have been verified and extended by many people—e.g., Marchiafava, Celli, Bignami, Dionisi, Daniels, Stephens, and Christophers, etc.—but the account of their work will be given later. Thus, out of the fevers all classed as malaria there issued a type clearly defined, to which the term 'malaria' must be restricted.

In 1901 Forde and Dutton discovered a trypanosome, called by Dutton *Trypanosoma gambiense*, in a case of a peculiar irregular fever in the Gambia. In 1902 Dutton and Todd observed this organism in several other cases presenting the same type of fever, which became known at the time as trypanosome fever, Gambia fever, or Dutton's disease (Laveran and Mesnil). In 1902 and 1903 Castellani found a trypanosome in the cerebro-spinal fluid of cases of sleeping sickness, and first associated it with the ætiology. Further investigation by Bruce, Nabarro, and numerous observers in various regions of Africa confirmed and greatly extended this work. In 1903 Sambon and Brumpt independently promulgated the hypothesis that the human trypanosome was carried by a tsetse-fly, in all probability the *Glossina palpalis*, and Bruce and Nabarro experimentally proved that the *Trypanosoma castellanii* is in reality introduced into human beings by the bite of *Glossina palpalis*. Bruce and others considered the transmission as purely mechanical, but the researches of Kleine show that the parasite undergoes true development in the body of the tsetse fly. In 1903 Castellani stated that man in analogy with the lower animals might be infected by several species of trypanosomes. In 1909 Chagas discovered a form of human trypanosomiasis in South America, and showed that the trypanosome causing it (*S. cruzi* Chagas, 1909) was carried by a Conorhinus. In 1910 Stephens and Fantham created a new species (*T. rhodesiense*), which Kinghorn and Yorke in 1912 showed to be transmitted by *Glossina morsitans* (Westwood).

Trypanosomes were found in the lower animals long before they were discovered in man. Gruby first used (1843) the term 'trypanosoma' for a flagellate he had found in the blood of frogs in 1842. A similar parasite had been found by Valentin in 1841 in the common trout (*Salmo fario*). Very little progress was made in the investigations of these organisms until 1878, when Lewis, in India, described a trypanosome in the blood of rats, which was named by S. Kent *Trypanosoma lewisi*. In 1880 Evans discovered a trypanosome in animals affected with surra—*Trypanosoma evansi* (Steel 1885). This was a most important discovery, as it showed that trypanosomes were capable of producing disease, while previously it had been believed that these parasites were harmless. In 1894 Bruce discovered the Nagana trypanosome, *Trypanosoma brucei* (Plimmer and Bradford, 1899), and experimentally proved that the organism was conveyed by a species of tsetse-fly (*Glossina morsitans*). Rouget in the same year observed a trypanosome in the blood of horses affected with dourine—*Trypanosoma equiperdum* (Doflein, 1901).

Elmassian in 1901 described a trypanosome observed by him in mal de caderas —*Trypanosoma equinum* (Voges, 1901). Theiler, in 1902, in South Africa found a trypanosome in the blood of cattle affected with a peculiar disease known locally as 'galziecté' The parasite was named by Bruce *Trypanosoma theileri*. Recently several other forms of trypanosomiasis have been described in the lower animals by Dutton and Todd, Cazalbou, Lingard, Ed. and Et. Sergent, Schilling, Martini, Ziemann, and others.

In the meanwhile, Colonel Sir W. B. Leishman, in the year 1900, discovered some peculiar bodies in the spleen of a soldier who had died of what was called 'dum-dum fever,' but did not publish an account of his discovery till 1903, in which year Donovan also found the same parasitic bodies in Madras. This parasite was first considered to be a piroplasma by Laveran and Mesnil, and called *Piroplasma donovani*; but Ross created a new genus for it, using the term *Leishmania*. Wright of Boston found similar bodies in Oriental sore, which he called *Helcosoma tropicum*. The knowledge of these bodies and the diseases they cause has been considerably extended by Christophers and by Martzinowsky and Bogroff, while a great advance was made by Rogers, who in 1904 showed that by artificial cultivation *Leishmania donovani* developed into flagellate organisms. The life-history of *L. donovani* outside the human body has partially been traced by Patton, of the Indian Medical Service, in the bed-bug. In 1904 Laveran and Cathoire discovered a Leishmania in films from the spleen of a child in Tunisia. In 1905, Pianese, in Italy, found a Leishmania in the spleen of children suffering from febrile splenic anaemia. Nicolle completed the study of the parasite, and called it *Leishmania infantum*. Gabbi, and later Cardamatis, Feletti, and others, have emphasized the frequency of this disease in the Mediterranean littoral and islands. Gabbi considers the disease to be identical with Indian kala-azar.

In 1903 peculiar parasitic bodies, certainly protozoa, were discovered in rabies by Negri of Pavia. Negri's important discovery has been confirmed by many authors, and in the tropics by Cornwall.

In this section may be described the discovery of the causes of disease due to spirochaetes, the nature and relationship of which are not yet clearly known. Obermeyer, as far back as 1873, described the spirochaete of relapsing fever, which was thought to be spread by the bed-bug. In 1904 Nabarro, Ross, and Milne, in Uganda, discovered a spirochaete in the blood of persons suffering from tick fever—i.e., a fever supposed to be due to the bite of *Ornithodoros moubata*—and independently in the same year Dutton and Todd, working in the Congo, described a spirochæte causing tick fever. This spirochaete has been proved by Breinl and Kinghorn to be distinct from the *Spiroschaudinnia recurrentis*, and in 1906 they gave it the name of *S. duttoni*, in honour of the late Dr. Dutton, of the Liverpool School, who had done so much for Tropical Medicine, and who himself had fallen a victim to this disease. Novy and Knapp had a little time previously assigned the name *Spirillum duttoni* to the same parasite. In 1914 Inada and Ido discovered a spirochæte in Weil's disease, which they called *S. icterohæmorragiæ*. In 1918 Noguchi cultivated from cases of yellow fever a spirochæte which he has named *Leptospira icteroides*. Other spirochætæ have recently been described, as will be mentioned later.

In 1905 Schaudinn discovered the presence of a spirochæte-like organism in syphilis, which he called *Spirochæta pallida*. Later he created for the organism a new genus—Treponema. In the same year Castellani demonstrated the presence of a spirochæte or treponema in yaws, and named it *Spirochæta pertenuis* (*Treponema pertenue*), and in 1906 described Bronchospirochætosis.

Reference must here be made to the discovery of a small protozoan parasite in sheep suffering from a disease called 'carceag' by Babès in Roumania in 1888. The name applied to this parasite—viz., hæmatococcus—could not be maintained, as it was already used in botany, hence the generic name of Babesia was given to the group by Starcovici in 1893. The term 'piroplasma,' which should be used, was introduced by Patton in 1895. It is, however, mostly due to the work of Smith and Kilborne on red-water in cattle that Piroplasma has become well known, together with the fact that it is spread by a tick. The parasite *Piroplasma canis*, discovered by Piana and Galli-Valerio in 1895, has been thoroughly described by Celli in 1900 and Nuttall in 1904, and the life history in the tick has been worked out by Christophers. At the present time, thanks to the researches of Koch, Theiler, França, and others, several species of Piroplasma especially affecting cattle are known.

As to whether a Piroplasma is the cause of the tick or spotted fever of the Rocky Mountains appears open to grave doubt, although it has been described by Wilson and Chowning in 1902, and supported by Westbrook and Cobb in the same year, and Anderson in 1903, because other observers have failed to find any such organism. There is, however, strong evidence in favour of a tick being the spreader of the disease.

Mycology. Pathogenic mycology takes its origin in 1677 with Hooke's description and illustration of fungi causing the blighted or yellow specks on the leaves of the damask rose, and by his illustration of the blue moulds. This pioneer work is continued by Malpighi (1686), Ray (1706), Plukenet (1720), Micheli (1729), and their discoveries were systematized and extended by Linnæus (1753), Persoon (1801), Fries (1821), Link (1824), and so on to the days of Saccardo, Vuillemin, and last, and by no means least, Pinoy; but more detailed information with regard to this history will be given later.

Special attention must be drawn to the discovery by Gruby, in 1844, that ringworm was due to a parasitic fungus, and to the extension of that discovery by Malmsten in 1845, and to the great list of investigators of this particular feature down to the classical work of Sabouraud.

This work by Gruby produced world-wide interest in parasitic mycology, and for a time it made great progress, but fell back into a second-rate place when bacteriology came forward, and is only now being rescued from this position thanks to the labours of Manson, Blanchard, Böllinger, Eyre, Carter, Vincent, Nocard, Pinoy, and Brumpt.

Bacteriology. From the most remote times the suspicion that the mysterious cause of contagious and epidemic diseases must be sought in living entities has flashed through the minds of many observers. Columella, a contemporary of Seneca, records the belief, apparently popular in his time, of the living nature of miasmata and contagion. The idea of a *contagium vivum* was not extinguished even in the darkness of the Middle Ages. Thus, for instance, in a book written in the twelfth century, and wrongly stated to be by St. Hildegard, the abbess of a convent, we find notices of minute animals which produce disease.

Fracastoro's sixteenth century work is considered above, while in 1641 Athanasius Kircher, a friar, stated that he had observed minute living organisms in the blood of a patient during an epidemic of plague. Linnaeus supported the theory that disease was due to minute forms of life by inserting papers on the subject in his 'Amœnitates Academicae.' But the first to promulgate scientifically a bacterial theory was Agostino Bassi, a country practitioner of the north of Italy in the early nineteenth century. At that time a peculiar disease was destroying the silkworms, bringing ruin to the country in which the silk industry was paramount. Bassi, by means of the microscope, discovered the germ which is the cause of the disease. The organism received later the name of *Botrytis bassiana*. From analogy, Bassi believed and stated that human diseases were also due to micro-organisms. Bassi's work was not appreciated by his contemporaries.

In 1849 Pollender, and in 1850 Davaine, noted the *Bacillus anthracis* in the blood of sheep suffering from anthrax, but it was not until Pasteur, in 1857, had shown that fermentation was due to a yeast and that butyric acid fermentation was due to a bacillus, that Davaine, in 1863, considered that the rodlets which he had seen in the sheep's blood were the cause of the disease.

In 1882 Koch discovered the tubercle bacillus, and from 1877 to 1911 he introduced and improved methods for the separation and pure culture of bacteria, and laid down the proofs required to demonstrate that a given bacterium is the cause of a disease; and acting on these lines, Hansen in 1879 discovered the so-called bacillus of leprosy, Eberth in 1880 that of typhoid fever, Nicolaire in 1884 that of tetanus, Koch in 1884 that of cholera, Bruce in 1886 that of Malta fever, Yersin and Kitasato in 1894 that of plague, Shiga in 1898 and Kruse in 1900 that of bacillary dysentery.

The discovery of the typhoid, paratyphoid, and allied organisms has been of importance in enabling the differentiation of fevers previously massed together into a chaotic group labelled 'malaria.'

Serums and Vaccines.—The discovery of the immune serums, and their application to the treatment of disease, marked a great step forward in the history of medical science.

Still more important are the labours of Roux, Haffkine, Wright, Strong, Lustig, Galeotti, and others, in perfecting and applying vaccines to the prevention as well as to the treatment of disease.

Those of greatest tropical importance are Haffkine's plague vaccine, the same worker's cholera vaccine, and Wright's monovalent typhoid vaccine and his pyogenic vaccines.

A further advance was the introduction of Castellani's multiple vaccines for the prevention and treatment of disease. For long it was thought that a vaccine must be monovalent, but Castellani's triple vaccine for typhoid and the paratyphoid fevers has now been used on a very large scale for the British and other armies with success, and the tetravaccine typhoid, para A, para B, cholera has been adopted by the Serbian Army since 1916. He has also prepared tetravaccines, which include undulant or Malta fever, and has prepared and advocated the use of penta- and hexa-valent vaccines.

Entomology. It is obvious from the preceding sections that insects play a great part in the spread of protozoal diseases, and the same holds good for worms and bacteria.

Filaria can be spread by Culex, Stegomyia, or Anopheles; malaria by several species of the Anophelinae; Piroplasma and spirochaetes by ticks; *Leishmania donovani* perhaps by bugs; *Leishmania infantum* probably by fleas; trypanosomes by tsetse-flies, and possibly by some kind of flies.

But apart from these diseases, of which we know the cause, there are two infections the unknown agent of which is carried by mosquitoes. Thus Finlay, in 1881, formulated definitely the hypothesis that yellow fever was spread by a mosquito, which in 1900 was proved by Reed, Carroll, Agramonte, and Lazear to be a fact, the mosquito being *Stegomyia fasciata*, now *Stegomyia calopus*.

With regard to dengue fever, Graham of Beirut, in 1903, thought that he had discovered a protozoon in the red corpuscles of persons suffering from this disease, and that this parasite underwent development in *Culex fatigans* (Wied). Doubt has been thrown upon Graham's parasite, but the idea that *Culex fatigans* (Wied) is responsible for the spread of dengue fever has been strongly supported by Ashburn and Craig in 1907.

Turning now to bacterial diseases, the work of the Indian Plague Committee, published in 1906-1908, proves that the rat-flea (*Xenopsylla cheopis*) is the main means of the spread of plague. With regard to typhoid, it was conclusively proved in the army concentration camps of the United States in the Spanish-American War of 1898 that flies were great spreaders of the disease, a fact already emphasized by Celli and others; and this has been further supported by the work of Firth and Horrocks (1902), Chantemesse, and numerous other observers. Dysentery may also be spread by flies.

A knowledge, therefore, of ticks, biting flies, and other insects is of the greatest importance to the doctor who is to practise in the tropics. We refer the reader interested in this subject to the classical work of Nuttall on insects as carriers of disease in the Johns Hopkins Hospital Reports, 1899.

The idea that the house-fly and its allies are capable of spreading disease originates from the time of Mercurialis, who in 1577 suggested that the virus of plague might be disseminated by this means. In 1666 Sydenham remarked that the presence of numerous flies in the summer indicated that there would be much sickness in the autumn, while in 1808 Crawford stated that he believed insects to be the carriers of infection. In 1853 Moore referred to flies as the possible carriers of cholera, typhoid, tuberculosis, anthrax, and leprosy. In 1869 Raimbert performed the first experiments, showing that anthrax could be disseminated by flies. Tizzoni and Cattani made observations on the spread of cholera by the same means, Grassi and later Stiles demonstrated the possibility of the carriage of parasitic worms, and one of us the transference of the *Treponema pertenue* by the same means. Gayon in 1903 indicated the possibility of the dissemination of fungi by flies.

Toxicology.—Micro-organisms are not the only causes of disease to be found in the tropics, for poisons from plants and animals are also of the greatest importance.

It has been shown that the most primitive peoples have definite knowledge of poisons, and it has already been mentioned how early the study of snake and other animal venoms began.

It will suffice here to indicate that the scientific study of snake-venom, begun by Prince Lucien Bonaparte in 1843, has been extended by Fayrer, Martin, Lamb, Calmette, Noguchi, and many others, and leave a fuller description of this and the history of other poisons to a later chapter.

Climatology.—Tropical medicine does not confine itself to diseases caused only by parasites and poisons, for there are such conditions as heat-stroke, which are entirely due to physical causes, and also there is the important question of the influence of tropical climates on man, which must be dealt with in a later chapter.

Dietetics.—But little work has so far been done with regard to this important subject in the tropics, though pioneer struggles have been undertaken most successfully by McCay in India, and his example deserves to be followed.

Clinical Medicine.—Clinical researches into the diseases affecting Europeans and natives in the tropics began with the earliest modern travellers, non-medical as well as medical, and the earliest references to tropical diseases are to be found in these early works on travel. Thus, as Singer has pointed out, De Oviedo in 1526 gives a reference to a disease bubas, which we now know to include *Frambœsia tropica*, a form of Leishmaniasis, and probably a form of Blastomycosis. In 1558 Thevet described the jigger as a little worm called '*Tom*,' which entered into the feet, and wrote descriptions of *Frambœsia tropica* under the term 'Pians.' In 1598 G. W. wrote an account of Calenture (heat-stroke), and Tabardillo, which is derived from the Spanish word *Tabardo*, a cloak, and was applied to the typhus fever epidemic in Spain in 1557; and therefore G. W. may have meant typhus by this term, though it is possible that he also included yellow fever under the same name. He also describes

Espinlas, possibly due to the bite or sting of some venomous animal; Cameras de Sangre, or dysentery; erysipelas, which probably included filariasis: and Tiñoso, or scurvy. In 1642 Bontius wrote his work, 'De Medicina Indorum.' Chalmers and Archibald have drawn attention to the description of dracontiasis, dermatophiliasis, epidemic gangrenous rectitis in South America; simple continued fever, malarial fevers, dysenteries, smallpox, climatic bubo in India; malaria, endemic yellow fever, dengue, smallpox, filariasis, diarrhœas, dysentery, and yaws in West Africa, as indicated by D. L. F. in 1726 and by Aubrey in 1729; but these and many others are briefly mentioned at the end of this chapter under the heading 'Special Works on Tropical Medicine,' and need not be further described here.

It is not possible for us to trace out in detail the history of treatment, but we may briefly mention a few points with regard to quinine, arsenic, antimony, thymol, and emetine.

Treatment--*Quinine*.- In the seventeenth century the epoch-making discovery of the value of cinchona-bark in the treatment of malarial fevers took place.

In 1638 the Countess of Chinchon, wife of the fourth Count, Viceroy of Peru, after nine years' residence in that country, was seized with tertian malarial fever. Don Lopez de Canizaries, the Corregidor of Loxa, hearing of this, sent her a parcel of the bark of a tree called by the Indians of Loxa 'quina-quina.' The duplication of the name of the tree is said to indicate that it has medical properties.

The value of this bark in the treatment of fever appears to have been only known locally, but was understood by the Spaniards in Loxa as far back as 1600. How the Indians became acquainted with the bark is not known, and the tales of the curing of their fevers by drinking the water of a lake into which a cinchona-tree had fallen, or of a sick puma chewing the bark, are considered to be myths invented later in Europe.

Dr. Don Juan de Vega administered the bark to the Countess, who quickly recovered, and four years later returned to Europe with a large supply of it, which she distributed to persons suffering from fever on her estates near Madrid. Hence the bark was often known as *Pulvis comitissæ*. In 1670 Jesuit missionaries sent some of the bark to Rome, whence it was distributed throughout Europe by Cardinal de Lugo. Hence the names 'Jesuit's' or 'Cardinal's' bark.

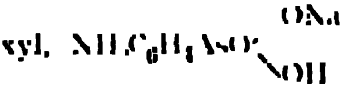
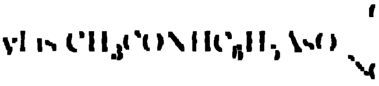
Linnæus named the tree after the Countess, but spelt her name wrongly, calling it *Cinchona officinalis*. A curious strife now rose in Europe as to whether fever should be treated by bark or not, but the labours of Morton and Sydenham, together with the dramatic cure of the Grand Dauphin, enabled its true value to be known. The tree has since that time been introduced into several parts of the world, and grows well in India, Ceylon, and Java.

Finally in 1820 Pelletier and Caventou prepared the alkaloid quinine from cinchona-bark. For further particulars see Chapter XL. on Malaria.

Arsenic and Antimony.—Thanks to Morgan's work it is possible to give a brief history of these two metalloids, which belong to the nitrogen group of the fifth vertical series of the periodic classification, and are related to the non-metals phosphorus and nitrogen and to the metal bismuth.

Arsenic occurs in nature in combination with cobalt, as smaltite and cobaltite, both of which are included under the term *cobalt*, which was found by a German artist to be capable of making *sympathetic ink* when acted upon by aqua fortis, the action of which was studied in 1737 by Hellot and in 1760 by Cadet de Gassicourt, who produced a highly inflammable stinking fluid therefrom, and this Thenard concluded was a *complex acetate containing arsenic*.

During the years 1837-1843 Bunsen isolated this complex, to which Berzelius gave the name *cacodyl*, and in 1858 Baeyer, having first made *primary methyl arsenicals*, produced methylarsenic acid, the soluble salts of which are employed medicinally as new cacodyl and arrhenal. In 1860-1863 Béchamp made the *first aromatic arsenical*, and in the seventies Michaelis, in collaboration with other workers, not merely extended this knowledge, but prepared the *first aromatic antimony compounds*. In 1902 Béchamp's compound was first tried in medicine by Thomas and Breinl for sleeping sickness, being called *atoxyl* because of its comparatively non-toxic action, and it is the drug which has been used with such success in sleeping sickness in the Sudan. Atoxyl was shown in 1907 by Ehrlich and Bertheim to be the sodium salt of *p*-arsenilic acid, being a derivative of quinquevalent arsenic.

Atoxyl,  $NH_2C_6H_4AsO\begin{matrix}ONa\\OH\end{matrix}$ contains from 25·05 to 20·78 per cent of arsenic according to the amount of water of crystallization. Mono-acetylated atoxyl is  $CH_3CONHC_6H_4AsO\begin{matrix}ONa\\OH\end{matrix}$.

According to Mesnil and Nicolle's experiments, and the observations of Nierenstein, it is not the arsenic in these compounds which is to be looked upon as the effective agent, but the amido group, which may possibly be the effective agent in trypan red, afridol blue, afridol violet, and parafuchsin, which do not contain arsenic but possess amido-groups, and affect trypanosomes in a similar manner to atoxyl. According to Ehrlich, Levaditi, and Yamanouchi, atoxyl undergoes a reduction in the animal tissues. Ehrlich has prepared two derivatives of atoxyl, one of which, already mentioned (arsenophenylglycin), is very effective in mice on atoxyl-resistant trypanosomes. Levaditi and Yamanouchi have also prepared an active derivative of atoxyl, which they call trypanotoxyl. Nierenstein thinks that atoxyl is oxydized in the tissues, and it is only in the nascent state that it becomes efficacious.

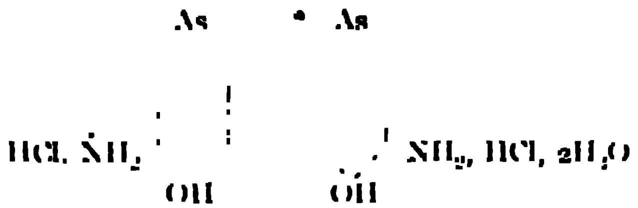
Owing to the fact that large doses of atoxyl lead to such unpleasant results as optic atrophy, gastro-intestinal inflammation, and peripheral neuritis, other arsenical preparations have been recommended; and the firm Burroughs and Wellcome has introduced, under the trade name of *soamin*, a preparation somewhat similar to atoxyl, but said to be less poisonous. It is given in the same doses as atoxyl, but the therapeutic results do not appear to have been very successful. *Soamin*, according to the published formula, is $C_6H_4NH_2AsO(OH)(ONa)5H_2O$.

Atoxylate of mercury was introduced by Uhlenhuth, but is less satisfactory than atoxyl.

Combinations of Mesnil's afridol and atoxyl, Ehrlich's parafuchsin and atoxyl, picric acid, safranin, trypaflavin, and other dyes and atoxyl, have been suggested in the treatment of trypanosomiasis, but in man the results have not been so successful as in the lower animals.

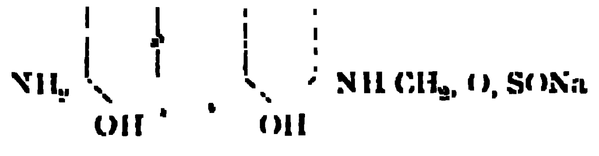
Mercury was first introduced in 1902 for the treatment of sleeping sickness by Low and Castellani, using intravenous injection of Baccelli's sublimate solution (hydrargyri perchloridi, 0·10 gramme; sodii chloridi, 0·50 gramme, aquæ destillatæ, 100·00 c.c.; 1 to 4 c.c. per intravenous injection), in association with arsenic and quinine by the mouth. A fall of the temperature was observed in some cases, but the fatal course of the disease was not influenced. Moore, Nierenstein, and Todd have used mercury and atoxyl in combination or alternation, with the idea that mercury might act upon the latent form of the trypanosome, while atoxyl would influence the active form. In man this combined treatment has apparently not given any better results than atoxyl alone. This combined treatment, consisting of atoxyl and an inorganic salt of arsenic such as orpiment has been recommended by Laveran and Thiroux and has already been used in man with good results. The orpiment should be given in pills, in the dose of 2 grains of orpiment two or three times daily. The administration of orpiment frequently causes diarrhœa. Thiroux therefore incorporates in the orpiment pills some opium.

Ehrlich observed that the aromatic compounds of tervalent arsenic were more efficacious in attempts to kill protozoan parasites, and after 605 attempts in 1909 he evolved *Salvarsan, or 606, also known as Kharsivan and Arsenobillon*, which is a pale yellow powder soluble in dilute hydrochloric acid or aqueous sodium hydroxide or carbonate. Its formula is the hydrochloride of 3 : 3'-diamino-4 : 4'-dihydroxy-arseno-benzene-*i.e.*:—



On account of its phenolic and feebly basic properties Salvarsan fails to give neutral salts, and the free base is very insoluble in water or in normal saline solution; therefore an approximately neutral solution has to be prepared immediately before use, which is inconvenient, and led to the search for a compound with soluble salts giving a neutral reaction in solution. Such a preparation had been foreshadowed by Ehrlich's 418 Spirarsyl, or the sodium salt of arsenophenylglycine, which was the most successful of the arsenic compounds prior to Salvarsan.

It was found that Salvarsan dihydrochloride could be made to produce a compound called Ehrlich's 914, or Neosalvarsan, also called Neokharsivan, Novarsenobillon, Novarsenobenzol, or Sodium 3 : 3'-diamino-4 : 4'-dihydroxy-arsenobenzene-N-methylene sulphurate:—



This is a pale yellow powder, with (commercially) generally small proportions of inorganic salts. It is soluble in water and the solution is quite neutral, but its arsenical content is lower than that of Salvarsan, and hence its average dose is larger, and the efficacy of the preparation should be tested by intravenous injections into rabbits.

Galyl, discovered by Mouneyrat, is 4 : 4'-dihydroxyarsenobenzene-3 : 3'-phosphamic acid, and forms a neutral solution when added to aqueous sodium carbonate, and is useful in syphilis and also kills spirochætes and trypanosomes. It is very slightly toxic. Ludyl is a complex disulphonamide discovered as

1,151 of Mouneyrat's series, and like galyl is given intravenously and for the same conditions.

We have already referred to *Spirarsyl*, and we may mention that *Arsenophenylmethylglycine* has been used experimentally by Oechslin to kill *Trypanosoma evansi* and *T. rhodesiense* in experimental animals.

In 1913 Ehrlich found that Salvarsan and other derivatives of arsenobenzene could join with salts of copper, silver, gold, and platinum, forming combinations which could be administered intravenously and in which the heavy metal appeared to aid the arsenic in its germicidal action. Luargol is an example of this type of chemical body

Further new types of compounds of organic arsenicals with antimony, selenium, etc., are being tried. Especial attention is said by Morgan to be directed at the moment to certain partly methylated hexaminoarsenobenzenes, which give stable solutions with soluble bicarbonates, and so the final word has yet to be said with regard to these compounds, which the chemist is preparing for trial by the physician.

With regard to the organic antimony derivatives, the salts of antimonyl tartaric acid, in the form of lithium antimonyl tartrate, were first used in the experimental trypanosomiasis of mice by Plimmer and Thomson in June, 1907. Their results were confirmed by Mesnil and Brimont in January, 1908, while in March, 1908, Manson used it on man, giving it by the mouth. Also in 1908 Boosten and Rodhain used tartar emetic in human trypanosomiasis.

In 1913, Tsuzuki introduced potassium ammonium antimonyl tartrate, as *antiluetin*, and in the same year Vianna and Machado gave tartar emetic intravenously in cases of espundia, with good results, which have been confirmed by Terra da Silva, Carini Carwalho and Christopherson, and by Low. For the same complaint Ludeberg tried trioxide of antimony intramuscularly, and Martindale prepared an *injectio antimonii oxidi*, which Morgan considers to contain, probably, a glyceryl antimonite, and this has been reported in 1917 as curative of American Leishmaniasis when used subcutaneously, intramuscularly, and intravenously.

Also in 1913 Vianna and Aragão reported that tartar emetic was useful in the treatment of ulcerating granuloma.

In 1914 Castellani used tartar emetic, together with other drugs, in a case of Indian kala-azar, with satisfactory results, and came to the conclusion that the drug was the cause of the striking result, and therefore he recommended it for routine treatment. In the previous year he had originated his yaws mixture (now generally called Castellani's mixture), which contains tartar emetic, potassium iodide, and both carbonate and salicylate of soda.

In 1915 Di Cristina and Caronia reported the cure of eight cases of infantile Leishmaniasis by antimony therapy, and later Rogers confirmed and extended this use of tartrate of antimony in kala-azar, a line of treatment well accepted at the present time.

Emetine.—For many years it was known that ipecacuanha and emetine were valuable in the treatment of certain cases of dysentery, and this was crystallized down to the treatment of amœbic dysentery, and more especially to the presuppurative stage of amœbic hepatitis by Rogers from 1909 onwards. Later Vedder in the Philippine Islands studied its action on entamœbæ, and Rogers devised the clinical application of the drug by subcutaneous injection, which to-day is used as the correct treatment of that form of dysentery and its complications.

Thymol.—Bozzolo, in 1880, was the first to introduce this drug for the treatment of ankylostomiasis. He obtained satisfactory results which have been confirmed all over the world.

Prophylaxis.—The knowledge of the causal agent and its method of dissemination have enabled reasoned and scientific methods of prophylaxis to be devised and carried out, of which perhaps the most striking is that performed in Panama by Gorgas.

It is to be hoped that in years to come these methods will be extended, and that many diseases at present hampering civilization will cease to be terrors; indeed, the present war has amply proved the wisdom of prophylactic and sanitary measures, especially the polyvalent prophylactic treatment against the enteric fevers, cholera, and other diseases, and it is to be hoped that now the war is over international action will be taken all over the world to combat disease

Research. Notwithstanding the fact that so much has been done to elucidate disease, still there is a great field for research, and one of the direct blessings of the recent war will be the stirring up of Governments to provide funds for this work, which should never be left, as it used to be, entirely, or almost entirely, to individual generosity.

The State and Tropical Medicine. Tropical medicine has been fortunate in that at the commencement of modern tropical medicine there was at the head of the British Colonial Office a far-seeing and exceedingly wise statesman Mr. Joseph Chamberlain - who clearly realized the duties of the State in regard to the formation of Schools of Tropical Medicine in London and Liverpool, and of the foundation of laboratories in British Colonies. This policy, continued and extended under the auspices of the Advisory Committee of the Tropical Diseases Research Fund, has produced the *Tropical Diseases Bulletin* and other publications of great value.

The example set by the British Government has been followed by those of other countries, and to-day all over the world the State supports tropical medicine.

In many tropical countries, however, it appears to us that the State should exercise more authority over the medical practitioner, native or modern trained; that registers of such practitioners should be kept, and that this should not be confined to medical practice only, but also to dental and veterinary work.

The War and Tropical Medicine.—The recent war has disseminated tropical diseases in such a manner that many of them may become cosmopolitan. The Anophelines of England have now a chance to become infected with malaria, and, in fact, cases of endemic malaria have already occurred, but we doubt whether there is any real danger of an epidemic. Bilharziosis has the opportunity to spread from Egypt to other countries. Are sufficiently strong measures being taken to combat the spread of these diseases and many others like them, *e.g.*, amœbic dysentery?

Another point which the war has brought into prominent notice is that so-called tropical diseases exist in abundance in Europe—*e.g.*, in the Balkans and that agents like lice are as prone to spread disease in the Temperate as in the Tropical Zone.

Certainly the massed formations of medical knowledge at work in the recent war at the study, treatment, and prevention of disease will produce results which would have been but slowly evolved in years of peace.

It is not possible to close this history without acknowledging the debt which tropical medicine owes to the officers of the Royal Army Medical Corps, of the Royal Navy, the Indian Medical Service, the Colonial Service, and to their training schools, as well as to the officers of the Medical Services of the armies and navies of France, Italy, and the United States of America.

MODERN JOURNALS.

The very excellent *Tropical Diseases Bulletin* enables the tropical practitioner to keep himself abreast of the day as regards current events in tropical medicine while the *Tropical Veterinary Bulletin* permits him, if he so desires, to obtain the same up to date information with regard to the diseases of animals. Both these publications are issued by the Tropical Diseases Bureau, the Imperial Institute, London, S.W. 7.

If he desires more information with regard to bacteriological work he may find this and much more in the *Bulletin de l'Institut Pasteur* which is issued by that Institute in Paris.

If he wishes more detail with regard to Japanese medical work, he will find a review in English, written by the Research Staff of the Severance Union Medical College, Seoul, Korea, published in *The China Medical Journal*. The names of some of the Japanese medical journals are as follows:—

Chugai Iji Shimpo, or Home and Foreign Medical News, *Juzenkai Zasshi* or Journal of the Perfection Medical Society Alumni of Kanazawa Medical School; *Nisshin Chiryo* or Modern Therapeutics, *Taiwan Igakukai Zasshi*, or Journal of the Formosa Medical Society, *Tokyo Iji Shinshi*, or Tokyo Medical News, *Tokyo Igakukai Zasshi* or the Proceedings of the Medical Society of Tokyo; also *Acta Scholae Medicinalis Universitatis Imperialis* in Kioto, *Japanische Zeitschrift für Dermatologie und Urologie*, *Kyoto Igakukai Zasshi*, *Mitteilungen aus der Medizinischen Fakultät der Kaiserlichen Universität zu Tokyo*, *Sei-i-kwai* (*Medical Journal*) of Tokio, *Tokyoer Medizinische Wochenschrift*, *Mitteilungen aus der Medizinischen Fachschule zu Keijo*.

If resumes of German literature are desired, they can be found in the *Archiv für Schiffs- und Tropenhygiene* and in the *Archiv für Bakteriologie*.

Apart from these the following journals usually contain original papers dealing with tropical medicine:—

1. Annali di Medicina Navale e Coloniale (Rome).
2. Annales d'Hygiène et de Médecine Coloniales (Paris).
3. Annales de l'Institut Pasteur (Paris).
4. Annali d'Igiene (Turin).
5. Anales del Instituto Médico Nacional (Mexico).
6. Annales Paulistas de Medicina e Cirurgia (San Paulo).
7. Annals of Tropical Medicine and Parasitology (Liverpool).

8. Annual Reports of the Principal Medical Officers of British, French, Italian, and Dutch Colonies.
9. Archives de Médecine et Pharmacie Navales (Paris).
10. Archives de Parasitologie (Paris).
11. Archiv für Protistenkunde (Jena).
12. Archiv für Schiffs- und Tropen-Hygiene, and separately 'die Beihefte' (Leipzig).
13. Arquivos de Hygiene e Pathologia Exoticas (Lisbon).
14. Archivos do Instituto Bacteriologica Camara Pestana (Lisbon).
15. Archives de Médecine (Athens).
16. Archivos Brasileiros de Medicina (Rio di Janeiro)
17. Archives de l'Institut Pasteur de Tunis (Tunis).
18. Atti della Società per gli Studi della Malaria (Rome).
19. Australian Institute of Tropical Medicine, Collected Papers (Townsville).
20. Boletin del Instituto Nacional de Higiene de Alfonso XIII. (Madrid).
21 Boletin de la Association Médica de Puerto Rico (San Juan)
22. Brazil Medico (Rio di Janeiro)
23. British Guiana Medical Annual (Demerara).
24. Bulletin de l'Office International d'Hygiène (Paris)
25. Bulletin de la Société de Pathologie Exotique (Paris).
26 Bulletin de l'Académie Royale de Médecine de Belgique (Brussels)
27 Bulletin de la Société Portugaise des Sciences Naturelles (Lisbon).
28 Bulletin de la Société Medico-Chirurgicale de l'Indochine (Hanoi and Haiphong).
29 Bulletin de la Société Médicale de l'Ile Maurice (Mauritius)
30 Bulletin of Entomological Research (London).
31. Bulletin de l'Institut Pasteur d'Algérie (Algiers).
32. China Medical Journal (Shanghai).
33 Cronica Medica (Lima)
34 Cronica Medica Mexicana (Mexico).
35. Commonwealth of Australia. Quarantine Service Publications (Melbourne)
36. Folia Microbiologica (Delft).
37. Gaceta Medica de Caracas (Caracas).
38. Geneeskundig Tijdschrift voor Nederlandsch Indie, Rijswijk (Batavia).
39 Grèce Médicale (Athens)
40. Illinois Biological Monographs (Urbana).
41. Index Medicus (Washington)
42. Indian Journal of Medical Research (Calcutta).
43 Indian Medical Gazette (Calcutta)
44 Interstate Medical Journal (St. Louis)
45. Journal of the Ceylon Branch of the British Medical Association (Colombo).
46 Journal of Comparative Pathology and Therapeutics (Edinburgh;
47 Journal of Hygiene (Cambridge)
48. Journal of Pathology and Bacteriology (Cambridge)
49. Journal of the Royal Army Medical Corps (London).
50. Journal of Tropical Medicine and Hygiene (London)
51. Journal of Parasitology (Urbana).
52. Kitasato Archives of Experimental Medicine (Tokio)
53. Lister Institute, Collected Papers (London)
54 Malaria e Malattie dei Paesi Caldi (Rome)
55. Malay Medical Journal.
56. Malariologia (Naples).
57. Medicina Contemporanea (Lisbon).
58. Mededeelingen van den Burgerlijken Geneeskundigen Dienst in Nederlandsch-Indie (Batavia)
59. Medical Journal of South Africa (Johannesburg).
60 Memorias do Instituto Oswaldo Cruz (Rio di Janeiro).
61 Monthly Health Reports of the Department of Health of the Panama Canal (Washington).
62. Pacific Medical Journal.

63. Panama Canal Record (Balboa Heights Canal Zone).
64. Parasitology (Cambridge).
65. Philippine Journal of Science, Section B. Philippine Journal of Tropical Medicine (Manila).
66. Proceedings of the Canal Zone Medical Association (Mount Hope, Canal Zone).
67. Proceedings of the Society for Experimental Biology and Medicine (New York).
68. Records of the Egyptian Government School of Medicine (Cairo).
69. Review of Applied Entomology, Series B, Medical and Veterinary (London).
70. Revue de Médecine et d'Hygiène Tropicales (Paris).
71. Revista Medica de Yucatan (Yucatan).
72. Repertorio de Medicina y Cirugia (Bogotá).
73. Revista Clinica (Colombia).
74. Revista Medica de San Paulo (San Paulo)
75 Revue Médicale d'Alger.
76. Riforma Medica (Naples).
77 Sanidad y Beneficencia, Bolito de l'Secretaria (Havana)
78 Southern Medical Journal (Nashville, Tennessee)
79 South-Western Medicine El Paso (Texas).
80. Sperimentale (Florence)
81. Studies from the Institute for Medical Research (Federated Malay States).
82. Transactions of the Society of Tropical Medicine and Hygiene (London).
83. Texas State Journal of Medicine (Fort Worth).
84. Veeartsenijkundige Bladen voor Nederlandsch Indie (Batavia).
85 Zeitschrift fur Chemotherapie (Leipzig)
86 Zeitschrift fur Hygiene und Infektionskrankheiten (Leipzig).
87. Zeitschrift fur Immunitätsforschung und Experimentell Therapie (Jena).

The following journals have, from t [illegible] time, valuable papers on Tropical Medicine and Parasitology:—

1 Arbeiten aus dem Kaiserlichen Gesundheitsamte (Berlin).
2. Archives of International Medicine (Chicago).
3. British Medical Journal.
4. Boston Medical and Surgical Journal (Boston).
5. Bulletins and Reports of the United States Departments concerned with:— (*a*) Animal Industry; (*b*) Hygienic Laboratory, (*c*) Public, Health (Bulletins and Reports separately), (*d*) Naval Medical; (*e*) War Department (Washington).
6. Canadian Medical Association Journal (Toronto)
7. Collected Studies from the Research Laboratory, Department of Health (City of New York).
8. Comptes Rendus de la Société de Biologie (Paris).
9. Deutsche Medizinische Wochenschrift (Berlin).
10. Johns Hopkins Bulletin.
11. Journal of the American Medical Association (Chicago).
12. Journal of Experimental Medicine (New York).
13. Journal of Infectious Diseases (Chicago).
14. Journal of Laboratory and Clinical Medicine (St. Louis).
15. Journal of Immunology.
16. Journal of Medical Research (Boston).
17. Journal of the Royal Naval Medical Service (London).
18. Lancet (London).
19. Medical Journal of Australia (Sydney).
20 Münchener Medizinische Wochenschrift (Munich).
21. New Zealand Medical Journal (Wellington).
22. Policlinico (Rome)
23. Presse Médicale (Paris).
24. Proceedings, Series B, and Transactions of the Royal Society of London.
25. Quarterly Journal of Microscopical Science (London).
26. South African Medical Record (Cape Town).

JOURNALS WHICH HAVE CEASED PUBLICATION.

Since the appearance of the second edition of this book the following journals have either ceased to be published as separate entities or have stopped publication altogether:--

1. *American Journal of Tropical Diseases and Preventive Medicine.* This is now included in the New Orleans Medical and Surgical Journal. Three volumes were issued 1913-1916.
2. *Journal of the London School of Tropical Medicine.* Two volumes were issued 1911-1913.
3. *Journal of Tropical Veterinary Science, Calcutta.* Seven volumes appeared 1906-1912.
4. *Paludism, Simla.* There are five numbers only, 1910-1912.
5. *Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India.* New Series, Calcutta. These are exceedingly valuable publications, and numbered some sixty volumes from 1902-1913. Their place and that of *Paludism* is taken by the *Indian Journal of Medical Research.*
6. *Yellow Fever Bureau Bulletin, Liverpool.* There are three interesting volumes in existence which appeared from 1911 to 1915. Its work is carried on by the *Annals of Tropical Medicine and Parasitology.*

No *Reports of the Wellcome Tropical Research Laboratories, Khartoum,* have appeared since 1911. In the meanwhile much of the original work performed during the last five years has been published in medical, chemical, and entomological journals. Up to date four reports and two reviews of tropical literature have appeared between 1904 and 1911.

SPECIAL WORKS ON TROPICAL MEDICINE.

(*In Chronological Sequence.*)

De Oviedo, F. (1526). Hystoria Natural de las Indias (Toledo). (1547). Coronica de las Indias (Madrid). (Accounts of Yaws and Jiggers.)

Thevet, F. A. (1558). Les Singularitez de la France Antartique autrement nommée Amerique. (Jiggers, Yaws, and Native Practice.)

Da Orta, G. (1563). Coloquios dos Simples e Drogas da India. (This book is the first European work published in India, and contains descriptions of many Indian plants and their application to the treatment of Cholera, Dysentery, etc.) Garcia de Orta was physician to Dom Marten da Sousa, Governor of Goa, with whom he travelled in India and Ceylon in 1534. Antwerp, 1567, translation by Clusius into Latin. The English translation (1913).

W., G. (1598). The Cures of the Diseased in Remote Regions (London) Heat Stroke, Typhus, Yellow Fever (?), Erysipelas (Filariasis?), Espindas Dysentery, and Scurvy. (1916) Reprinted at Oxford.

Bontius, J. (1642). De Medicina Indorum (Lugduni, Batavia). (Remarks on drugs, preservation of health, treatment, and morbid anatomy.)

Alpinus, P. (1645) De Medicina Ægyptiorum (Parisiis). (The first book contains articles on the state of Egyptian medicine, on diseases endemic and epidemic, including plague; the second on blood-letting; the third on scarification, extraction of stone from the bladder, baths, and friction; the fourth on medicines.)

Pison, G. (1648). Historia Medica Brasiliæ (Lugduni, Batavia). (This work is divided into two parts, of which the first treats of Brazilian climatology; the second, of Brazilian diseases—*e.g.*, catarrhs, diseases of the eyes, spasm, stupor of the members, obstructions of the viscera, hydropsy, fluxes, tenesmus, colic, dysentery, liver troubles, worms, syphilis, ulcers, etc.)

PISON (GULIELMUS) ET GEORGIO MARCGRAVO DE LIEBSTAT (1648). Historia Naturalis Brasiliæ

PISON, G. (1658). De Indiæ Utriusque de Natura et Medica (Amsterdam).

CLEYER, A. D. C. (1682). Opuscula Medica ad Mentem Sinensium (Francofurti).

SLOANE (1707-1725). A Voyage to the Islands of Madeira, Barbadoes, and Jamaica, to which is prefixed an Introduction wherein is an Account of the Inhabitants, Air, Water, Diseases, Trade, etc., of that place.

KAEMPFER, E. (1712). Amœnitatum Exoticarum Politico-Physico-Medicarum Lemgoviæ. (This well-illustrated book, dealing with Persia, India, and Japan, is composed of five fascicles, of which the first is political; the second antiquarian, the third physico-medico containing descriptions of the Torpedo, *Dracunculus persarum*, Asafœtida, Hydrocele, Hypersarcosis ulcerosa pedum malabaricæ genti vernacula—i.e. Madura-foot, acupuncture, cauterization; the fourth and fifth are botanical.)

F. D. L. (1720). Traité des Maladies Particulières aux Pays Orientaux (Paris). (Bound with Luillier's Voyages; contains descriptions of Sea-Sickness, Scurvy, Colic, Venereal Disease, Fever, Guinea Worms, Jiggers, Serpent Bite, Smallpox, etc.)

AUBREY, T. (1729). The Sea Surgeon, or the Guinea Man's Vade-Mecum (London). (Contains accounts of Fevers, Erysipelas, Diarrhœa, Cholicks, Yaws, Negroes and their Food, etc., as seen on the Coast of Guinea.)

ATKINS, J. (1734). The Navy Surgeon (London). (Contains an appendix on 'The Sleepy Distemper in the Negro.')

ATKINS, J. (1737). A Voyage to Guinea, Brazil, West Indies. 2nd edition 1810.

PERRY, C. (1743). View of the Levant, particularly Constantinople, Syria, Egypt, and Greece in four parts, containing information with regard to Medicine and Surgery in the East.)

BROCKLESBY, R. (1764). Observations on Camp Diseases, with an Appendix on the Climate and Diseases in Africa (London).

LIND, JAMES (1768). Essays on Diseases incidental to Europeans in Hot Climates (London). (Other editions 1771, 1777, 1788, 1808, 1811. Translated into German 1773. Also edition 1792.)

HILLARY (1752). Observations on the Changes of Air, etc., in the Island of Barbadoes (London). 1766.

CLARK, JOHN (1773). Observations on the Diseases in Long Voyages to Hot Countries, and particularly those of the East Indies (London). (Other editions 1792, 1809. Translated into German 1778.)

ROBERTSON, R. (1777). A Physical Journal kept during Three Voyages on the Coast of Africa and the West Indies in the Years 1772-1774 (London).

ROLLO, J. (1781). Diseases in the Army on St. Lucia (Barbadoes).

FONTANA, N. (1781). Osservazioni intorno alle malattie che attaccano gli Europei nei Climi Caldi (Livorno). (Translated into French in 1818.)

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BALFOUR, F. (1790). Treatise on Putrid Intestinal Fevers (Edinburgh).

THOMAS, R. (1790). Medical Advice to the Inhabitants of Warm Climates (London).

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WADE, P. (1793). Prevention and Treatment of the Disorders of Seamen and Soldiers in Bengal (London).

HUNTER, JOHN (1796). Observations on the Diseases of the Army in Jamaica and on the Best Way of preserving the Health of Europeans in that Climate (London).

THOMAS (1801). Modern Practice of Physic of all Climates.

CLARK (1801). Fevers and Diseases of the West East Indies and America.

CAMPET, P. (1802). Traité pratique des Maladies graves qui régnent dans les Contrées situées sous la Zone torride et dans le Midi le l'Europe (Paris)

BLANE, G. (1803). Observations on the Diseases of Seamen (London).

WINTERBOTTOM, T (1803) An Account of the Native Africans in the Neighbourhood of Sierra Leone, to which is added an Account of the Present State of Medicine among them 2 vols (London) (The second volume contains the medical information)

HUNTER, W (1804). An essay incident to Seamen or Lascars in Long Voyages (Calcutta)

M'GREGOR (1804) Medical Sketches Expedition to Egypt from India

CURTIS C (1807) Diseases of India (Edinburgh)

JOHNSON J (1812) Influence of Tropical Climates on European Constitutions (London. Other edition 1818 1821 1824 1826 and 1827, and a sixth edition

ASSALINI (1810) Observations on the Disease called the Plague or the Dysentery the Ophthalmy of Egypt and New York

FRANK (1812). Collection d'Opuscules de Médécine Pratique (Paris)

JOHNSON J (1813) Influence of Tropical Climates on European Constitution London

REECE (1814) Medical Guide for Tropical Climates (London)

SIMPSON (1820) Exposition of Elementary Principles specially concerned in the Preservation of Healthiness and Production of Distempers amongst Mariners Travellers etc in Tropical Climates (London)

CHISHOLM, C (1822) A Manual of the Climate and Diseases of Tropical Countries (London)

BALLINGALL, G (1823). Observations on Fever, Dysentery, and Liver Complaints in European Troops in India (Edinburgh)

BOYLE, J (1828) Letter, on the Prevention and Cure of Diseases peculiar to Hot Climates (London)

M'CABE J. (1825) Military Medical Reports containing Pathological and Practical Observations illustrating the Diseases of Warm Climates (Cheltenham)

JOHNSON J (1827) An Essay on Morbid Sensibility of the Stomach, etc to which are added Observations on the Diseases and Regiments of Invalids on their return from Hot and Unhealthy Climates (London).

HASPER M (1831) Die Natur und Behandlung der Krankheiten der Tropenländer (Leipzig)

BOYLE, J (1831) Medico Historical Account of the Western Coast of Africa (London)

ROSER (1837) Ueber Einigen Krankheiten des Orients (Augsburg)

THÉVENOT (1840). Traité des Maladies des Européens dans les Pays Chauds (Paris)

McWILLIAM, J O. (1843) The Medical History of the Expedition to the Niger 1841-42 (London)

SIGAUD, J. F (1844). Maladies du Brésil (Paris).

FERGUSSON, W. (1846) Notes and Recollections of a Professional Life (London). (Deals with Military Hygiene, Ophthalmia, Plague, Yellow Fever, Typhus, Marsh Miasmata and Cholera)

REID, McC. (1846). Fever, Contagion Quarantine, and Cholera (London). (Deals with Yellow Fever, Typhus, Plague and Scurvy)

WILSON, J. (1846). Medical Notes on China (London).

BRYSON, A. (1847). Climate and Principal Diseases of the African Station (London). (This is a book on the diseases in the vessels of the West African Squadron from 1820 till 1845, giving graphic descriptions of the ravages of Yellow Fever, and, in addition, chapters on the Topography of the Station, the Causation, Treatment, and Prevention of Disease in the Station, and the Diseases most prevalent among captured slaves)

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Moore, W. J. (1861 ?). Manual of the Diseases of India (London). Second edition, 1880.

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Gauthier (1865). Des Endemies au Sénégal Thèse (Paris).

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Bachoué (1876). Étude sur la Constitution Phys. et Méd. de Zanzibar (Paris).

Roy, G. C. (1876) Burdwan Fever (London).

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Sullivan, John (1877) The Endemic Diseases of Tropical Climates (London).

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Nielly, Maurice (1881) Elements de Pathologie Exotique (Paris).

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Gordon, C. A. (1884) Medical Reports—Chinese Customs Service (London). (Almost a textbook of tropical medicine, with valuable reports by Manson on Filariasis, Paragonimiasis, etc)

Maclean, W. C. (1886). Diseases of Tropical Climates (London).

Burot (1886). De la Fievre dite bilieuse inflammation à la Guyane (Paris).

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Corre, A. (1887). Traité Clinique des Maladies des Pays Chauds (Paris).

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GRALL ET CLARAC (1910) Traité de Pathologie Exotique (Paris) (Several volumes: not yet fully published).

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HISTORY OF TROPICAL MEDICINE.

The most excellent book is Garrison (1918), 'History of Medicine,' 2nd edition, Philadelphia, and the important periodicals are 'Annals of Medical History,' commenced in 1917, and published in New York; and the 'Archiv für Geschichte der Medizin,' started in Leipzig in 1908, and Janus, as well as the Transactions of the 'Medical Historical Section' of the Royal Society of Medicine.

Neuberger (1910), 'History of Medicine,' vol. i., English translation by Playfair, gives good accounts of Byzantine and Arabic medicine; and Elliott (1914), 'Outlines of Greek and Roman Medicine,' London, is most interesting.

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Rush (1818). Medical Inquiries and Observations. (The first volume contains an account of medicine amongst the North American Indians.)

Seligmann, C. G. (1902). Journal of the Anthropological Institute (London). (The Medicine, Surgery, and Midwifery of the Sinangolo, an inland tribe inhabiting the Rigo District of British New Guinea.)

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CHAPTER II

TROPICAL RACES

The Tropics—Tropical Races—Primitive man—Classification—Caucasic division—Ethiopic division—Mongolic division—Amerind division—References.

THE TROPICS.

SUPAN suggested that climates should be classified as follows:—

1. *Tropical or warm climates*, extending from the Equator to the mean annual isotherm of 20° C. or 68° F.

2. *Temperate climates*, extending from lands possessing a mean annual isotherm of 20° C. or 68° F. to those which have a temperature of 50° F. for the warmest months of the year.

3. *Cold climates*, lying polewards of the isotherm of 50° F. for the warmest months of the year.

In Fig. 1 we have depicted the tropical or warm climates as delineated by Supan's lines marked B B., indicating the mean annual isotherm of 20° C. or 68° F. in north and south latitudes. Both lines are very wavy, the northern being situate about 35 degrees north latitude, and the southern at rather less than 30 degrees south latitude. This region Supan has divided into two zones, the *Tropical Zone* and the *Subtropical Zone*, by lines indicated on Fig. 1 as A.A., which represent isotherms of 20° C. or 68° F. for the coldest months of the year in both northern and southern latitudes.

These lines A.A. correspond more or less to 23½ degrees north and south latitude—*i.e.*, more or less to the Tropics of Cancer and Capricorn.

1. **The Tropical Zone.**—Examining the map a little more in detail, it will be noticed that, starting in the extreme west and travelling eastwards, the isotherm both north and south of the Equator is nearly the same as the latitude 23½ degrees north or south, but as the coast of America is reached it dips a little to the south in the Northern Hemisphere, and considerably to the north in the Southern Hemisphere. This variation is caused by cold currents in the sea running along the west coast of America, the more important of which (marked I. on the map) is the cold current from the Antarctic.

Tracing the line farther eastward, it will be noticed that it rises towards the north in the Northern Hemisphere, and falls towards the south in the Southern Hemisphere. In the Northern Hemi-

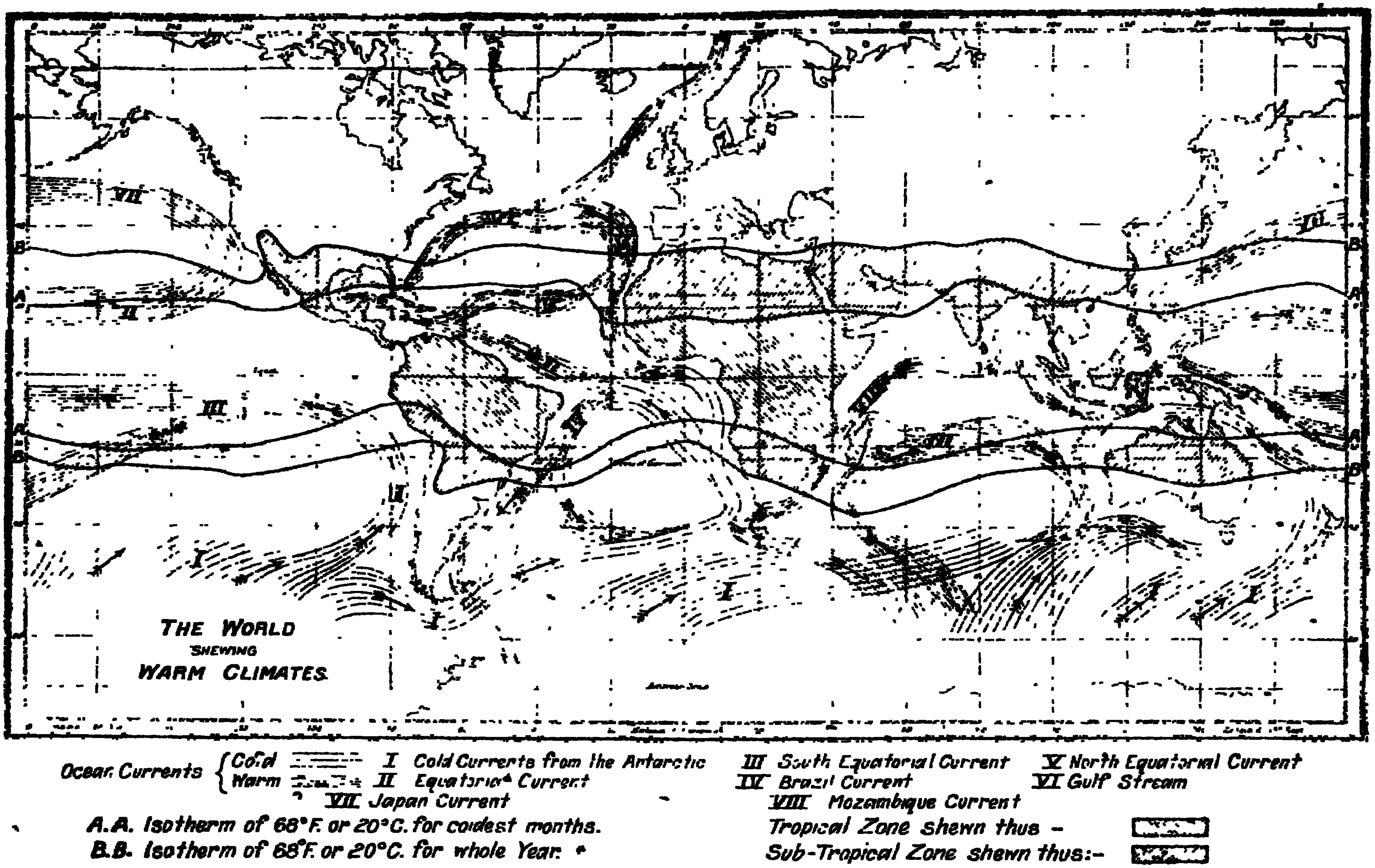
THE WORLD
SHEWING
WARM CLIMATES
Ocean Currents {Cold / Warm
I Cold Currents from the Antarctic
II Equatorial Current
VII Japan Current
III South Equatorial Current
IV Brazil Current
VIII Mozambique Current
V North Equatorial Current
VI Gulf Stream
A.A. Isotherm of 68°F. or 20°C. for coldest months.
B.B. Isotherm of 68°F. or 20°C. for whole Year.
Tropical Zone shewn thus -
Sub-Tropical Zone shewn thus:-
A
B
I
II
III
IV
V
VI
VII
VIII

FIG. 1.—THE WORLD, SHOWING WARM CLIMATES AS DELINEATED BY SUPAN'S LINES.

sphere this is due to the warm Equatorial Current (II.), and in the Southern Hemisphere to the warming effects of the land and to the warm Brazilian Current (IV.).

With reference to the different effect of land and sea, it is necessary to remember that though 25 per cent. of the heat of the sun's rays which fall on the outer limit of our atmosphere are absorbed, still these rays do not really warm the air to any appreciable extent. The real warmth of the air is obtained from the dark heat radiated from land and sea.

Land not only absorbs the radiant heat from the sun more quickly than water, but also more readily gives off the dark heat to the air; therefore the presence of a large area of land upon which the sun's rays fall more or less vertically at noon all the year round will raise the temperature of the air, and will tend to extend the area of the warm climates. Hence the land may become extremely hot--incredibly high temperatures have been mentioned by authors—while water never becomes very warm. The reason of this is that water, being a liquid, by convection and by currents tends to keep at a more even temperature than land, though, as already noted, the currents, cold and warm, have a marked influence on the climate.

Turning again to the map, and tracing the isotherm eastwards towards the west coast of Africa, it will be noticed that again both the northern and the southern isotherms approach the Equator, and again this is due to cold currents- in the north to the North Equatorial Current (V.); and in the south to the cold Antarctic Current (I.). Crossing the continent of Africa, the effect of land is seen, and on passing into the Indian Ocean the effect of the Mozambique and the South Equatorial Currents may be noted, and finally, to the west and east of Australia the cold Antarctic Currents produce effects.

Thus the Tropical Zone is alternately decreased and increased in area, the most marked diminutions being on the west coast of America and the west coast of Africa.

It will be observed that this zone includes Central America, a large portion of South America, the West Indies, a large portion of Africa, Madagascar, a portion of Arabia, India, Ceylon, Indo-China, Sumatra, Java, Borneo, the Philippine Islands, New Guinea, and a portion of Australia, and many other smaller islands.

2. **The Subtropical Zone.**--The Subtropical Zone lies between the isotherms of 68° F. (20° C.) for the temperature of the coldest month, and the same isotherms for the mean temperature of the year.

It is depicted in Fig. 1, and will be noticed to include a portion of North America and considerable portions of South America, Africa, Asia Minor, Arabia, Persia, North India, China, and Australia.

Another method of subdividing warm climates, based upon the winds, rainfall, and altitude, will be given in the next chapter.

TROPICAL RACES.

It is now desirable to inquire very briefly into the races of mankind inhabiting these tropical or warm climates as defined above, in order that the tropical practitioner may understand the racial relationship of the peoples amongst whom he is working: and for this purpose we give the following very condensed account, starting with primitive man.

PRIMITIVE MAN.

From geological, zoological, and botanical considerations there can be little doubt that in early tertiary times there existed an Indo-African continent where, at present, the Indian Ocean lies. This continent, embracing the Deccan, Madagascar, and South Africa, is more extensive than Sclater's Lemuria, and is now known as Gondwanaland.

This Indo-African continent may, for many reasons, have been the site of the primitive home of the human race, and indeed it was in Java that Dubois found those remarkable teeth, calvarium and femur, which to-day are recognized as belonging to *Pithecanthropus erectus* Dubois 1891, which, geologically, belongs more probably to the early Pleistocene rather than to the Tertiary Pliocene, as was at one time considered possible. These remains belong either to a very early form of man or to an immediate precursor.

Once evolved, there can be no doubt that the main factor in man's further evolution has been the development of the brain, and this may have been stimulated by his remarkable migrations, for, driven by food requirements, geological or meteorological disturbances, man migrated from his primeval home and spread westwards into Africa, where, in the then fertile and well-watered northern regions of the Sahara, Caucasic man probably evolved. He also migrated northwards into Asia, evolving there the common ancestor of Mongolic-Amerind man, which eventually formed Mongolic man in Asia, while the further migration into America gave rise to Amerind man. Migrations from the south were easier in those days, because the Himalayas were much lower than they are to-day.

In the meanwhile the non-migrating common ancestor may have evolved into Ethiopic man, who was eventually compelled by the subsidence of the land to migrate westwards into Africa and eastwards into Oceania.

With regard to these early migrations, it must not be forgotten that the climatic conditions were probably very different from those of to-day, and, as it was a warm interglacial period, were distinctly favourable to these movements; while the abundant land connections of Africa to Europe, Asia to America, and America to Europe, of those days materially facilitated them. Neither must it be forgotten that these migrations, as well as subsequent migrations, were not single, but multiple, taking place in successive waves, and spread over a long space of time.

When considering the different divisions of mankind in greater detail, it will be noted that they spread from their original homes in various directions and at various times, until the whole world was populated.

The first dispersal of man over the globe must have resembled the migrations of animals in that it must have been performed unconsciously under the influence of the factors just mentioned, though it is possible that the food factor was the most potent, because, as Seligmann has pointed out, the hunting man of to-day requires a relatively large area in which to obtain his food, and it is equally possible that primeval man soon found that a given district was unable to feed his rapidly increasing family or tribe. Under these circumstances the family or tribe in question would move into a more suitable region. When man became more evolved migrations would still take place under compulsion as described above, but might also have taken place under the influences of attraction or expulsion, by which one means that a powerful tribe might be attracted to an area held by a weaker tribe, which latter would be compelled to submit to the conquerors or to migrate to some other area. If the weaker tribe remained with the stronger, there would possibly be a race fusion, as has so often taken place all over the world, and a new mixed race would appear, or the two races might live together with little fusion. During these early times must have appeared many of the diseases, especially the infectious diseases, which to-day afflict mankind, but what part the disease factor played in these migrations we do not know. What part epidemic parasitic diseases have played in evolution cannot be stated, but that they must have played some part in the extinction of animals seems possible; and it appears also possible that parasites transferred from animals to man at this period by the agency of blood sucking insects, etc., may have formed the basis of certain of the diseases of man to-day.

These migrations must have been delayed or stopped by meeting with natural barriers, such as deserts, dense forests, or broad expanses of water; and probably at these places settlements would be made, from which reflux migrations into parts originally occupied, or passed through, might arise, due again to the influence of the factors above mentioned.

In this way tribes, now modified by selection, environment, etc., re-entered the districts through which they had originally passed, and, finding them more or less occupied by differently evolved peoples, brought about fusion of the early divisions and subdivisions of mankind. And thus at an early period arose the first of these race fusions which are ethnologically so confusing to-day. One factor in these early refluxes must be mentioned, and this is the changed meteorological conditions brought about at the Glacial period or periods, for during these man must have been driven towards the Equator, while in the intervals he could wander polewards.

These early migrations and refluxes must have acted as potent stimuli to the already rapidly evolving brain of man, but this evolution does not appear to have gone on equally all over the world; in fact, it is in the so-called *Culture Zone*, situate between 25° and 50° north latitude, that brain development began to be highly specialized. In the eastern part of this region arose the Accadians, the Egyptians, and the early Cretans, from whom all the culture of Europe, Asia, and Africa evolved; and separately in the west the Mexicans, Peruvians, Columbians, and inhabitants of Yucatan, whose advance was ended once for all by the Spanish conquests, leaving only the culture of Accadian, Egyptian, and Cretan origin to supply the world with knowledge.

In other regions man has lagged far behind; indeed, in New Guinea and in other places we have the native peoples just emerging from a contemporary Stone Age side by side with the newly migrated and highly cultured Caucasic.

The tropical regions of to-day have therefore a most curious and most complex congeries of mankind. First, the indigenous inhabitants or natives of the land in question, together with the descendants of peoples arising from the intermingling of the original native race with other races brought thither by migrations of long ago; secondly, peoples whose native habitat is a temperate or cold climate, and who are derived from the quite recent and still continuing Caucasic migration; and, thirdly, the half-castes, derived from the intermingling of these Caucasic races and the native races

From the above it will be comprehended that the study of the ethnology of man in the tropics is indeed complex, but some elementary knowledge of the origin and relationships of the people among whom he is to work may be of use to the practitioner in the tropics, and therefore we give the following brief classification, leaving anyone interested in this subject an opportunity of further study by means of the works mentioned in the references at the end of the chapter.

Classification.- All classifications are more or less artificial, and based upon the generally accepted knowledge of the day, and are therefore ephemeral, and the various classifications, suggested by Bernier in 1684, Linnæus in 1735, 1740, and 1758, Blumenbach in 1775, Virey in 1801, Des Moulins in 1825-26, Bory de Saint-Vincent in 1827, Agassiz in 1850 and 1853, Isidore Geoffroy Saint-Hilaire in 1858, Pruner Bey in 1863, Haeckel in 1873, Broca and Topinard in 1885, Flower in 1885, Deniker in 1889, and, finally, Keane in 1895, form no exception to this rule.

The most useful classification is that of Keane, in which the human species is divided into four divisions--viz.:--

The Caucasic Division.
The Ethiopic or Negroid Division.
The Mongolic Division.
The Amerind Division.

We will now briefly consider these divisions.

Caucasic Division.

This division of man is thought to have evolved in Northern Africa at a time when the Sahara was a well-watered and inhabitable region.

Characters.—The characters of Caucasic man are:—*Height*, average or above the average; *colour*, florid or pale; *hair*, long, wavy, soft, and flaxen, or long, straight, wiry, and black, in either case oval on transverse section; *skull*, dolichocephalic or brachycephalic; *eyes*, moderately large, straight, blue or black; *nose*, straight or arched leptorrhine; *cheek-bones*, small; *jaws*, orthognathous; *teeth*, small; *beards*, full. Three types are recognized of these physical characters: the Nordic, with cephalic index 74-79, and blue or grey eyes, fair hair, and height 5 feet 8 inches to 6 feet; the Alpine, with cephalic index 80-90, brown or black eyes, dark hair, and height 5 feet 5 inches to 5 feet 6 inches; the Mediterranean, with cephalic index 72-78, black eyes, black hair, and height 5 feet 4 inches to 5 feet 6 inches. *Speech*, inflecting—*e.g.*, the Hamitic, Semitic, and Aryan languages—except in some instances, when it is agglutinating—*e.g.*, Basque; *temperament*, active, enterprising, and imaginative. *Medicine* varies from the highly evolved European medicine to the primitive Oceanic medicine.

Migrations. From his Saharic home the primitive Caucasic man wandered in Palæolithic and Neolithic times eastwards into the Valley of the Nile and on into Asia, where he met Mongolic man, and later into Southern Asia, and so into Oceania, reaching, as we shall presently see, its farthest islands. He also wandered northwards in successive migrations across the bridges between Africa and Europe, where he was succeeded by the early race to which belong the Cannstadt cranium found in 1700, the Neanderthal cranium found in 1856, the Spy cranium found in 1886, the skeleton of *Homo primigenius* found in 1908 in the Valley of Vézère, and the various skeletons and skulls found in 1909. All these skulls belong to the type called 'Neanderthaloid,' after their best-known member, and are considered by some authorities as not belonging to *Homo sapiens*, but to a separate species—*H. primigenius* (*H. neanderthalensis*)—which is approached to-day most closely by the Australian type. This earlier type was followed by more highly evolved Caucasic types, as, for example, the Cro-Magnon race of the French anthropologists found at Les Eyzies in Périgord. It is almost certain that these early peoples did not speak an Aryan language, but more probably a language allied to that of the Berbers, and therefore to the present Basque language. In Asia a fusion took place of certain Caucasic races with Mongols, forming the Turkoman and many Tatar peoples, such as the Uzbeg Tatars.

In both prehistoric and historic times there have been migrations of Semitic Caucasians from Asia into Africa, of which the most important were the Arabic migrations, which have produced a great impression on the peoples of Northern and Eastern Africa.

In recent times migrations of the highly evolved types of Caucasians have taken place from Europe into America, Oceania, Asia, and Africa, and to-day new races are arising from the fusion of native races with Spaniards and Portuguese in America, with Dutch in South Africa, and with French in Indo-China. It is, however, a curious sociological trait of the Anglo-Saxon not to amalgamate with the aborigines of the land into which he has migrated.

Population.—At the present time the Caucasic division is estimated to number 770,000,000 of the 1,570,000,000 of peoples which are supposed to inhabit the world, but there can be no doubt that this division is rapidly increasing in numbers. These 770,000,000 are distributed as follows:

Europe, 355,000,000; Asia, 280,000,000; America, 115,000,000; Africa, 15,000,000; Oceania, 5,000,000.

Classification.—Ethnologically, Caucasic man may be classified into the Xanthochroi and the Melanochroi, while an early wave passing across Asia gave rise to the Indonesians, which type is difficult to define, though Haddon considers that its least modified representatives are to be found among the dolichocephalids of the forests of Borneo.

THE XANTHOCHROI, or fair subdivision, is characterized by possessing light hair and light-coloured eyes. It contains the modern Europeans, who can be subdivided into the Teutonic branch, consisting of Germans, Dutch, Anglo-Saxons, and Norse races, and the Slavic branch, consisting of Russians, Poles, Serbs, Bulgars (in part), and Croats. It is the Teutonic branch which has supplied many of the peoples of the recent Caucasic invasion of the tropics.

THE MELANOCHROI, or dark subdivision, has long, straight, wiry black hair, black eyes, and only average height, while their characters are fiery, impulsive, and fickle. For the present purposes the Melanochroi may be subdivided into Hamites, Semites, Hindus, and Dravidians.

The Hamites may be further divided into a western division and an eastern division. The Western Hamites are the Berbers, sometimes referred to as Libyans, who are spread from the Canary Isles in the west to the Oasis of Siwa in the east, and from the Mediterranean in the north to the Senegal River and southern boundaries of the Sahara in the south.

The original strain of the Berbers has become altered by admixture with Arab blood in the north and negro blood in the south. In the north they have suffered much from the irruptions of Phœnicians, Romans, Greeks, Vandals, Arabs, and the European nations of to-day.

Two important sections of the Berbers must be recognized—the Agriculturists, as, for example, the Kabyles of Mauretania, who live settled lives, and the Nomads, represented by the Tuaregs of the Sahara. Tracing the various groups of true and mixed Berbers from west to east, there are first of all the Guanches, or original inhabitants of the Canary Isles, who show an affinity to these peoples; then the Trarza and Brakna of the Coast Sahara just north of the Senegal River, who have a negro strain. The Moors of Morocco must be considered to be Berbers with a strong Arabic strain. The principal groups of these are the Riffians of the north of Morocco, the Brábers of the Atlas, the Shluh of Western Morocco, the Sus between the great and small Atlas and the Tafilat to the south of the Atlas; but the last two have a negroid strain, as have the Wargla. East of these come the Kabyles of Jurjura and the Shauia of Aurès, who are interesting because, according to authors, some of them have chestnut hair and grey eyes. The Uled-Naïls of the Biskra district are mixed Berbers and Semites.

South of the territories of these peoples are the interesting veiled Tuaregs, with their centre in the *Haggar* Mountains, and their division into Asgers (Asjars) in the east, Haggars (Ahaggars) in the west, and Kelowis in the south; and Awelimmiden on the Central Niger. The veil, or *litham*, is used to protect them from the wind-blown sand of the desert. In the south of Algeria there are mixed Berbers, Arabs, and negroes, such as the Beni-Mzab, the Wargla, and other inhabitants of the oases. The Shaamba are Berbers between the south of Tunis and the west of Tripoli. In Tripoli itself there are Berbers mixed with Semites. South of these and east of the Tuaregs lies Tibesti, the headquarters of the Tibus, who are now Mohammedans with a slight mixture of Paganism. Far south there are the Fulahs, who are Berbers with a great admixture of negro blood, who are dispersed among the Sudanese negroes. They took their origin on the Senegal, but later invaded the Hausa States and formed the Empire of Sokoto.

The eastern division of the Hamites includes the Egyptians, the Abyssinians, and the so-called Ethiopians or Nubians. The Egyptians of to-day exist as the Christian Kopts and the Mohammedan Fellahîn. The Ethiopians include the Bejas or Bisharû, of the land between the Red Sea and the Nile; the Afar or Danakil, between Abyssinia and the Gulf of Aden; the Somals of Somaliland, who are much intermingled with negroes, Arabs, Afars, and Abyssinians; the Gallas or Ilm'Orma, in Southern Ethiopia or Gala-land proper; and the Masai of Masailand intermediate between the Galla and the Wahuma or Wahima, who are dispersed among the Bantu peoples of the great lakes, and are believed by some to be the originators of the Bantu dialects

The Semites have their primeval home in Arabia, from which they wandered in various directions e.g., the Himyarites or Southern Arabs to Abyssinia, the Arabs proper to North Africa and to the east coast of Africa, producing profound effects They may be classified into South Arabians, including Himyarites and their derivatives, certain tribes of the Abyssinians and the Northern or true Arabs, the Assyrians, Amorites, and Canaanites, which included the Hebrews and Phœnicians, both of which have produced effects upon man in Africa, where to day the Jew is found in numbers in Tripoli and Algeria.

The Hindus. The Aryans are thought by Keane to have arisen as a fusion of many Caucasic and some Mongolic elements with an original xanthochroid basis, and to have lived in a Eurasian home, probably in the steppes between the Ural and Caucasian Mountains and in the Aral-Caspian depression and the regions of Turkestan; for, as he points out, in Neolithic times this region was very suitable for human life, being then well watered, but the gradual drying of Asia would compel these primitive Aryans to wander westwards into Europe, and south-eastwards into the Iranian plateau and India, and it is with this last migration that we are at present concerned. In this extent there is only one non-Aryan survival- viz., the Brahui of Eastern Baluchistan. The important groups are the Hindus, Bengalis, Punjabis, Kashmiris, Gujaratis, and Sinhalese.

The Dravidians include a vast congeries of tribes, which, if the so-called Pre-Dravidian jungle peoples be excepted, form everywhere in India the basis of the population. The pure Dravidian

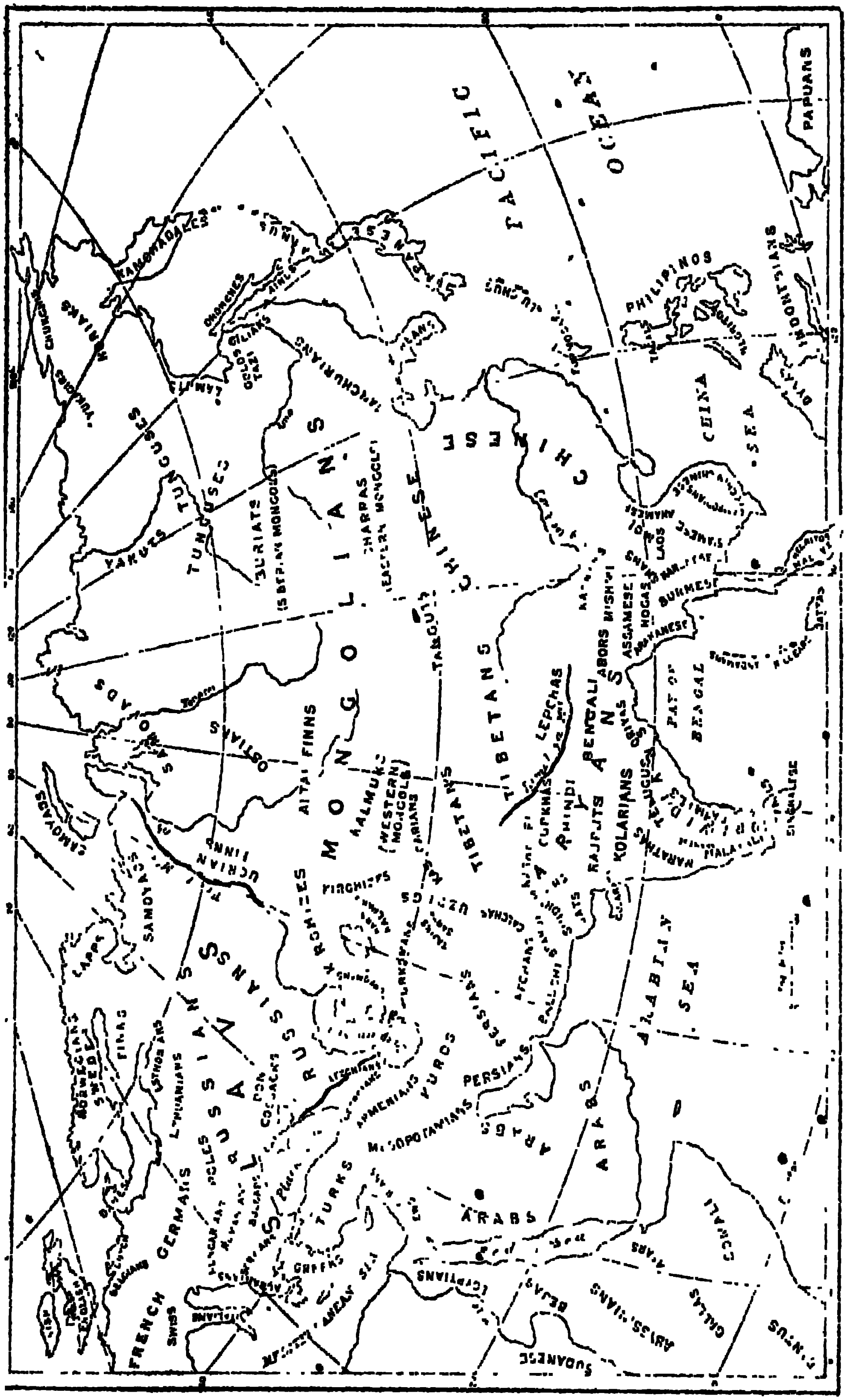

FIG. 2.—THE RACES OF ASIA.
(From Hutchinson's 'Living Races of Man.')

stock is represented by the short, dark, broad-nosed, dolichocephalic peoples (recalling the noseless Daezu of the invading Aryans), but they have everywhere been modified by fusion with immigrant peoples, giving rise to the Aryo-Dravidian, Scytho-Dravidian, and the Mongolo-Dravidian types. The Aryo-Dravidian type is principally found in Northern India and Ceylon, its upper strata being exemplified by the Hindustani-speaking Brahman of Northern India and the Tamil-speaking gentleman of Northern Ceylon, while its lower strata are exemplified by the Chamar. The complexion of these people varies from medium brown to very dark, and their noses from medium to broad. The Scytho-Dravidian type of Western India is characterized by a fair complexion, with little or no hair on the face, with broad heads and moderately fine noses. Riseley considers that this type is a fusion between Dravidians and immigrant Scythians, and Haddon suggests that it is a fusion with the Alpine race from the hills of South-West Asia in prehistoric times. The Mongolo-Dravidians are best represented by the inhabitants of Lower Bengal and Orissa. They are of medium stature, and usually of dark complexion with abundant hair on the face, with broad heads and broad or medium noses.

INDONESIANS.—The greatest divergence of opinion is found with regard to the inhabitants of Malaysia and Oceania. It would appear probable that the earliest inhabitants belonged to the undifferentiated negroid type, of which the negritoes gave rise to the Andamanese, the Semangs of Malaysia, the Aëta of the Philippines, and the pygmies of New Guinea, while the negroes formed the Tasmanians, the Papuans, and the majority of the Melanesians. In among these peoples came the brachycephalic Mongols, called by Haddon the Proto-Malays, who were to be found first in the Peninsula, and later, driven south by the Caucasic migrations to be presently described, in the islands.

Earlier migrations still, perhaps of lowly developed Caucasian stocks, may have given rise to the Pre-Dravidian jungle tribes of India and Ceylon, and perhaps to the Kakhyens of Northern Borneo and the Sakai of Malaysia, and to one element in the Australian race.

An early migration fused with the Proto-Malays, forming the Proto-Polynesians of Haddon, who migrated into the Western Pacific, and, fusing with the early black peoples, gave rise to the Melanesians; while others, passing through or round Melanesia, went on to Tonga and Samoa, and later to Tahiti and Raratonga of the Cook Islands, spreading later to Hawaii and the Marquesas, and still later to New Zealand. These migrations or voyages are supposed to have begun by a migration to Java as late as 65 B.C., and did not cease till A.D. 1350. In this way the mixed populations of many of the islands of the Pacific arose.

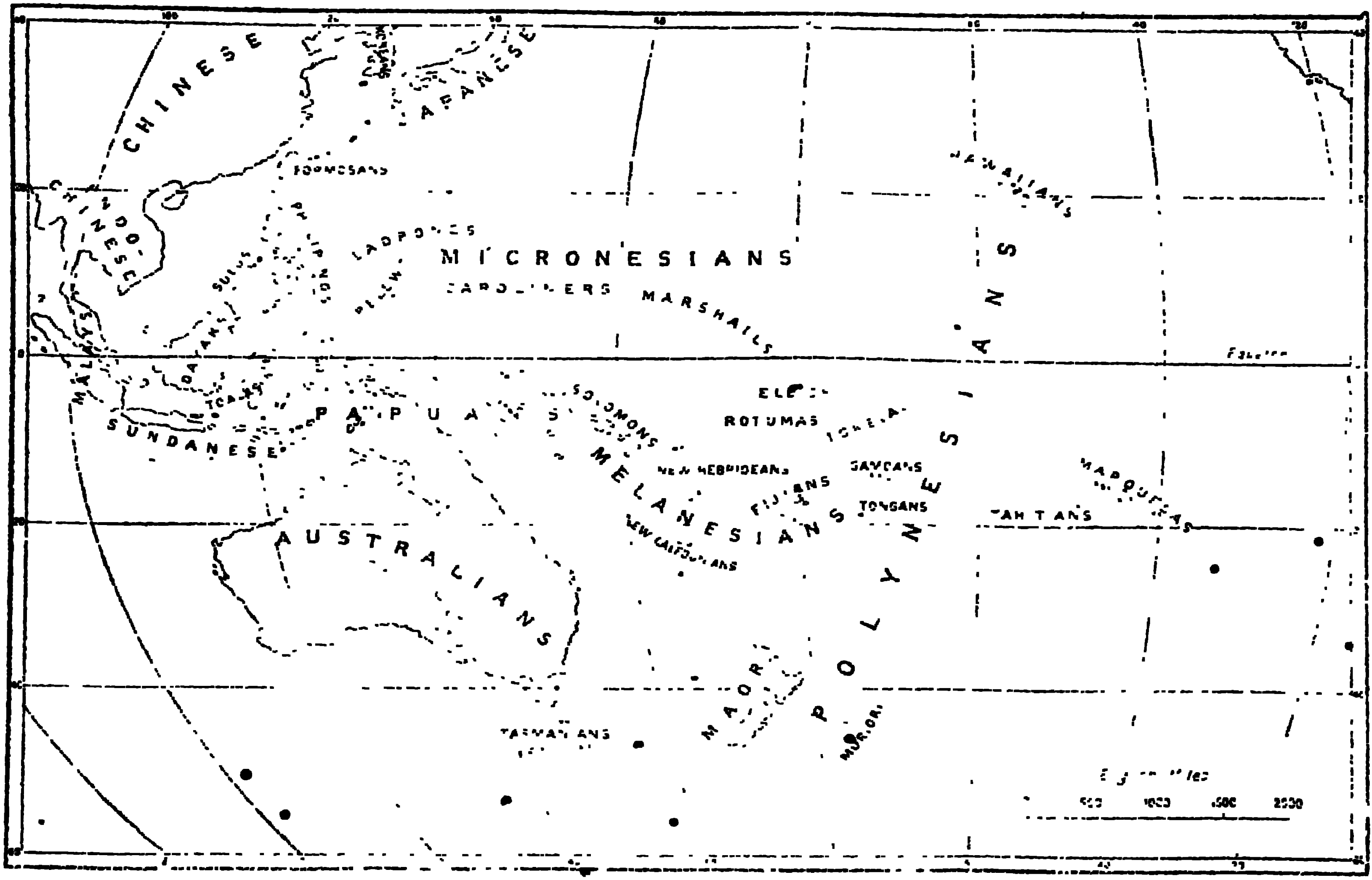

FIG. 3.—THE RACES OF MALAYSIA AND OCEANIA.
(From Hutchinson's 'Living Races of Man.')

Ethiopic Division.

It is possible that this division took its origin in the Indo-African continent.

Characters.—The characters of Ethiopic man are.—*Height*, either above the average (negro) or dwarfish (negrito); *colour*, blackish or yellowish brown; *hair*, short, frizzy, flat in section, or reddish-brown and woolly; *skull*, dolichocephalic (negro) or brachycephalic (negrito); *eyes*, large, round, prominent, black, with yellowish cornea; *nose*, flat and broad, platyrhine, *cheek-bones*, small; *jaws*, prognathous; *teeth*, large, *beards*, absent or small; *speech*, agglutinating, with prefix and postfix types, or inflectional. In negroid Africa there are numerous languages in the Sudan and West Africa, but in the east, centre, and south there are only variants of the Bantu stock language; in the far south there are the Hottentot and Bushmen languages. In Madagascar and Oceania the Malayo-Polynesian stock language is prevalent. In America the speech of the negroes has approached that of the European languages. *Temperament*, indolent, sensuous, passionate, and cruel. In Africa there is a lack of self-respect, thus readily permitting slavery. The development of the mind is believed to be arrested at puberty by the closure of the cranial sutures, and there is also a belief that the negro, left to himself, without Caucasic migrations, would have retrograded enormously, some stating that he would have retrograded to the condition of an animal (these statements may be received with caution). *Religion*, fetishism, nature and ancestral worship, *medicine*, primitive, being closely associated with religion, and therefore with the fetish priest, and therefore with magic, charms, invocations, and sacrifices; but there is a knowledge of poisonous plants, which are used in trials by ordeal, in hunting, fishing, and war.

Population.—Ethiopic man is guessed to number some 175,000,000 of persons, of whom perhaps 155,000,000 are in Africa, 3,000,000 in Madagascar, 20,000,000 in America, and 2,000,000 in Oceania.

Migrations.—From his Indo-African home Ethiopic man wandered westwards into Africa and eastwards into Oceania.

Africa.—One of the first of the westward waves must have been that caused by Palaeolithic man migrating into Africa, wherein he spread north and south. Another very early wave was that of the pygmies, who gave rise to the Bushmen and negritoes or negrillos, and spread along the whole east side of Africa from the Mediterranean to the extreme south. With, or perhaps not long after, the pygmy migration came the taller negro, who possibly wandered into East Africa and through the forests, together with the pygmies, to the west coast, and possibly northwards as far as the northern shores of the Mediterranean; but these migrations of Ethiopic man in Northern Africa were stopped by the evolution of Caucasic man, who not merely drove the negro southwards, but made some remarkable race fusions with him. Thus, for example, the Hottentots are believed by some to be of Hamitic-Bushmen origin, although others consider it safer to place them as intermediates between the Bantu peoples and the Bushmen. These Hottentots were stronger than the Bushmen peoples, but not so strong as the Bantu peoples, by whom they were eventually driven into Southern Africa.

Another remarkable race fusion is that which produced the Fulani, who are believed to have been originally Berbers (Caucasics), but who have intermingled with the negro races among whom they have migrated. Thus their residence on the Senegal River is traced by the Wolofs of the Senegambia, who are a negroid Fulani race; and along the Niger by the Mandingoes, who possibly have also Tuareg and Arab infusions. These Mandingoes, driven by Fulani migrations, have to-day approached the coast south of the Senegal River, displacing the Krus and Kpwesi, who now live in Liberia. Migrating farther inland, these Fulanis compelled the Ashantis and Fantis to travel coastwards, and then settling in the Hausa States, and forming the Sokoto Empire, they compelled the Hausas to move southwards and to force the Yorubas to approach the coast, who in their turn drove the weaker indigenous

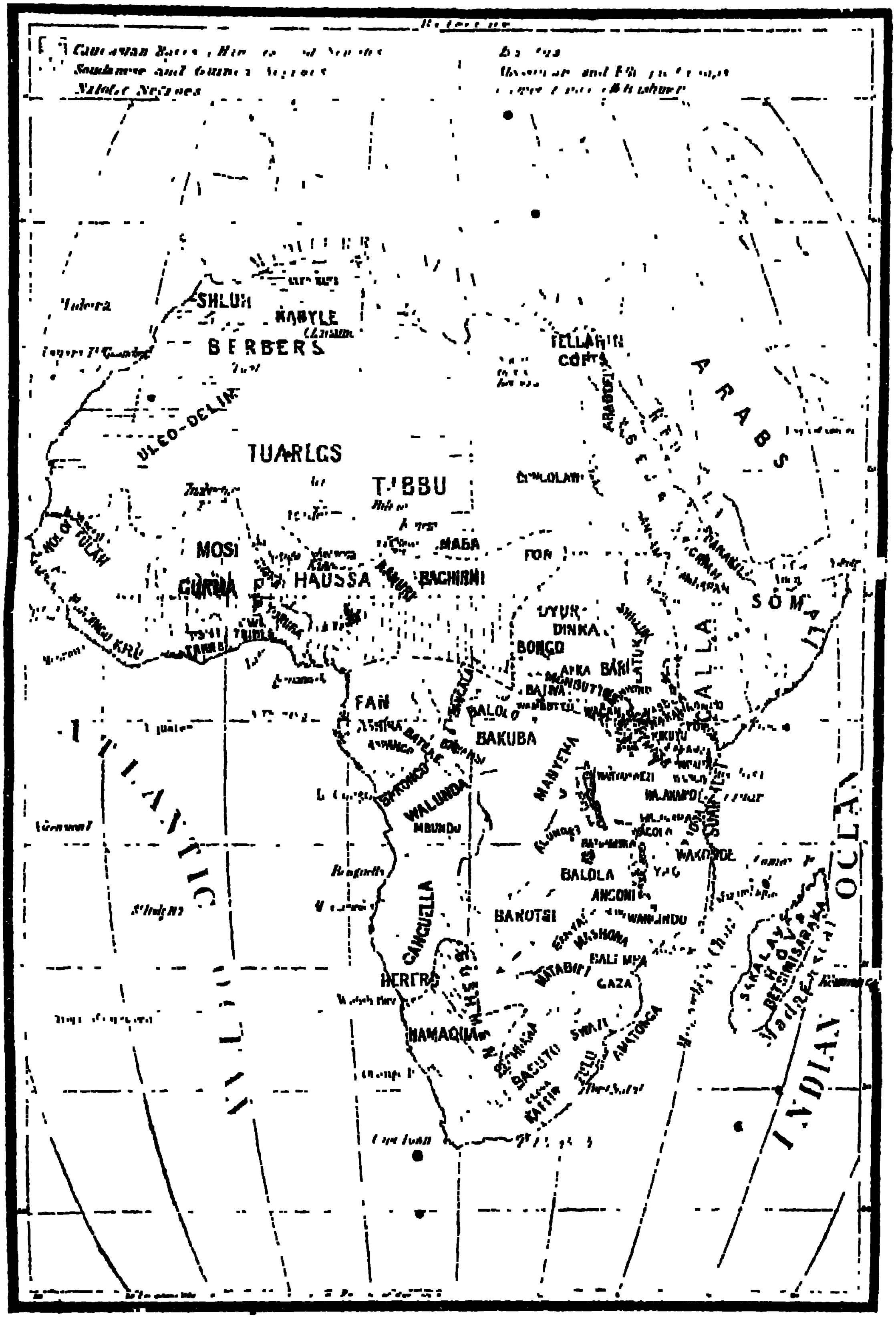

FIG. 4.—THE RACES OF AFRICA.
(From Hutchinson's 'Living Races of Man.')

tribes into the unhealthy delta of the Niger. The Fulani can also be traced by their language right across Africa to Dar-Fur.

All these negroes, pure and mixed, living in that region of Africa which is called the Sudan, from the Arabic *Belad-es-Sudan* (Land of the Blacks), speak languages of various stocks, but very different is the language of the Bantu speaking peoples of the portion of Africa south of a line approximately drawn eastwards from the Rio del Rey River, near the northern boundary of the Kamerun, which separates the Bantu peoples from the Sudan peoples.

It is quite impossible here to mention the many changes which have been brought about in the position of the various Bantu tribes by the slave-trade, migrations of local tribes, as well as those of Caucasians; but these influences have produced many changes even during the nineteenth century, of which some are known, particularly in South Africa.

The slave raids began with the expeditions of the ancient Egyptians, and continued until quite recently, when the last Arabic raiders were checked by the Caucasic migration.

Locally, movement of Congo tribes southwards, and southern tribes northwards and interior tribes coastwards, have caused much confusion; but perhaps of all the movements, those of the Ama Zulu and their descendants, the Zulu especially under Chaka, together with those of the Barotse and the Mantati, and the Ova Herero, are the most remarkable or best known. Curious causes have called forth these migrations. First of all, the physical features of Africa have had a great effect upon the occupations, and hence upon the migrations of its people; secondly, the urgent need for salt in vegetable-feeding peoples, driving them coastwards; and, lastly, the endemic and epidemic disease factor, which is demonstrated by the weaker tribes being driven into the most unhealthy regions. The Caucasic migrations of the Dutch and English in South Africa have also had great effect in driving the native tribes northwards and in exterminating them.

Oceanic. The eastward or Oceanic migration of Ethiopic man is extremely difficult to follow, and may have taken place largely on foot over land bridges, which at that time existed, and later in canoes by water.

The negritoes, or pygmies, are represented to-day by the Andamanese, the Semangs of Malaysia, the Aeta of the Philippines, and the pygmies of New Guinea; while the Oceanic negroes gave rise to the extinct Tasmanians and the Papuan people, the latter forming the ground-stock of Melanesia.

Classification. Ethnologically, the Ethiopic millions are classified into two principal sections—the Western or African, and the Eastern or Oceanic, section.

The stature of the Ethiopics of the Oceanic section is less than that of the Africans, the hair is more wiry, the nose is large and straight, the lips are not so thick, and are not everted as they are in the Africans. The Oceanics are more savage, but they show artistic taste and execute wood carving.

The Western or African Section contains negritoes and negroes. The negrito is dwarfish, with yellowish-brown colour, reddish-brown woolly hair, and brachycephalic skull; while the negro is tall, of blackish colour, with jet-black frizzy hair and dolichocephalic skull.

The African negro may be subdivided into negroes living north of the Equator and not speaking the Bantu dialects, which include the West and Central Sudanese, the Welle River groups, the Nilotic groups, and the Nubas of Kordofan, and into groups living south of the Equator and speaking the Bantu dialects; while in the extreme south are found the Hottentots and Bushmen.

The Eastern or Oceanic Section contains also negritoes and negroes, distinguished as above mentioned.

Mongolic Division.

Mongolic man probably evolved in the Tibetan Plateau of long ago.

Characters.—The characters of Mongolic man are: *Height*, rather under the average; *hair*, black, lank, coarse, round on transverse section; *skull*, brachycephalic; *eyes*, small, black, oblique, with outer canthus slightly higher than the inner, and with a vertical fold of skin over the inner canthus; *nose*, very small, mesorrhine; *cheek-bones*, prominent laterally; *jaws*, mesognathous; *teeth*, medium; *beard*, slight or absent, but moustache present; *speech*, agglutinating, with postfixes, the families being Ural-Altaic, Tibeto-Indo-Chinese, and Malayo-Polynesian; *temperament*, reserved, sullen, and apathetic in the Mongols, industrious in the Chinese, and indolent in the Malays; they are all gamblers; *religion*, animism, Shamanism, Lamaism, Buddhism, Mohammedanism, Confucianism, Taoism, etc.; *medicine*, mostly theurgic, associated with invocations, but in China there has been an attempt to evolve a higher state of efficiency. The Hungarians have the usual highly evolved modern medicine.

Population.—The total number of Mongols is estimated to be 540,000,000 persons, of whom 380,000,000 are believed to reside in China, 55,000,000 in Japan and Korea, 35,000,000 in Indo-China, 30,000,000 in Malaysia, 10,000,000 in Mongolia and Manchuria, 6,000,000 in Tibet, 7,000,000 in Turkestan and Siberia, 13,00 in West Asia, and 4, elsewhere, but estimates vary very much.

Migrations.—The common stock of Mongol-Amerind man, migrating from the primeval home in the Indo-African continent, passed into Asia, and while the Amerind division travelled through that continent into America, it is probable that the Mongolic division made its home in Tibet. This would be in later Pliocene times, when the Tibetan Plateau would not be the elevated region which it is to-day.

In Tibet to-day the original type is best preserved among the Drupa, who are about 5 feet 4 inches in height, with light brown skin, somewhat resembling that of the Amerindians, with brachycephalic skulls, long black hair, brown eyes, slightly prominent cheek-bones, depressed nose, wide nostrils, and large ears. They are semi-nomadic pastoral peoples, living at a height of about 14,000 feet above the sea-level. The other groups in Tibet are the Bodpa, the dominant peoples, who are of mixed descent, and the Tanguts, predatory peoples along the north-east boundary.

From this Tibetan home Mongolic man wandered westwards, giving rise to the celebrated Akkads and Sumerians of Babylonia, and much earlier entered Europe, giving rise to the many Asiatic invasions of that continent. With regard to the Akkads and Sumerians, it may be stated that they early evolved a form of culture which grew and flourished after their fusion with their early Semitic conquerors, thus laying the foundations of one of the most ancient forms of human civilization. According to some authorities (though by no means proved), the Chinese took their origin from early Akkadian emigrants.

Another migration from Tibet was southwards along the valleys of the Irawadi, Salwin, and Mekhong Rivers into Indo-China, giving rise to the Mishmi, the Abors (with whom there has been trouble recently), the Kuki, the Luohai, the Chins, the Nagas, the Karens, the Khas, and the Moi, who, though perhaps not the makers of the stone implements recently discovered in the Irawadi Basin, may be looked upon as the aborigines of these regions, because there is at present no evidence as to who these earlier peoples were. The above-mentioned tribes have remained in a primitive condition, but others have developed, under Hindu influences, a high degree of civilization—as, for example, the Burmese. An immigration from the north brought the Malayans and the Tai race, which, coming from Central China about the Yang-tse-Kiang, gave rise to the Shans, the Laos, and the Siamese; while yet another migration, this time from the valley of the Si-Kiang and South-Eastern China, gave rise to the Annamese, Tongkinese, and Cochin Chinese.

In Oceania, taken in its widest sense to include all the islands of the Indian Ocean, as well as what is generally known as Oceania, the Mongol peoples are often known under the term 'Malays,' which is, properly, only applied to the Mohammedan tribes of Malay Peninsula, who are the Malays proper. These Malayans are found in Sumatra, Java, Borneo, Celebes, Bali, Lombok, Billeton, Bangka, the Spice Islands, and the Philippines, but are much mingled with other races—*e.g.*, with the negroes of Bantu origin in Madagascar, and the Caucasic Indonesians in Malaysia generally.

Keane says that the term 'Malay' was originally applied to the Orang-Maláyu, a small tribe of the Menangkabau district of Sumatra, who rose into prominence about a thousand years ago and spread over the archipelago, and whose language is the chief medium of intercourse throughout Malaysia.

Reverting to the primeval home of the Mongols, there are still further offshoots to mention—viz., the Hyperboreans of Northern Siberia and the Mongol-Túrki. These latter, who are often called Mongol-Tatars, from two words—'Mongol,' meaning 'brave,' and 'Tatar,' the plural of 'Tata,' 'an archer' (while 'Turk' is an Aryan word meaning 'swift'), which, again, is often spelt 'Tartar'—spread in two directions—eastwards and westwards. The eastward-migrating Mongol-Túrki gave rise to the Mongols proper, who include the Kalmuks, Sharras, Buryats, Tunguses, and Manchus, and the Mongoloid Koreans and Japanese. The Tunguses of the Amur Basin and East Siberia are interesting because the great bulk of them are Shamanists, their Shamans being medicine men, often called 'priests,' who heal by magic, uttering oracles by which they establish communication with the invisible world, and thus are able to coerce good spirits and evil spirits to work for the good of the patient, and even to expel devils. The Manchus are the celebrated imperial caste of the Chinese Empire. The Koreans, so called after the powerful Koryo dynasty of A.D. 918-1392, are of mixed Caucasic and Mongolic origin, and are the precursors of the Japanese, who are of mixed Caucasic origin from the Aïnus, Mongolic origin from the Manchus and Koreans, and Malayan from the Malays coming through the Philippine Islands and Formosa.

The westward-migrating Mongol-Turki need not detain us, except to state that they gave rise to the Túrki proper, the Samoyedes, the Lapps, the Magyars and Finns, and the Bulgars, probably only in part.

Classification.—The Mongolic division (*vide* Figs. 2 and 3) may be classified into:—

1. *Mongols*, who include the Mongols proper, the Tunguses, the Manchus, the Koreans, and Japanese.
2. *Túrki Peoples*, who are the Yakuts, Kirghizes, Turkomans, Anatolian Turks, and Osmanli Turks.
3. *Ugro-Finns*, comprising the Finns, Lapps, Samoyedes, Mordvins, and Magyars.
4. *Tibeto-Chinese*, with the Tibetans, Burmese, Nagas, Shans, Siamese, Annamese, and Chinese.
5. *Malayans*, who are classed into the Malays proper, the Javanese, including the Sundanese, Madurese, and Javanese proper; the Achinese, Rejangs, and Passumahs of Sumatra; the Bugis, Mangkassaras, and Minahasans of Celebes; the Tagalas, Bisayas, etc., of the Philippines, the Dyaks of Borneo, the Formosans, and the Hovas of Madagascar.

Amerind Division.

The Amerind or American-Indian division of mankind has a twofold origin—from Europe and from Asia. From Europe dolichocephalic Caucasic peoples made their way in Pleistocene times along land bridges connecting Britain with the Orkneys, the Shetlands, the Faroë Islands, Iceland, Greenland, and Labrador. These peoples, making their way across the continent, met with later and more numerous arrivals, the brachycephalic peoples of Mongol-Amerind stock, arriving from Asia by the land connections about the Behring Straits and the Aleutian Islands. These two races fused and formed the Amerind division of man. These Palæolithic races were apparently uninterrupted by any Caucasic, Mongolic, or Ethiopic migrations until the discovery of America by Columbus, after which all three divisions made their migrations thereunto. Therefore all the culture of the Mayas, Aztecs, and Incas, etc., was an inbred culture, not dependable for its origin on outside sources. Hence the absence of the ordinary animals and plants of Asia, Africa, and Europe, and the presence of peculiar animals and plants. Hence, also, the presence of only stone and copper ages until the introduction of iron by the Caucasians, and also the possible source of certain peculiar diseases, such as yellow fever, and perhaps Frambœsia tropica, and, according to some authors, syphilis, which, when introduced into Europe, Asia, and Africa, produced such ravages.

Characters.--The characters of Amerind man are --*Height*, above the average; *colour*, coppery or yellowish, *hair*, long, coarse, and black, on section round; *skull*, mesaticephalic; *eyes*, small, round, black, sunken, and straight; *nose*, large, bridged, or aquiline mesorhine, *cheek bones*, moderately prominent; *jaws*, mesognathous, *teeth*, medium, *beard*, absent; *speech*, divided into a very large number of linguistic families, said to number more than those of the rest of the world, but peculiar to America by being polysynthetic or holophrastic *i.e.*, sentences made from single long words. The most important of these linguistic families from a tropical point of view are the Ut-Aztecan, the Mayan, Carib, Arawak, Quichuan, and Guaranian. The Ut-Aztecan speech is used by the Shoshoneans, or Snakes, who include the Utahs and the Nahuas, who also include the Aztecs, while the Quichuan comprises the Incas. *Religion*, Shamanism in the north, Nature-worship, and polytheism; *medicine*, very primitive, especially when associated with Shamanism, but was somewhat more advanced among the Aztecs and Incas. Cinchona bark was a native Ecuador remedy.

Population.--There are believed to be some 10,000,000 Amerinds and 13,000,000 to 40,000,000 half-breeds, but the numbers are by no means easy to estimate even approximately. It is clear, however, that the Amerinds are rapidly dying out in Canada and the United States.

Migrations.--The brachycephalic peoples whom we have already noticed proved superior to the dolichocephalic people from Europe, and drove them northwards, where they became Eskimo, and southwards, where they became the Tehuelche or Patagonians and the Fuegians. The brachycephalic peoples then evolved the North American Indians, of whom we are only concerned with the members of the Ut-Aztecan linguistic family, because the Aztecs are members of this family in common with the Shoshoneans, and it is probable that the Nahuan family to which the Aztecs belong migrated southwards from the district of British Columbia.

Coming to Mexico proper, it is found that the archaic peoples—the Popolcans, Mixe, Chinantecs, Zoque, Mazatec, Cuicatecs, Chocho, and Magahua—have all been pressed by the migrations presently to be mentioned into secluded valleys, where alone traces of them can be found at the present time. The Mexicans proper are the Otomi, who are related to the Magahua, and are still to be found in the valley of the Upper Moctezuma and in Guanjuato.

A northern immigration may have brought the Tarascos of Michoacan into Mexico, or they may belong to the primitive Mexicans. In either case, they are to be found to-day in Guanjuato; with these may be joined the Ulmecs, Xicalancas, Mestecs, and Zapotecs among the early tribes of Mexico. Of all these, the most important would appear to be the Mistecâ-Zapotecâ family, because they are known to have evolved a degree of civilization before the days of the Mayas. This culture is exemplified by the monuments of Mitla and of Monte Alban in Oajaca.

The Maya people are variously believed to have been immigrants into Yucatan, from which they spread into Guatemala, Salvador, and Honduras, or to have been original settlers therein. Be that as it may, there is no doubt that they extended into Mexico, both along the coast, where one of their tribes, the Huantecs, were found about Tampico, and into the plateau. They very early produced some degree of civilization, and constructed the celebrated monuments of Guatemala and the pyramid of Cholula in Mexico, on the top of which was the temple of Quetzatcoatl They invented picture-writing and an almanac. They were divided into the Mayas proper of Yucatan, the Choulats of Mexico, the Quichés, the Pocomans of Guatemala, the Chortes, and the Huantecs of Tampico.

Such must have been the constitution of the tribes of Mexico when the Nahuans broke their way in. This tribe is allied to the Shoshonics, who occupy the wide tract from Oregon to California and New Mexico, and are believed to have come from the region of British Columbia. They moved down to the west of the Rocky Mountains, and spread as far south as Oajaca and eastwards to the Atlantic between Vera Cruz and Coatzacoalcos. The first waves may have been the Toltecs, but there is great doubt as to who these people were. The Alculhuaques and the Tepanecs followed, while the last immigration was that of the powerful Aztecs, who, though probably but little civilized when they entered Mexico, soon became so, and remained the masters of that part of America until subdued by the Caucasic migration.

Enumerating, therefore, the tribes from the north to the south, there would be first the Shoshonies in the west and south-west of the United States, extending into Mexico; the Yumas of Arizona and the Pueblo-Indians, characterized by their curious rock structures; then would come the Otomi, Totonacs, and Zapotecâ, with their Nahuan conquerors, especially the Aztecâ, all in Mexico. In Central America the Maya people would be found in Yucatan, Guatemala, and Honduras, along with the Xicaks of Northern Honduras, the Leukas and Guatusos of Central Honduras. Farther south would be the Choulats of Nicaragua, the Soumoo, the Micos of the Mosquito Reservation, the Moscos of the Blewfields Lagoon, and the Rinos of an island therein.

Passing into South America, there is the great linguistic family of the Chibcha of Colombia, whose empire extended southwards until it met that of the Incas. These peoples, as well as the Incas, are Andeans—that is to say, are peoples belonging to the highlands of the Andes. It is curious that all the South Amerind civilizations should have developed in these highlands, but it is probable that the lakes and rapid streams were suitable for the extension of agriculture, and thus led to the settlement of peoples, for without a permanent abode any great degree of civilization is impossible. The Chibchas, also called 'Muyscans,' influenced the whole Panama region as far north as the northern boundary of Costa Rica.

South of the Chibchas comes the ancient empire of the Incas, extending from Quito as far south as the Rio Maule in Chili. It would appear from the megalithic remains and the ruins of Tiahuanacu that there was an early civilization in this region, especially about Lake Titicaca. Who these people were we do not know, but they must have been conquered by the Quichuas or Aymaras, who are allied to them, as both speak derivatives of the Quichuan language.

At the same time there existed near Truxillo the Chimu people, speaking Mochica, a language quite different from Quichuan. They reached to a degree of civilization, but both they and the Quichuans were conquered by

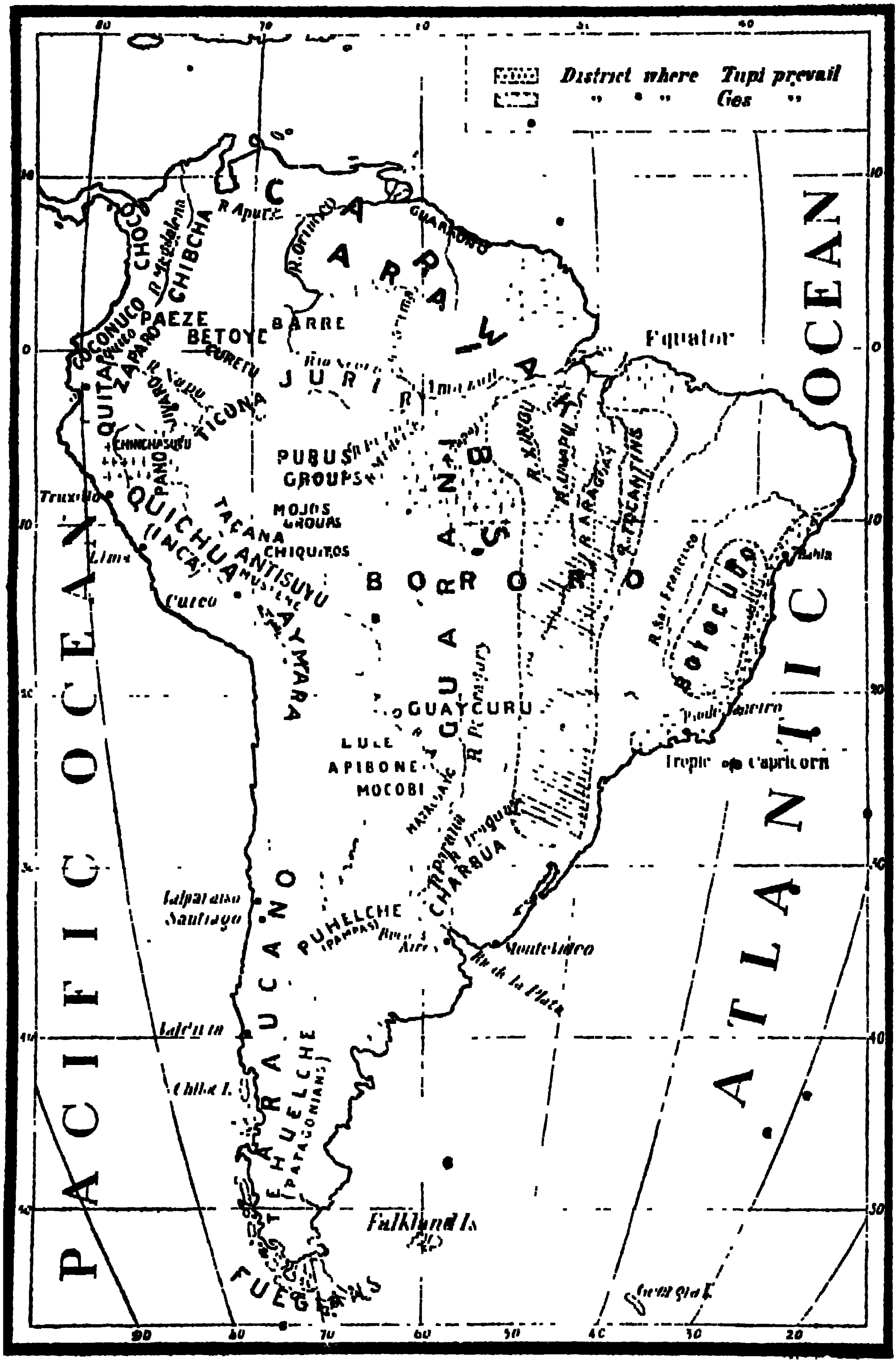

FIG. 5.—THE RACES OF SOUTH AMERICA.
(From Hutchinson's 'Living Races of Man.')

the Incas. To-day the descendants of the Chimu are called the 'Yuncas,' and live along the coast from 5 degrees to 10 degrees south latitude. In the provinces of Catamarca, Tucuman, and Salta of the Argentine lived a civilized race, now extinct, called the 'Calchaqui,' who were also subdued by the Incas.

The Incas are possibly the descendants of the unknown peoples of the early civilizations who, defeated by the Quichuan peoples, fled into the Apurimac region, whence they subsequently issued forth to subdue their ancient conquerors. Their rule was very despotic, and their subject peoples were very carefully divided into tens, fifties, five hundreds, and ten thousands, the last being under a chief taking orders direct from the Inca. Their system was very artificial, and absolutely without any freedom for the individual, and hence the easy Spanish conquest. They possessed no written language, everything being preserved by oral information handed down from generation to generation.

Except in the Andes, there are no civilizations in South America, and the peoples whom we now come to consider were all backward in their culture evolution at the time of the advent of the Spaniards. They are the members of the linguistic families called 'Arawak,' 'Tapuya,' 'Tupi,' and 'Carib,' in the regions lying east of the Cordilleras as far south as the Rio de la Plata, while farther south lived the Pampeans and Fuegians, with whom we are not concerned.

The Arawak would appear to be the original inhabitants of the low-lying lands to the east of the Cordilleras, and it is possible that they originally spread to the north-east, the east, and the south-east from a primeval home on the eastern slopes of the Bolivian Cordilleras; but their most important migration appears to have been that to the north east, where they populated the, until then, vacant valleys of the Orinoco and Amazon, especially along the north bank and up the Xingu River. In the east of Brazil, from the Xingu River to the coast, lived the Tapuya, who were probably the aborigines of these regions. They include the Ges and Botocudos of to-day, of which the latter are degraded savages.

The Caribs, according to Van der Stein, took their origin about the sources of the Xingu and Paranatiga Rivers, where the Caribbean tribes called 'Bakairi' and 'Nahuqua' live. From this source they travelled, probably by water, along the Amazon, meeting with the Arawak, till they reached its mouth, when they turned northwards, probably because they met the Tupi people coming from the south, and spread through Guiana to Venezuela, where their progress was checked by the civilized Chibchas, though some of them entered the valley of the Magdalena River. From the north of South America they proceeded to the Antilles, into which they were still migrating when stopped by the arrival of the Spaniards.

The Tupi people had their primitive home, according to Haddon, in the northern portion of the basin of the Rio de la Plata, down which they spread to the mouth, and then, migrating northwards along the coast, reached the mouth of the Amazon, meeting there the Arawak and possibly the Carib peoples, and, travelling westwards along the southern bank of the Amazon, reached the Xingu River, up which they went, founding the Kamayura and Aneta tribes in its upper basin. They went still farther westwards, forming the more civilized Omagua between the Putumayo and Caqueta Rivers, and the Cocama peoples at the junction of the Amazon with the Ucayali River.

In Uruguay and Paraguay the Tupi peoples are called 'Guarani,' or 'Warriors,' and hence the whole family is called the 'Tupi-Guaranian family.'

Into the races mentioned above penetrated the great Caucasic migration, headed by Columbus, in the fifteenth century of our era, which, though stopping the autochthonous evolution of civilization in America, introduced the more highly evolved culture of the Old World at the cost of millions of lives of the Amerindians.

The Latin races of this migration have fused with the aborigines to a great extent, and thus have laid the foundations of the new Latin-Amerindian races which are arising to-day.

The Anglo Saxon in North America did not fuse with the Amerind, who to-day is rapidly approaching extinction.

The negro migration was compulsory, as the negroes were introduced as slaves, but it suited the race, which is rapidly increasing in numbers. The Mongolic migration is at present very small, and of quite recent date.

Classification.—The Amerinds may be classified for our purposes into those belonging to the Northern Section, to the Central Section, and to the Southern Section of America, but only the two last need concern us here.

The Central Section is formed from Mexico and Central America as far south as the northern boundary of Costa Rica. It contains the Opata-Pima linguistic family, composed of the Pimas and Papajos of the Gila Valley, where the Gila Monster (*Heloderma suspectum* Cope 1869) lives, the Capitas, Coras, Yumas, and Torahumeras, though these last are mixed with Caucasic blood. The Nahua or Aztecs come next, and include the Aztecs proper, the Pipils of Guatemala, the Niquirans, and the Chichimecs.

The Huaxtecan group, often called the Maya-Quiché group, includes the Huaxtecs of Tamaulipas and Vera Cruz, the Mayas of Yucatan, the Choulats of Mexico, the Mopans of Northern Guatemala, the Quiché farther south in Guatemala, the Pocomans around the city of Guatemala. The Mayas proper are divided into the Itzas and the Lacandons. The Chortegans include the Chorti living around the ruined city of Copan as well as the Bribri and others.

In the Southern Section are the nations which we have sufficiently described above, viz., the Chibchas, Quichuas, Chimus, Calchecaquis, and Incas, all of whom were civilized, and the Arawak, Tapuya, Carib, and Tupi peoples, who were far more primitive and savage, as well as the Pampeans and Fuegians, which are not tropical races.

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CHAPTER III

TROPICAL CLIMATOLOGY

Preliminary remarks — Climate — Tropical climates — Temperature and humidity — Pressure — Winds — Electrical conditions — Sun's rays—Moon's rays—Acclimatization—References.

PRELIMINARY REMARKS.

We have delineated the tropics by Supan's lines, as this appears to us to be the most suitable method of bounding warm climates, and we have noted the characters of the races of mankind which occupy the lands so defined. These, we may incidentally mention, amount to a little less than one-half of the surface of the earth, and now we must consider what is meant by the terms 'climate' and 'tropical climates,' and then turn our attention to the effects of these climates on mankind.

CLIMATE.

Climate may be defined as the combined effects of the sun, the atmosphere, and the earth upon living objects at any one place on the earth's surface. The factors which produce a climate are therefore threefold—viz., the sun, the atmosphere, and the earth; and the living object with which we are concerned being man, we must study the effects of these factors upon him, but we restrict our attention to mankind as seen on that portion of the earth's surface called the tropics.

TROPICAL CLIMATES.

In the previous chapter we have noted Supan's simple division of warm climates by isotherms, but there is a better subdivision given by Ward, and based upon wind systems and their control over rainfall (*vide* Fig. 7).

Around the Equator lies the region of equatorial calms, called the doldrums (Fig. 7), while north and south of this region are the trade winds (Fig. 6). These zones of calms and winds are not stationary; on the contrary, they move so as to reach a maximum extension northwards of some five to eight degrees of latitude in July and a maximum extension southwards of some three to four degrees in January.

These movements are dependent upon the changes in the inclination of the axis of the earth towards the sun, but are not coincident with these changes.

A locality may therefore lie entirely in the equatorial belt, or it may lie entirely in the trade-wind belts, or it may be polewards of these belts; but with the movement of the system polewards, as indicated above, some of the places in a trade-wind belt must come into the equatorial belt, while others usually situate polewards to the trades must be included in these belts.

Were the tropics flat this classification would suffice, but there are high mountain ranges in tropical lands, and therefore it is necessary to make a division to include these, because it is possible in the high lands of the tropics to pass through every degree of temperature, if you ascend high enough, as if you proceeded from the Equator to the Poles.

There are therefore four divisions of warm climates—viz.:

I. The Equatorial Belt.
II. The Trade-Wind Belts.
III. The Monsoon Belts.
IV. Mountain Climates.

I. **The Equatorial Belt.**—Localities situate within a few degrees of the Equator are always more or less subject to rain and cloud, because the heated air is full of aqueous vapour brought by the trade winds from the sea; and as aqueous vapour is lighter than air in the ratio of 0·623 to 1·0, it can rise to high and cold altitudes, and there be condensed into small droplets of water forming cloud or larger droplets forming rain.

As the capacity of air to hold water is doubled for every 27° F. increase in temperature, and as in air saturated at 85° F. and then cooled to 60° F. every cubic foot yields 7 grains of water, the excessive violence of these equatorial and tropical rains is easily understood.

This belt is subject to alternate seasons of wind and calm—*e.g.*, in January it will be subject to the north-east trades, followed by a period of calm; and in July to the south-east trades, succeeded by another period of calm. There are, therefore, two maximal and two minimal temperatures after the two zenithal and solstitial positions of the sun, and two short wet seasons and two short dry seasons.

Such places are Southern India, Ceylon and Java in Asia, Columbia in South America, and in Africa parts of the Valley of the Nile. and the Gold Coast.

With the inclination of the North Pole towards the sun, which begins on March 21 and ceases on September 22, the shifting of calms and trades northwards begins some time after the first date and lags behind the last date, and during this period a locality may be in the equatorial belt for six months in the year and have six months' drought and six months' rain. Such places are Bengal, portions of the Nile Valley, Northern Australia, and Central America. The Sudan receives its rains when the equatorial belt is passing northwards—*i.e.*, from May to August—and its vegetation grows rapidly, but when it is in the trade-wind belt, from November or December to March or later, the climate is dry.

It is the northern migration of the Equatorial Belt which brings the heavy rains to the Uplands of Abyssinia, and causes the rise of the Blue Nile and the Atbara, which produce the rise of the Nile.

The same features are to be noted in the movement southwards; thus rain comes on the pampas of Brazil in the months from October to April, while the dry season lasts for the rest of the year.

Some few places—*e.g.*, Wady Halfa—show only one maximum and one minimum temperature—*i.e.*, the so-called tropical type of temperature variation.

II. **Trade-wind Belts.** The lands which lie just outside the polar boundaries of the equatorial or rain belt are situate some 20° to 35° north or south latitude, and are among the driest in the world, except in India, where the south west monsoon brings a little rain into the dry regions of the Punjab and Sind.

The worst places are the dry zones of California and other parts of North America, the Sahara and Nubian Deserts, parts of Arabia and Persia, Argentina, Eastern Patagonia, South-West Africa, and the interior of Australia. The only rain these regions are likely to get will come from the extension equatorially of the polar winds.

We may, therefore, summarize the character of the trade-wind belts as very regular annual and diurnal ranges of temperature, with a complete absence of rain or with slight showers at infrequent intervals. The range of temperature in the desert is often very great; thus during the day the temperature may be very high, with dry winds carrying dust and sand, and the nights, with the clear sky free from cloud allowing active radiation, may be cool if not cold, or even at times very cold.

III. **Monsoon Belts.**—The word 'monsoon' is believed to be derived from the Arabic word *Mausin*, meaning 'a season.'

The monsoons (Fig. 6) are classifiable into three groups:—

1. North-East and South-West Monsoons.
2. North-West and South-East Monsoons.
3. West Monsoon.

1. **North-East and South-West Monsoons.**—These are typically met with in the Indian Ocean and its coasts.

Dove's explanation of these monsoons is generally accepted—viz., that, owing to heating of the great plains of Asia, where the air ascends in the months of May, June, July, and August, the south-east trade-wind, which is blowing south of the Equator, is drawn northwards, at the same time being deflected to the west, thus forming the south-west monsoon. Conversely, when the plains cool in November, December, January, February, and March, there is a breeze from the north east towards the Equator, which, though called the north-east monsoon, is really a trade-wind.

The interval between the two monsoons is characterized by changeable winds, which blow alternately in opposite directions—north-east and south-west.

The south-west monsoon is laden with moisture, and on it Southern India largely depends for rain, and a failure will mean a famine, because a large portion of the population is agricultural, for the natives depend for food upon

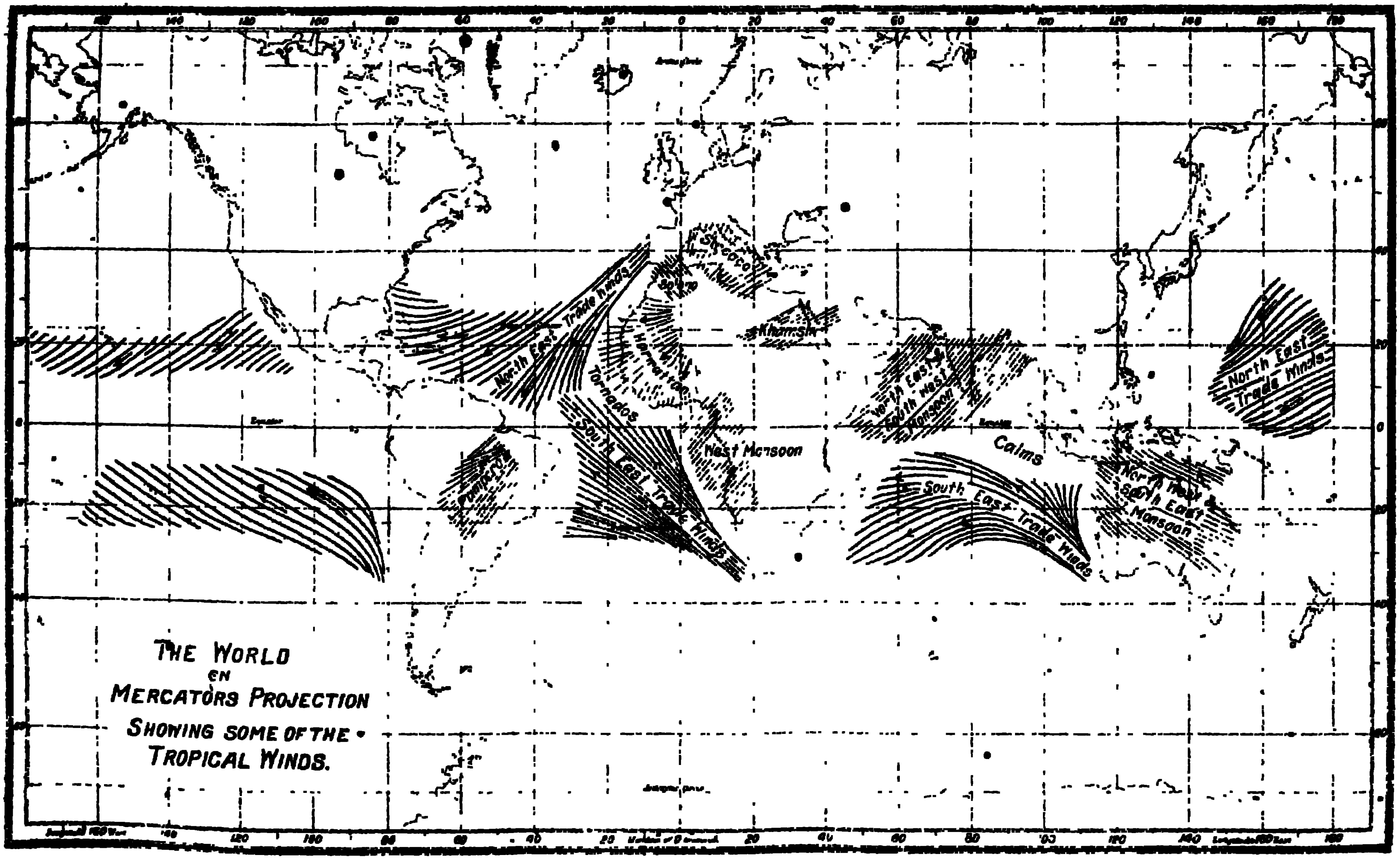

FIG. 6.—TROPICAL WINDS.

their own cultivation; and so densely are they placed that a failure to produce their own crops results in a most severe famine, which can only be coped with by the most energetic action of the Government.

2. **North-West and South-East Monsoons.**—These are to be found in the Southern Hemisphere, and are depicted in Fig. 6 in the region of Australia.

3. **West Monsoon.**—Dove described as the west monsoon of the line a wind which blows in a south-westerly direction along the coast of Africa from Cape Verde down to Walfisch Bay. These winds, however, are variable, and in the Gulf of Guinea are interrupted very often by calms.

Some people describe the winds along the eastern and western coasts of South America as monsoons, but they hardly come under this term.

In typical monsoon regions the rains follow the vertical sun, and the type of temperature is the so-called tropical type, with one maximum and one minimum.

It must be admitted that this simple classification, like all classifications, fails to explain everything, and there are numerous exceptions showing combinations of equatorial, trade-wind, and monsoon types.

IV. **Mountain Climates.**—We have already pointed out the effect of altitude in lowering the temperature, and, indeed, Herschel, many years ago, showed that for every 300 feet of increase in altitude there was a decrease of 1° F. in temperature, and for every 180 metres a decrease of 1° C. These statements are only partially correct, for the temperature at a given altitude depends upon the expansion and humidity of the air, the clearness of the atmosphere, together with the quantity of earth at the given locality, and the nature of the wind blowing at the time of the observations. Perhaps of all these the most important is the expansion of the air, for, as is well known, it expands when heated—*i.e.*, the energy represented by heat is converted into motion, and hence the temperature falls. This will in part be counteracted by the heat produced by the condensation of aqueous vapour, even at high altitudes, and upon this condensation and cloud-formation will depend how much of the heat, radiating from the earth into the air, is retained. The lessened amount of earth in high altitudes is also a factor, as there is less earth to retain heat, and hence less heat is given off into the air. It is obvious that movements of the air—the winds—must have a great effect, depending upon their origin from warm or cold sources. Hence, though in general the rule mentioned above as to a relationship between temperature and altitude holds good, it is only approximate, as the connection between the two is complex, not simple.

In the tropics, therefore, the low country possesses the true tropical climate, while the climatological conditions of the hills are quite different. Indeed, as Ward has said, the climates of many tropical plateaus and mountains have the reputation of having a perpetual spring, but though that may be so at certain latitudes, if considerable elevations are reached a perpetual winter exists, with snow all the year round, even on the Equator.

The great blessing of these elevations in the tropics is that they provide cool hill stations to which the resident of the plains may resort during the hottest months, and in which sanatoria may be built for the treatment of persons convalescent from lowland complaints.

This brief sketch of tropical climates must suffice for our present purpose, and we now turn to consider the various climatic factors and their effects upon man; but the reader interested in this subject may find it useful to consult Chapter II., pp. 28 to 58, in our second edition, in which more details will be found.

TEMPERATURE AND HUMIDITY.

Heat derived from the sun is capable of traversing the atmosphere surrounding the world, and thus reaching the earth, because this atmosphere is diathermanous to rays with short wave-lengths coming from so hot a body as the sun. Dry air is diathermanous for all rays, but aqueous vapour is almost athermanous for infra-red rays, though largely diathermanous for other rays.

In passing through the atmosphere, about 25 per cent. of the heat which has entered it is absorbed before it reaches sea-level.

The position of the sun is, however, of the utmost importance with regard to the quantity of heat reaching the earth. If the sun is quite vertical, probably only 20 per cent. is lost; whereas, if the beam is nearly horizontal, probably none reaches the earth.

The heat rays falling upon the earth are absorbed and converted into dark heat—that is to say, into frequencies with longer wave-lengths—and these are radiated back into the atmosphere (terrestrial radiation). This dark heat is absorbed by the atmosphere, which is, as already stated, almost athermanous to this kind of energy. This atmospheric heat is one of the most important factors in determining the nature of a climate, and shows daily and annual periodic variations, of which the first is due to the sun's rays heating the earth, and therefore this disappears at sea or during an arctic winter, while the second depends largely upon the inclination of the world's axis as it passes round the sun in its yearly orbit. As the sun is vertical in the sky at noon twice a year in the tropics, there is or ought to be a wet season at these times, and in their intervals a dry hot season.

It is impossible, however, to consider the effects of temperature upon man without at the same time taking into account the humidity of the atmosphere.

Man can bear very high temperatures easily, provided the air is dry, but not if there is much moisture or humidity in it. The humidity of the atmosphere is, in fact, of the utmost importance in the study of climatic effects upon man. This humidity is due to aqueous vapour, caused by the constant evaporation which takes place from the surface of all collections of water.

The humidity of the atmosphere presents three problems: atmometry, or the measurement of the quantity of water being taken into the air; hygrometry, or the determination of the quantity of aqueous vapour present in the air at any given time; and hyetometry, or the quantity of water being condensed from the atmosphere.

Evaporation takes place most quickly in hot dry air, and causes a considerable amount of heat to be rendered latent. This fact can be made use of in hot climates, where it is a common practice to wrap flannel or felt round a bottle of water, and after damping the flannel, to hang the bottle in the breeze, so that the contents may become cooled by the evaporation of the water from the flannel. The same principle applies to the porous stone or earthenware basins which are commonly used in Ceylon, Uganda, Egypt, and other parts of the tropics to filter and cool water. Hence, also, the value of collections of water in keeping the temperature of places equable.

The amount of aqueous vapour in the atmosphere is generally spoken of as the humidity. Two kinds of humidity are recognized: absolute humidity, which is the weight of aqueous vapour actually present in a definite volume of air at a given temperature; and relative humidity, which is the ratio of the weight of water actually present in a known volume of air to the weight of water which is required to saturate the same volume of air at the given temperature, and is generally expressed as a percentage.

We have already stated that the humidity of the air is of the greatest importance in considering the effects of a tropical climate on man. The most trying climate would be one with a high air temperature and a high relative humidity, for it is obvious that when the air is full of aqueous vapour, evaporation from the surface of the human body must be considerably diminished; and as this is one of the methods of regulating the bodily temperature, it is apt to rise and cause great discomfort, as will be described later.

A warm place with a high humidity is less bearable than a much hotter but drier place. A fairly high relative humidity can, however, be borne if there is a breeze, without which a much lower humidity is most unbearable. In fact, Giles points out that Abusher, in the Persian Gulf, in August, with a mean maximum temperature of 96·5° F. (35·7° C.), and a relative humidity of 65 per cent., with no rainfall during the month, and little or no breeze, constitutes one of the most unbearable climates in the world, though neither the temperature nor the humidity by themselves are high.

When the aqueous vapour in the atmosphere condenses, the result may be dew, fog, mist, cloud, rain, hail, or snow, of which the two last are rare in the tropics. Clouds in the sky prevent to a great extent the heating of the earth during the day, and at the same time they prevent radiation of heat from the earth during the night, and even reflect this back to it. Hence cloudy nights may be very hot in the tropics.

Effects.

We must now consider briefly the effects of high air temperatures with and without high atmospheric humidity upon man, and we will commence with a consideration of its effects upon the bodily temperature.

Normal Temperature.—The normal temperature of man is the resultant between the heat produced by the oxidation of foodstuffs in the muscles, glands, and other organs and tissues of the body, and the heat lost by warming the urine, fæces, and expired air, by evaporation from the lungs and skin, and by radiation and conduction from the skin. In other words, the temperature of the body is controlled both by chemical and by physical heat regulation.

1. **Chemical Heat Regulation.**—By this is meant regulation of the bodily temperature by increased or diminished production of heat, which can be brought about by alterations in metabolism. Diminished heat production is, however, rare, being usually pathological, though it is possible that it occurs more frequently in the Tropics than in the Temperate Zone, owing to the lessened disposition for muscular or mental work.

2. **Physical Heat Regulation.** The body temperature is usually regulated by increasing or diminishing the loss caused by radiation, convection, and evaporation. According to Hill, a man weighing 70 kilogrammes loses 77·1 per cent. of his heat by radiation and convection and 22·0 per cent. by evaporation. This regulation is brought about by the dilatation of the cutaneous vessels bringing more blood to the skin and by the increased perspiration. The loss of heat caused by radiation and convection depends upon—

1. Temperature and conductivity of the skin.
2. Temperature and radiation from the skin.
3. Temperature of the air.
4. Rate of motion of the air.

Clothing may, however, affect the loss of heat from the skin, for, as a rule, it is composed of substances which are bad conductors of heat, and hence the loss may, according to Rubner, be diminished no less than 47 per cent. Wet clothing, on the other hand, is a good conductor, because of the water in its interstices, and hence the danger of chills while wearing damp clothes. This latter fact is well known to the old resident of the tropics, who has generally learnt its danger by personal experience.

Radiation takes place best when the air is still, dry, and cold, conduction when it is damp. Convection is only of importance when the air is in motion, in which case the loss of heat is proportionate to the square root of the velocity, and is more marked when atmospheric humidity is high.

With regard to evaporation, Rubner has shown that it is best at medium, greater at low, and still greater at high temperatures, as is shown by the following table taken from his book of an observation on a man of 58 kilogrammes weight lightly clad:—

Air Temperature.	*Grammes of OH_2 per Hour.*	*Grammes of CO_2 lost per Hour*
2° C.	37	29·8
10° to 15° C	28	25·1
15° to 20° C	19	24·1
20° to 25° C	23	25·0
25° to 30° C.	43	25·3
30° to 35° C.	84	23·7
35° to 40° C.	112	21·2

This evaporation is very markedly diminished by humidity, as is shown in the following table:—

Temperature in Centigrade.	*5 to 8 per Cent. Humidity.*	*81 to 89 per Cent. Humidity.*
15·0°	30·3	9·0
20·4°	54·1	15·3
25·3°	75·5	23·9
28·9°	105·0	—

It is also diminished by a moderately strong wind, but is increased by the sun's rays and by work in a hot climate.

To determine accurately the temperature of a man in the tropics is not the easy matter which most people consider it to be, and the principles applying thereto should be understood even by those *not likely to be deceived by an air temperature so high that a maximum thermometer rises and keeps above normal without any reference to the patient*, a fact which we have seen lead to curious mistakes. Under such conditions, the thermometer must be kept and examined in cold water.

The temperature of man, being the resultant between the heat produced and the heat lost, must vary considerably under many circumstances, and there is no doubt that it varies in different individuals.

In investigating the temperature of the body, one ought to seek that which most nearly represents the temperature of the blood, for though the different organs of the body manufacture or lose heat in different proportions, the circulation of the blood tends to bring about a mean internal temperature for the whole body.

The possible methods of investigating the temperature of the body are by placing the thermometer—

1. In the axilla,
2. In the mouth,
3. In the rectum,

to which might be added placing the thermometer in the stream of issuing urine; but this method is only open to limited application, and there may be considerable loss from evaporation and radiation, and, therefore, though it is an excellent method when used with care, will not be further considered.

If the thermometer is placed in a *dry, well-closed axilla,* and kept there long enough, the result will be not unlike that in the *mouth;* but if it is thought that any resemblance to the internal temperature of the body is to be obtained by placing a thermometer in a perspiring axilla for half to one minute, then the greatest mistakes as to the real temperature of the patient are possible. In our experience it has not been unusual in the tropics to find several degrees of difference between the axilla and the mouth.

As a rule, it may be stated that the axilla is not a good place in which to take thermometric observations which are meant to indicate the true temperature of the body.

With regard to the mouth temperature there has been a great deal of discussion, but the most careful observations are those of Pembrey and Nicol, who have shown that the mouth temperature is apt to vary considerably, and that it is not a reliable indicator of the internal temperature of the body in cold weather or after exercise. Haldane, in his valuable experiments to be quoted presently, finds that it varies greatly with the individual.

In warm and moist air, however, the mouth temperature approaches the rectal temperature.

The reason why the mouth temperature is apt to be lower than the rectal and the real temperature of the body is apparently the cooling owing to the proximity of the skin, and possibly of the nasal cavity, and therefore in warm air this difference frequently does not exist. In India Crombie found in fifteen carefully taken observations that the mouth temperature was 0·22° F. below that of the rectum, whereas Pembrey found it as much as 4·5° F.—*i.e.*, 2·5° C.—below that of the rectum in cold weather in England. It is possible, therefore, that it is a better site for thermometric observations in the tropics than in Europe.

Rectal temperatures under ordinary conditions give the highest readings and are the truest indicators of the internal temperature of the body; but this is not a method open to clinical use, except in children and in states of coma.

The conclusion is that if care be taken that neither hot nor cold articles have been recently placed in the mouth, and particularly if the mouth has been kept closed for a short time, the temperature from the thermometer placed under the tongue is, without doubt, the most accurate for ordinary clinical work in the tropics, for in that position the thermometer is as completely as possible protected from the influence of the nose and the skin.

A thermometer, however quickly it reacts to its surroundings, must be left a reasonable time in the mouth, by which is meant two or three minutes, so that the temperature of the closed mouth may approach that of the rest of the body. Crombie gives the time for the accurate recording of the temperature in India as:—

Ten minutes in the well-closed and dry axilla.
Eight minutes in the mouth.
Three to four minutes in the rectum.

The mean daily temperature of man for the hours 8 a.m. to 12 midnight in the Temperate Zone is as follows:—

98·45° F. (36·90° C.) in the axilla.
98·36° F. (36·87° C.) in the mouth.
98·96° F. (37·20° C.) in the rectum.

The so-called normal temperature of man in the mouth may be placed at 98·40° F. (36·90° C.) or 98·6° F. (37° C.), and was determined as the mean temperature from 8 a.m. to 12 midnight by John Davy in 1837, and by some mistake it has been interpreted into the mean temperature for the twenty-four hours, which is different, being probably lower.

Crombie gives the following as the means of the observations of Ogle, Allbutt, Casey, and Rattray:—

Mean Morning Temperature.	*Mean Afternoon Temperature.*	*Mean Twenty-four Hours' Temperature.*	*Maximum Daily Range.*
97·763° F.	98·341° F.	98·084° F.	1·41° F.

But at present there are insufficient data upon which to base a definite conclusion as to the mean temperature of human beings for the whole twenty-four hours.

The average temperature in the mouth varies from between 96° F. and 97° F. to a little under 99° F., and the rectal temperature from 97·2° F. (36·28° C.) between 2 to 5 a.m. to 99·4° F. (37·45° C.) between 4 to 7 p.m.

Pembrey gives the mean daily temperature as being 98·6° F. (37° C.), the maximum 99·5° F. (37·5° C.), and the minimum 96·8° F. (36° C.)

Effect on Temperature.—Having now defined what we mean by a normal temperature in man, it is necessary to inquire into the effects of high atmospheric temperatures and varying humidity upon man.

The experiments of Lining (1738), Ellis (1758), Blagden and Fordyce (1775), established the fact that a normal man, suitably clothed, can regulate his temperature so that with high air temperatures it still remains within the normal limits, if the atmospheric humidity is low, and these experiments have been well borne out by life in the tropics.

It is, however, quite otherwise when the atmospheric humidity is high: as far back as 1775 Blagden and Fordyce noted that in a damp room with a temperature of 124·5° F. (51·4° C.) their bodily temperature rose to 100° F. (37·8° C.). Haldane observed that there was no abnormal rise of the bodily temperature until the wet bulb thermometer indicated 88° F. (31° C.), provided that the experimenters were stripped to the waist or clad in light flannel. If, however, the wet bulb exceeded this temperature by even one degree, then the bodily temperature rose hour by hour in proportion to the rise of the wet bulb thermometer above 88° F., but the bodily temperature increased more rapidly when high wet bulb temperatures were reached than when they were relatively low. With the abnormal rise of bodily temperature was associated increase of the pulse rate by about twenty beats per minute for each degree Fahrenheit and thirty-six for each degree Centigrade. All these bodily temperatures were taken in the rectum and with the patient standing. When this rectal temperature reached 102° F. hyperpnœa was observed, while other symptoms associated with the rise of the bodily temperature were profuse sweating and a general feeling of exhaustion and discomfort.

It was observations like these that caused Tyler to attempt to correlate personal sensations with meteorological data, and to formulate his 'hyther' degrees, by which he meant the degree of discomfort caused by high air temperatures associated with high relative humidity.

Haldane's experiments have often been repeated by ourselves on normal people by placing them alongside the condensers in the engine-room of steamers in the Red Sea during very hot months. Near the condensers one can usually find a corner where there is no obvious movement of the air, which is nearly saturated with aqueous vapour, and where there is a high atmospheric temperature. Placed in such a corner and clad only in loose pyjamas, the skin of the body flushes and burns, the perspiration rolls downwards in streams, and the temperature after a short pause commences to rise and goes on rising until the experiment is broken off, usually about 103° F.

This is not a pathological rise, though associated with throbbing vessels, etc., but is simply due to atmospheric conditions acting upon a normal man, and all symptoms disappear rapidly after removal to cooler air.

If such a climate existed no human being could live therein, but no such place is known, and although conditions of high atmospheric temperatures may produce fever, yet these are pathological and not physiological, and depend upon factors which will be discussed later.

From the time of Davy in 1839, observations have been made into the temperature of healthy men during the passage from the temperate to the tropical zone, during their residence in the tropics, and during the passage from the warm to temperate climates. In previous editions of this work we gave the known data, and anyone who cares to look at the pages from 91 to 97 in the second edition of this book will observe how confusing and contradictory are the results, while they will be struck with the relative paucity of these results. The truth is that the earlier observers omitted to take into consideration the atmospheric humidity, and this alone vitiated their conclusions.

Our own observations agree with those who have failed to show any change in the bodily temperature in passages to and from the tropics and in residence therein, provided that the individuals observed were normal.

Further, we have failed to observe any difference in the temperature between well-nourished healthy natives and Europeans, and with due allowance for individual and seasonal differences and the effects of exercise and clothing.

In previous editions we have consumed much space with discussions as to the pulse-rate, and so as not to weary the reader, we may say that we do not believe that there is any change in the pulse-rate of normal Europeans on entering or residing in the tropics, nor is there any appreciable difference between them and natives.

Bussière recently has invited attention to the action of cold on tropical natives brought straight to temperate climates, which tends to produce attacks of malaria, liver troubles, and inflammation of the bronchi and lungs. He especially lays stress on temporary albuminuria yielding to treatment in some one to three weeks

Effect on Respiration. As we have no personal experiments to record with regard to respiration, we give the work of other observers.

Rattray studied very fully the influence of tropical climates on respiration, and gives a table showing their effect on the capacity of the chest, as indicated by the spirometer, on a voyage from England to Bahia and back. The average of twelve observations is as follows (hygrometer indicates the difference between the wet and dry bulb of a Mason's hygrometer):—

Number of Persons, 12	*Temperature* 65° F., *Hygrometer* 2·5° F.	*Temperature* 78° F., *Hygrometer* 1° F.	*Temperature* 83° F., *Hygrometer* 4° F.	*Temperature* 65° F., *Hygrometer* 1·5° F.
Capacity of the chest as shown by spirometer ..	256·083	280·75	287·416	260·25
Gain or loss ..	—	+24·833	+6·5833	−26·333
Percentage gain		9·24		

The increased capacity, according to Rattray, is not due to any actual increase in the capacity of the size of the chest, but to a diminished quantity of blood in the lungs, which he considers has been diverted to the excited and congested skin and liver.

His results may be summarized by saying that the vascularity of the lungs is reduced by 23 fluid ounces, and owing to diminished number of respirations 7·5 per cent. less air is used daily, and 1·1 ounces less carbon, and 4·5 per cent. less aqueous vapour excreted.

With regard to these observations of Rattray, he is apparently supported by all observers as to the increase in capacity when Europeans enter the tropics. Jousset, however, states that this is only temporary, and disappears after acclimatization.

Rattray maintained that there was a diminution of capacity when a native of the tropics went to the Temperate Zone, and gave the following table:—

Condition.	*Race.*	*Temperature 79° F.*	*Temperature 78° F.*	*Temperature 32° F*
B. C., aged twenty-one; height, 5 feet 5½ inches	Native of Sierra Leone	210	207	185
J. C., aged twenty; height, 5 feet 4 inches	Native of Sierra Leone	171	166	156
J. W., aged thirty-one; height, 5 feet 4 inches	Half-caste	[illegible]	162	

He found that the frequency of respiration was slower in the tropics, as is shown in the following table:—

Climate		*Mean Shade Temperature*	*Highest Number of Respirations*	*Lowest Number of Respirations*	*Average Number of Respirations.*
England	Summer	62° F	18	13·5	15·08
	Winter	42·25° F	17·5	15	16·50
Equatorial doldrums	Outward..	78·74° F	14·5	11	12·74
	Homeward..	78·60° F	15	12	13·71

Jousset, Plehn, and others controvert Rattray's statement that the respirations are slower, believing, on the contrary, that they are augmented before acclimatization.

This shows clearly that the question is far from settled, and, in fact, requires reinvestigation.

Effect on Circulation.—Rattray investigated the pulse-rate carefully, and gives the following table:—

Time	*Number of Observations.*	*Tropics.*				*Temperate Zone.*
		Lowest	*Highest*	*Range.*	*Average.*	*Average.*
9 a.m. ..	53	66	112	46	86·4	91·7
3 p.m. ..	53	66	108	42	86·8	88·1
9 p.m. ..	49	73	110	37	87·3	90·5
Averages	—	—	—	—	87·5	90·1

He gives the following conclusions:—

1. The average pulse is lower by 2·5 beats in the Tropics than in the Temperate Zone.
2. This change holds good for the average morning and evening pulse.
3. The average afternoon pulse is higher in the Tropics than in the Temperate Zone, probably because the solar heat is greatest then.
4. The morning pulse has the greatest and the evening the lowest range.

He considers that this reduction in the pulse-rate is related to the diminished respiratory function. Parkes, Jousset, Crevaux, Feris, and Plehn, according to Huggard, maintain, on the contrary, that the pulse is increased by ten beats per minute. Plehn says, however, that on acclimatization the pulse-rate sinks to normal.

There is said to be a lowering of tension (associated, according to Huggard, with the dilatation of the peripheral vessels), as well as increased elasticity and dicrotism, all of which probably pass away on acclimatization.

Chamberlain in the Philippine Islands concludes that the average blood-pressure, measured by a Cook's modification of a Riva-Rocci's apparatus and a 12·5 centimetre armlet, in Filipinos and Americans of the same age dwelling in those islands, does not appreciably differ from one another, nor from that of similar Americans in the Temperate Zone, but that the pulse-rate of active Filipinos and Americans is a few beats above the usual standard of 72 per minute.

In our experience, in Europeans coming to the Tropics, the pulse-rate is *occasionally* slightly increased. This disappears after acclimatization, and the pulse-rate becomes the same as in Temperate Zones. We have never noticed dicrotism of the pulse in normal individuals.

As regards natives of the Tropics, it is stated by some authorities that their pulse is quicker than in the inhabitants of Temperate Zones, but we are unable to confirm this, and find it to be the same as in Europeans.

Effect on the Blood.—Mitchell, as the result of his work in the Persian Gulf, considers that damp heat *of itself* frequently produces anæmia, but gives no details of the blood examinations. In 1916 W. M. Strong, noting that persons who had lived for long in the Tropics became anæmic-looking, investigated this point, and concluded that the pallor was not due to deficiency in hæmoglobin nor to ischæmia of the cutaneous capillaries, but to pigment deposited in the epidermis, which becomes partially opaque to red light, which is important because the colour of the skin depends upon the relative amount of each spectral tint which is reflected back to the eye. Further, he considers that when more pigment is deposited the skin becomes yellow-brown.

The 'Arneth count' (see p. 1898) in healthy native children has been investigated by Breinl and Priestley; taking the figure for normal Europeans as 40, native children varied from 71·0 to 83·80, while in adult natives it stood at 74·04. They are of the opinion that the alteration of the blood picture is the outcome of climatic influences, and not, as suggested by Scott-Macfie, as the outcome of abortive inoculation with malarial parasites, though they think that the higher figure—viz., 83-86—may be accounted for by infection.

Sweet agrees that high 'Arneth index' is very regularly present in healthy children over the whole coastal area of Eastern Australia; he maintains that no factor apart from disease is found definitely to influence this index, but he says that external temperatures do apparently influence the index in animals, and that further research is required with reference to this in man.

We are disinclined to believe in a marked anæmia purely and solely due to climatic influences without any other causal factor, but diminished resistance against disease is certainly produced by long residence in the tropics, and is probably largely climatic in its cause, though food may also be a causal factor therein; but the chemical factors of resistance to disease still require investigation.

With regard to the sugar content in the blood, McCay finds that for Europeans it is 0·08 per cent., while for Bengalis it is 0·13 per cent., and the increase appears to be entirely due to the excessive amount of the carbohydrate in their diet. In the fat indolent classes it is 0·150 per cent., while in the poorest classes it is only 0·125 per cent., and he points out that there is a very close relationship, other things being equal, between the sugar content in the blood and the amount of fat deposited in the tissues, which again is a dietetic and not a climatic effect.

Effect on Digestion. With regard to the alimentary canal there is often less appetite and less desire for animal food, and greater demand for spiced articles of diet, all of which show a tendency to lower power of digestion; but we are convinced that the tropical hyperæmia, other than alcoholic, is a myth, and we base this statement on a large number of clinical and pathological observations spread over a period of some twenty-one years.

There is, however, one point to which special attention should be drawn, and this is to the danger of constipation in tropical climates with low humidity, and to the necessity of imbibing daily a sufficiency of water to combat the loss of moisture from the skin. This tendency to constipation in healthy people in very hot dry climates is usually aggravated by the difficulty in obtaining fresh vegetables and fruits in those regions during the driest times of the year. Constipation, if allowed to become chronic, may cause passive hyperæmia, but this is pathological, and due to the lack of free evacuation of the bowels and not due directly to the climate.

Effect on the Nervous System. It appears that the cells of the nervous system obey the general law that vital activity is increased with a higher temperature, but only up to a certain point, after which their functional activity becomes markedly depressed. This is the case in most Europeans, though a great deal of mental and physical work can be done in the tropics if the bodily health is maintained. Natives naturally are less prone to feel the depressing effects of continuous high temperature.

It is possible that this condition, together with the effect of the actinic rays of the sun, may result in weakening the control of the higher centres over the lower, and thus inducing outbursts of what Plehn calls 'tropical fury' (*Tropenkohler*), by which he means fits of passion caused by trivial incidents. This is seen not only in Europeans, but in natives, who are apt to do violent deeds under the impulse of unreasoning anger. It appears to be one of the causes of assaults and violent crime in certain parts of the Tropics.

Effect upon the Urinary System.—Urine is diminished in quantity in the tropics, and this is said to be due not merely to diminution of water, but also of solids, among which urea and chlorides may be noticeably mentioned. Lawson says that the pigments are increased.

The diminution of the urine is very markedly noticed in hot dry climates and should be carefully combated by drinking a sufficiency of watery fluids because of the danger of lithiasis.

Effect on the Generative Organs.—The generative organs act more vigorously in the tropics, but venereal excess is distinctly more deleterious than in the Temperate Zone.

Menstruation begins about one year earlier in European girls living in the tropics than in those living in the Temperate Zone. For instance, it begins in 48·4 per cent. at thirteen to fourteen years of age, and in 50·07 per cent. at fifteen to sixteen years of age. Eurasian and East Indian girls, according to Das, mostly begin to menstruate at thirteen years (54·8 per cent.), though a considerable number do so at twelve years (18·6 per cent.). Natives of India mostly begin about eleven to twelve years of age (63·51 per cent.), and high-caste Indian girls begin in their eleventh year (50 per cent.) or twelfth year (48 per cent.); but this early menstruation may be associated with child-marriage rather than climate. Puberty in boys appears at an earlier age than in temperate climates.

There appears no reason to doubt that the climacteric is a more trying time for the European woman in the tropics, and tends to produce neurasthenia. If possible, therefore, such a woman should be sent to the Temperate Zone during this period.

It is possible that fertility is not affected in Europeans, though there is some doubt on this subject, and evidence is increasing that it greatly decreases after the second or third generation. Abortions are said to be more common in the European in the tropics than in the Temperate Zone, and post-partum hæmorrhage is also said to be more common, but these statements require careful investigation before being accepted.

Effect on Growth.—Rattray made observations on the weight and growth of forty-eight naval cadets, aged from fourteen and a half to seventeen years, during four successive changes of climate during a voyage. He considered that they grew too rapidly and lost weight considerably in the tropics, and that their strength and health was impaired by the heat.

These conclusions of Rattray's are of the greatest importance, showing clearly the necessity (well known) of sending European children as soon as possible to live in the Temperate Zone, not merely, as some writers assert, for education, but, much more importantly, for their health.

Effect on the Skin.—The cutaneous system in all tropical regions is flushed with blood, and in the damper parts is more or less covered with visible sweat, which is apparently suitable for the growth of fungi.

In the dry hot climates the skin is dry, and in persons who possess few layers of horny cells it is liable to become inflamed and cracked. The hair, particularly on ladies who have resided some time in the dry tropics without a change, is apt to fall out.

PRESSURE.

The atmospheric pressure at different localities scattered all over the world may be measured by the barometer, due care being taken to correct the reading for index error, capacity, capillarity, temperature, and altitude; and the data so obtained may be entered on a map of Mercator's projection of the world, and finally points of similar pressure, as indicated in this map, may be joined together by curves, thus producing an isobaric chart.

The result of this investigation shows that, generally speaking, at sea-level there is high pressure at about 30 degrees north or south of the Equator, and that from this the pressure decreases towards the Equator.

The reason why the pressure is low at the Equator is partially due to the heating of the air by the sun's rays, but more especially to the considerable addition of aqueous vapour to the air in these regions, with the result that it ascends with considerable force, and goes on ascending to very high altitudes, owing to repeated warming from the condensation of aqueous vapour and the liberation of latent heat.

Though the pressure at 30 degrees is higher than that at the Equator at sea-level, it is considerably less than at higher altitudes. Consequently air passing upwards from sea-level at the Equator into higher strata will then flow either north or south towards 30 degrees; but as it flows it is compressed as the latitude increases, and hence the current of air flowing polewards becomes narrower and narrower, and finally, owing to this, is forced down by the increasing pressure, until it reaches sea-level at 30 degrees north or south, causing the high pressure about this latitude. This compression is helped by the cooling of the air as it proceeds polewards, and by the centrifugal force of the earth's rotation.

Apart from this general distribution, there are diurnal and annual variations in the pressure. The diurnal variation of pressure is best marked in the tropics, diminishing as the Poles are approached —*e.g.*, at Calcutta it is 0·12 inch, whereas at Greenwich it is only 0·02 inch. The cause of this diurnal variation is the heating of the air by the sun, but there is also another cause, producing, according to Blandford, a variation of 0·1 inch in India, and acting twice daily, the nature of which is not known.

The cause of these seasonal variations in the pressure is the heating or cooling of the land, which, in the case of Colombo, is associated with the monsoons. Thus, the low pressures occur in the season of the south-west monsoon, May, June, and July, when air is travelling from high pressure at the Equator to low pressure in the warm plains of Asia; and the high pressures are associated with the north-east monsoon, when air is travelling from the cold plains of Asia, where it is at considerable pressure, towards the Equator, where the pressure is less.

Effects.

The effects on mankind of the slighter variations of atmospheric pressure are quite unknown and unstudied, scientifically, as far as we know, though the subject merits careful research. It is possible that they are without effect, because they decrease with altitude in the same ratio in which the pressure diminishes, but without producing any obvious effect from a climatic point of view. When atmospheric pressure is increased considerably, as in the use of special apparatus for deep diving and in the caissons filled with compressed air which engineers use to lay the underwater foundations of bridges, then a series of symptoms are produced which are called caisson disease, and to this we shall refer in a later chapter, as the conditions are pathological and not physiological.

There is also the condition of diminished atmospheric pressure which is found in mountain climates. Thus, if the pressure at sea-level is 762 millimetres of mercury at 25° C., then at an altitude of 500 metres, and at the same temperature, this becomes 720; at 1,000 metres 679; at 2,000 metres 604; at 3,000 metres 530; at 4,000 metres 475; at 5,000 metres 420; and at 6,000 metres 370. But if the temperature at 5,000 metres were 0° C., instead of 25° C., then the pressure would be 394 millimetres, and at 6,000 metres 343 millimetres; while at 3,000 metres it is 517 at 0° C., and 536 at 25° C.

It must therefore be noted that the mean pressure is *not* the same at similar altitudes in the tropics and in temperate climates, but somewhat higher.

Mankind can live and has formed permanent habitations in Tibet at places over 4,900 metres above sea-level, and Hahn states that in the Bolivian province of Chichas people live at an altitude of 5,000 metres.

Hahn, quoting Pöppig and Reck, states that natives living on the high Andean plateaus suffer from certain disagreeable effects, but we have been unable to find what they mean exactly by this expression.

Mountain sickness belongs to the pathological portion, and will therefore be considered later; and all we can write with regard to the physiological effects of pressure is to invite the attention of observers, who live at or visit high altitudes, to the great lack of accurate information with regard to these matters.

WINDS.

The motion of the air in passing from regions of high to those of low pressure constitute the winds, which may be classified into permanent, periodical, variable, and local.

Permanent winds are caused by the expansion of the hot equatorial air which rises to high altitudes and passes polewards.

If Fig. 7, which demonstrated Ferrell's latest ideas as to the circulation of the air, be studied, in general it will be noticed that the zones of equatorial calms and rains are indicated, as well as the zones of subtropical calms and drought.

The unbroken arrows indicate the surface winds, and the broken arrows the upper currents. The margin of the circle shows a vertical section of the atmosphere in which the arrows indicate the movements. The equatorial area is marked in the centre.

If this figure be carefully examined, it will be seen from the section of the atmosphere on the sides of the figure that the heated air rises over the Equator to high altitudes, and flows to the poles;

but at lesser altitudes it descends in the region of subtropical calms, and either passes polewards or to the Equator. Within the area from 0 to 30 degrees there are winds called the 'trades,' which blow from 30 degrees towards the Equator, and which on reference to Fig. 6, can be noted as north-east trades and south-east trades, and it will also be observed that the only portion of the ocean free from them is the North Indian Ocean, where the south-west monsoons occur. The north-east monsoon is really a trade-wind.

Further, it will be noted that as the air moves in opposite directions along the surface in the region of latitude 35 degrees, there is an absence of prevailing winds. These belts of calms are called 'the subtropical belts,' or the calms of Cancer and Capricorn. Again, at the Equator there are calms for the same reason, and these are often called 'the doldrums.'

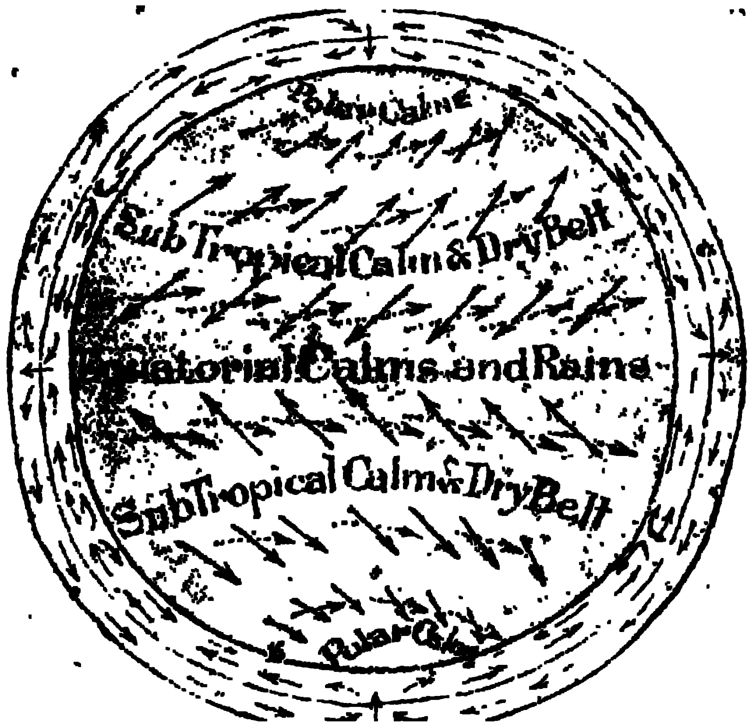
Polar Calms
SubTropical Calm & Dry Belt
Equatorial Calms and Rains
SubTropical Calm & Dry Belt
Polar Calms

FIG. 7.—DIAGRAM OF THE CIRCULATION OF THE ATMOSPHERE.
(After Ferrel.)

The trade-winds are only to be seen typically in oceanic regions, where the temperature is equable, and there are no local conditions to cause them to deviate from their course. But they, together with their intermediate zones of calms, shift their positions according to the temperature, having, therefore, different areas in such months as March and September. On an average the north-east trades extend from 7 degrees to 29 degrees north in the Atlantic, and the south-east to 20 degrees south. During the summer they advance a few degrees north, and in the winter recede to the south. In spring the centre of the doldrums is only 1 to 2 degrees north of the Equator, while in summer it is about 9 or 10 degrees north latitude, and, as will be explained later, the tropical rains of certain regions depend upon this movement. Their easterly direction is due to the rotation of the world.

Periodical winds are the movements of the air produced by the alternate heating (by the sun) and cooling of large tracts of lands, and the most important of these are the monsoons; to which reference has already been made.

Variable winds are found in the regions of calms interposed between the trades in the Atlantic and Pacific Oceans.

Local winds are of great importance in the tropics, constituting the so-called land wind, sea breeze, mountain wind, etc., and several others to be referred to later, to which special local names have been given.

The wind about which a great deal is spoken in every tropical country is 'the land wind.' During the day the land becomes heated by the sun, and causes the air to rise, thus lessening the pressure, and drawing the air from the sea, causing a sea breeze, which is, of course, very humid. During the night, however, by terrestrial radiation, the land becomes cooler than the sea, and the air travels from the land to the sea, and constitutes the land wind. This wind, as a rule, is dry, and has a very deleterious effect on men and animals by extracting moisture and abruptly cooling the body, and thereby lowering the resisting-power to disease. Hence the complaints made by old residents about the land breezes. On the other hand, new-comers delight in them, because they are so cool.

This land wind is more marked at certain seasons of the year than at others, being particularly felt in Colombo in those months when there is less cloud, because the terrestrial radiation is then more marked. There is, however, nothing like a definite season for a pronounced land wind, for it can take place at any time, only depending upon terrestrial radiation.

A few remarks may be useful with regard to some local winds:—

The Sirocco (Italian, *scirocco*).—The sirocco is a south-east wind with a high temperature, which, coming from the high land of North Africa, descends to the Mediterranean, and may reach Malta and some parts of Italy. It is considered to be very enervating.

The Solano.—The solano is a south-easterly wind, blowing from the Sahara into Spain.

The Harmattan.—The harmattan is a hot easterly wind, coming from the Sahara Desert, and carrying dust far out into the Atlantic.

In the months of November to March this wind meets with the north-east trade in its most southerly position, with the result that it is deflected southwards down the west coast of Africa. It is a very dry wind, and therefore extracts moisture from everything it comes across. Hence human beings feel their skin dry and hard, and may suffer from bleeding from the nose and lips while furniture creaks and groans in a most supernatural manner.

The Khamsin.—The khamsin, or khamseen, is the dust-laden wind which blows from the Sahara into Egypt at intervals during fifty days about Easter-time, and is very disagreeable, especially when associated, as it often is, with high air temperatures, when it may produce pathological changes in persons in poor health situate in places unsuitable for bearing heat, such as railway trains.

Pamperos.—These are the south-westerly winds of Brazil. Europeans have altered the significance of the name to squally cyclonic winds in the same vicinity.

Ghibli.—The ghibli is a violent south or south-east wind blowing into Tripoli from the desert, and carrying with it a quantity of sand, which causes irritation to the conjunctivæ and which may induce nervous symptoms.

The Foehn.—Though essentially a temperate or cool climate wind, still the foehn exists in the tropics. The foehn is to be seen in its home, Switzerland, as a warm dry wind which blows with great violence downwards from the crest of the Alps, and has marked effects upon man and animals, as it has a depressing effect upon the mind and the nervous system. It was thought at one time that this wind came from the Sahara, but all evidence is against this, and the present idea is that it is a local wind which is produced by a high south-east and a low north-west pressure, and attains its high temperature as well as its dryness in its descent from the summits of the Alps on their northern side, and less typical on the southern aspect when the pressure is high in the north-west and is low in the south-east.

Foehn-like winds occur in Trebizond, and on Lake Urmia, in Persia, where it is called *samum*, and blows down the eastern side of the New Zealand Alps on to the Canterbury Plains.

It also occurs at Resht, on the southern shores of the Caspian Sea; also in South Georgia, as well as in the Andes and at Kanazawa in Japan.

We have, above, given the usual explanation of the sirocco, but it must be noted that it is probably a 'foehn' wind, for Brydone, many years ago, noted that in Sicily it could not possibly come from the Sahara, because it would have been most violent on the south coast, whereas it is actually at its greatest violence on the north coast, especially at Palermo.

The 'sirocco di Levante,' between Pylos and Kyparissia, is also a 'foehn' wind, as is the sirocco of Algiers, and probably the solano of Spain and the vent d'Espagne on the northern aspect of the Pyrenees.

Cyclonic Storms.—Besides ordinary winds, cyclonic disturbances called storms occur. Cyclonic storms receive different names in various parts of the world, being called cyclones in India, Ceylon, and Mauritius, hurricanes in the West Indies, typhoons in the China Seas. Mild cyclonic storms met with on the West Coast of Africa and elsewhere are called tornadoes.

Electrical Conditions.

Silent electrical discharges are frequent in the tropics, and the acidity which they produce is supposed to be the cause of devitrification, which is so trying to persons working with all except the best microscopical and other lenses.

Thunderstorms of astonishing violence are frequent in many parts of the tropics, and generally cool the atmosphere for the time.

It is a popular belief that the electrical condition of the atmosphere has some influence upon life, but if this is so then it is an untrodden field, as far as we know, for we have been unable to find any definite scientific observations which can confirm or refute the popular belief. Hahn considers that there is no indication that atmospheric electricity plays a notable part in climatology.

Sun's Rays.

Sunlight contains heat rays (red), light rays (yellow), and chemical rays (blue, violet, and ultra-violet); that is to say, rays extending from the infra-red to as far as 291 $\mu\mu$ in the ultra-violet (Gibbs), but is much influenced by latitude, longitude, altitude, and the daily and hourly varying local meteorological conditions.

These rays reach the earth, according to Langley, in the following percentages:—

	Per Cent.
Ultra-violet	39
Violet	42
Blue	48
Greenish-blue	54
Yellow	63
Red	70
Infra-red	76

Freer, Gibbs, and Bacon have shown that, though the tropical light of Manila contains few, if any, more ultra-violet rays than the Temperate Zone, still the chemical rays have more effect there than in a temperate climate, and these effects vary on different days. Freer distinguishes 'actinic' and 'non-actinic' days, on both of which the sky may be equally clear. The cause of the difference between an actinic and non-actinic day is not understood. Gibbs does not believe that the normal intensities of the light in the tropics is different from that of any other region, the influence of local meteorological conditions being excluded, the most important of these being the humidity. Aron suspects that the deleterious influence of tropical sunlight is due to the long heat waves rather than to the short chemical waves, which we will now consider.

The chemical rays appear to have, first, a stimulative and beneficial influence, and, secondly, a harmful influence.

Stimulative Influence. Finsen, by experiments upon tadpoles, earthworms, beetles, flies, etc., came to the conclusion that the action of the chemical or blue-violet rays was very considerable as compared with light (yellow) or heat (red) rays, and that, though their action was probably very complex, still, it could be best considered as an excitation of the nervous system.

This excitation was so powerful as to produce reflex actions in tadpoles and movements in other animals, while in man he considers them to be the cause of the feeling of *bien-être* experienced on a bright, sunny day, which he compares with the depression felt on a dark, cloudy day.

Bactericidal Properties.—Downes and Blunt in 1877 showed that the chemical rays could kill bacteria, while D'Arsonval and Charrain showed that they could kill the *Bacillus pyocyaneus*. In 1903 Bernard and Morgan demonstrated that it was the middle third of the ultra-violet portion of the spectrum which caused these bactericidal effects.

Harmful Influences ACUTE SKIN IRRITATION.—Charcot in 1859 first expressed the opinion that it was the chemical and not the heat rays which produced sunburn, and showed that the dermatitis caused by strong electric light was identical with that caused by the sun.

In 1889 Widmark proved this definitely by using an electric arc of 1,200 candle-power, the light of which was first passed through water to absorb the heat rays, and then allowed to fall upon the shaven skin of a white rabbit, when the characteristic inflammation resulted. He then interposed a plate of ordinary glass to exclude the ultra-violet rays, when the skin remained unaffected.

In 1901 Finsen placed on the flexor surface of his forearm a plate of rock-crystal and pieces of different-coloured glass, and also wrote his initials in Indian ink. He then exposed the arm to the rays from an 80-ampère arc for twenty minutes, ten minutes at a distance of 50 metres and ten minutes at 75 metres. The result was that first all parts were slightly influenced by the heat, and then those parts which were unprotected or covered with rock-crystal became red and inflamed, and later desquamated and became pigmented, while the parts covered by glass and Indian ink, after the slight initial inflammation due to the heat, did not further react. This experiment is interesting as showing that the effects due to heat appear at once and pass off quickly, while those due to the chemical rays do not begin until after a lapse of three hours, which agrees with the well-known fact that a sunburn takes some time to develop.

Freund, as the result of his experiments, concluded that the chemical rays penetrated into the skin. Bernard and Morgan found that the ultra-violet rays were the active agent in producing sunburn.

The histology of solar erythema is not well known. Leredde and Pantrie made a biopsy on the skin of the shoulder of one of their friends who was suffering from sunburn of three days' duration. The skin was in a condition of acute erythema, without œdema or effusion. Under a low power of the microscope the epidermis appeared normal in thickness and disposition, but the horny layer was exfoliated in places. The dermis was richer than normal in cellular elements, and the connective-tissue bundles were swollen. Under a higher power the intercellular spaces appeared larger than normal. The vessels of the dermis were dilated, and there was a slight leucocytic infiltration, while the connective-tissue cells were swollen. These appearances are exactly like those produced by the rays of an electric light.

If the sun's action stops at this, the only change will be the deposit of the yellowish-brown pigment in the skin so well known in the tropics. If, however, the action is more intense, an exudation appears, which may be sero-fibrinous, cellular, or bloody, while the depth to which these changes may extend depends upon the intensity of the light. The epithelium becomes swollen, and bullæ may form, and the connective tissue of the dermis be swollen.

The pigmentation of the epidermis is important, and will be referred to at greater length in the next section.

Chronic Skin Irritation.—The chronic effects produced on the skin by the chemical energy of light are:—

(1) Pigmentation.
(2) Vascular modification.
(3) Disease.

(1) *Pigmentation.*—It is well known that pigmentation follows sunburn, but until recently it was not evident that it was of a protective nature.

In 1888 Wedding, confirmed by Charcot, first made this point clear, though Unna in 1885 was the first to say that it was to be regarded as useful, inasmuch as it prevented the rays penetrating too deeply, thus preventing inflammation.

In 1896 Finsen painted a black ring 2 inches wide round his arm with Indian ink to imitate the colour of a negro's skin, and then exposed it for three hours to a very hot sun. For a time the skin remained normal, showing only a little redness at the edge of the black paint, but in due course it became red and inflamed, except where it had been painted black. After several days the erythema disappeared, and the area which had been red was noticed to have become distinctly pigmented, or, in plain language, was sunburnt.

He then exposed it again to the sun, but this time the area which had originally been covered with Indian ink was unprotected. The result was that this part became red and inflamed, while the pigmented area was unaffected, except that it became a little more pigmented.

This experiment of Finsen's shows that the colour of native races living in the tropics is protective, and was possibly originally induced by the sun. Sambon and Baly found that the ultra-violet rays were entirely absorbed by a pigmented piece of skin, and therefore support the theory that pigmentation affords an efficient natural protection against ultra-violet rays.

Dyson studied cutaneous pigmentation in 1911, and concluded that the formation of melanotic pigment was a normal function of the nuclei of the epidermal cell, metabolism being due to a lipochrome, in which melanin is the chromatic protein portion. This pigment passes to the cutis by way of the lymph stream. The formation of the pigment can be increased by agents such as light, heat, and toxins, but the increase is usually transitory and tends to disappear; but if there is deficient drainage of the lymph from the cutis the pigment accumulates, and unless the drainage is improved tends to become progressively worse. Decreased vitality of the cells may possibly cause the overproduction of pigment due to diminution in nutrition, but if the cells become functionally inactive then pigment production ceases, and the existing pigment being carried away by the blood-stream, the part becomes depigmented, which is probably the case in vitiligo, in which, after hyperpigmentation, the skin becomes depigmented.

That the dark pigmentation is useful is shown also by the observation made by us on various occasions that natives suffering from leucoderma avoid going into the sun, as they state that the unpigmented portions of the skin become inflamed and painful. In this connection, an interesting case showing the importance of these rays came under our notice. A native, who had developed large leucodermic patches involving the whole of the face, noticed that he could no longer work in the sun, as each time he tried to do so the patches became painful and he felt sick, very weak, and giddy, and therefore asked to be relieved of his outdoor duties; but it was held that he was still fit to discharge his ordinary duties, with the result that the unfortunate man was compelled to resign his appointment a few months later. It is therefore well that the importance of skin pigmentation should be more widely known.

Generally speaking, in regions where the sunlight is very intense the race is densely pigmented. As a rule, the people who live nearer the Equator are more pigmented than those farther away—*e.g.*, the black colour of the West African can be compared with the red of the American Indian or the yellow of the Chinese. But this rule is not without exceptions, for the

Sinhalese, living nearer the Equator, are distinctly less pigmented than the Tamils of the warmer regions of Jaffna and South India.

There is also not the slightest doubt that the European living in tropical countries becomes darker, a fact which specially applies to the descendants of the settlers. On the other hand, according to Finsen, the dark colour of the negro diminishes to a sensible degree in Europe.

It must be noted, however, that a certain number of Europeans do not become sunburnt in the tropics. On the contrary, their skin, especially in localities where the climate is damp and hot, may take a peculiar whitish colour, even in cases in which the blood examination does not reveal any sensible decrease in the amount of hæmoglobin. As a result of an extended series of observations made by medical officers in the Philippine Islands, Chamberlain reports that the red cell counts averaged 5,200,000 per cubic millimetre in healthy American soldiers, averaging twenty-six years of age, after twenty months' service near sea-level, which count does not differ from the normal as at present recognized for healthy young men in the Temperate Zone. The hæmoglobin averaged 80·6 per cent., and the colour index 0·80 to 0·87, both of which were a little low, but not sufficiently so to indicate a definite anæmia. He believes that the pallor mentioned above is as a rule due to a superficial ischæmia.

The effect of tropical light on man has been made the subject of a special memoir by Woodruff, who points out that all over the globe the people who live nearer the poles are blonder than those residing near the Equator. He thinks that insufficient pigmentation, by permitting the penetration of the chemical rays, conduces to the increased activity of the mind and vigour in the muscles which is found in new-comers in the tropics. This condition of excitation causes them to overdo themselves sooner or later, and so to produce a feeling of exhaustion which he describes as tropical exhaustion.

He further considers that white men cannot become acclimatized in the tropics, and also that they should be protected by clothing opaque to the blue and ultra-violet rays. For this purpose he says that the outer clothing should be white, grey, or yellow, because heat will be least absorbed by these colours, while the underclothing should be black or yellow, to stop the ultra-violet rays. For office-workers and others not exposed to the direct sun-rays he advises black or dark blue, but he states that it is not known whether blue or black excludes the ultra-violet rays.

He also strongly advises opaque head-gear, as he says it is surprising how transparent the scalp and skull are to light rays, and that it is certain that the ultra-violet rays pass through them.

He points out the nuisance of the glare from houses painted white in the tropics, and mentions the better colours of green, dark yellow, and brown. The gradual disappearance of the white buildings in the business part of Colombo, and the appearance of new buildings coloured brown, indicates the correctness of his views.

While it is not possible to agree with all or even with many of Woodruff's statements, there is no doubt whatever that there is a great general truth in what he says, though many of the matters upon which he touches are purely speculative.

On the other hand, there is most urgent need for protection from sunlight both as regards the eyes and the whole body. With regard to the effect of the tropical sun on man and animals, some most interesting experiments have been performed in the Philippine Islands by Aron and Gibbs separately. Rabbits and monkeys—*i.e.*, animals with limited power of physical heat regulation—die if exposed to the sun's rays. The body temperature of these animals rises to febrile heights, while the post-mortem reveals hæmorrhages into the meninges, and in the case of monkeys into the heart. If, however, the increase of heat absorbed from the sun's radiation is compensated by increased loss from the animal by such means as a strong wind, the animal suffers no discomfort. Insolation of the skull alone is without effect if the body temperature is kept within normal limits. Our own experiments showed that rabbits died in about an hour if exposed to the sun with their head shaven, and lived if protected from these rays by means of red glass Aron and Gibbs have also shown that if the human skin is exposed to the sun's rays the temperature of the area so exposed rises as a rule more rapidly and reaches a higher maximum in a dark skin than in a light, until the nerve endings of the latter are irritated by the prolonged exposure. The black skin is protective because it guards the nerve endings from irritation, and because of the more rapid radiation by means of which heat is quickly lost, especially from the area in the shade, which is usually greater in extent than the part in the sunlight Further, it is probable that the relatively greater number of sweat glands in the dark skin is also protective. The air in the human hair, especially in black hair, under the influence of the tropical sun acquires exceedingly high temperatures. There is not the slightest doubt that the pigmentation of native races is protective, and that the older theories of Waltz that carbon was deposited in the tissues owing to imperfect oxidation due to heat, and that of Darwin that it was due to a survival of those best fitted to withstand tropical disease -for he believed that pigmentation prevented the native from being attacked by the fatal miasmata of the country -cannot now be seriously considered.

As to the origin of the pigment, this question must be considered as far from settled. There are two possible sources for the melanin, viz.: --

(a) The hæmoglobin of the blood.
(b) The cells of the epidermis.

(a) *The Hæmoglobin.* -This theory suggests that hæmoglobin is altered into melanin either in the blood-stream, in the connective-tissue cells, or in special melanoblasts, which by amœboid movement take the pigment to the epidermis.

(b) *The Cells of the Epidermis.*--This theory states that melanin is manufactured *in situ* by the epithelial cells, and is not derived from hæmoglobin, and in view of the histology given above this appears to be probably the correct solution of the problem.

Melanosis, which varies from mere freckles through the diffuse yellow and brown pigmentation to the jet-black of the African negro's skin, is caused by melanin granules lying in and between the cells of the epidermis.

With regard to the pigmentation of different races, it must be remembered that it is only absent in albinos, and that it occurs in the epidermis of the areolæ and mammillæ of the breast, the scrotum, labia majora, and around the anus in white races, being contained chiefly in the large basal cells of the Malpighian layer, and to much less extent in the more superficial layers, and the connective-tissue cells of the papillary layer of the corium. In negroes the pigmentation is deeper and more diffusely spread in the epidermis.

(2) *Vascular Modification.*—Associated with pigmentation there is said to be a persistent dilatation of the vessels and capillaries of the skin, and it is stated that hair and nails grow more rapidly in the tropics than in the Temperate Zone.

Light in general is believed to have an effect upon the blood, which absorbs the violet and ultra-violet rays, and the red corpuscles under these influences probably absorb more oxygen.

(3) *Disease.*—With regard to disease, there appears to be no reason to doubt that the irritating effect of light has at least a part in the ætiology of Kaposi's disease (*Xeroderma pigmentosum*), which we have met with in the tropics, where it would naturally develop rapidly in children prone to the disease.

There is also no doubt that these rays play a part in the production of the erythema of pellagra, as will be described later on, and they may have some effect in producing sunstroke.

Woodruff draws attention to the almost universal neurasthenia of white men in the tropics, among whom he says insanity is more common than in Temperate Zones. In support of the latter statement, he asserts that the insanity rate in the Philippine Army in 1901 was 2·02 per mille, while in the United States from 1889-1898 it was 1·13; but he remarks that the diagnosis was not confirmed on the arrival of several of the Philippine soldiers in the United States, as they recovered *en route*. He draws attention to the loss of memory in the tropics (*tropical amnesia*), a condition which is very prevalent on the West Coast of Africa, being often called 'coast memory.' He also mentions the midday siesta as useful in preventing this neurasthenia, and in this he is also probably correct, especially for ladies. Ordinary officials and business men, however, cannot afford to rest in the middle of the day.

Moon's Rays.—The extravagant stories by old writers, and especially the tales given by sailors with regard to the influence of the rays from the full moon, have thrown such discredit upon this subject that we have been unable to find any literature seriously considering the effects of its rays upon man.

Nevertheless, in our own experience, the rays of the full moon do produce headache and a certain amount of nervous irritability in persons who sleep in the open. The subject requires and deserves scientific study.

ACCLIMATIZATION.

Plehn seems to have been the first careful observer clearly to prove that the changes induced in the new-comer as he enters the tropics in due course disappear, and his organs becoming accustomed to the new work demanded from them, he virtually returns to the same condition of temperature, respiration, etc., as in the Temperate Zone—in other words, becomes acclimatized. Further, if constantly exposed to the sun's rays, his skin is apt to become more pigmented than normal, and to afford a certain degree of protection against its rays.

Sambon pointed out long ago that if proper sanitary and other measures against disease were introduced into the tropics, and if care were taken with regard to food, drink, excessive heat, and the rays of the sun, there is no reason why the European should not live healthily in these regions; and this is true to a certain extent, but in our experience the length of residence must be considered, as even with every care he may become debilitated by the direct climatic influences and require a change to a temperate climate, otherwise after a time, the length of which varies much in individuals, his health will be undermined and break down in some way.

The extraordinary success of the American sanitarians in the canal zone of Central America, once one of the most unhealthy regions of the world, but where now the sickness-rate has been diminished to less than half that of the death-rate of many a tropical town is often quoted. We feel that the basis of the largest proportion of illness and death in the tropics is bad sanitation and not climatic influences. Notwithstanding these facts, a permanent colonization of the low lying regions of the tropics by a white race is, in our opinion, not possible, as a uniformly damp, hot climate endured for years diminishes the resistance against disease, and has a markedly deleterious effect on the nervous system. Fertility probably also decreases after the second or third generation. The climate greatly deteriorates the physique of the children, as can easily be observed in any district of the tropics at sea-level. In the highlands, such as some parts of British East Africa, colonization by a white race may be possible, though Van Standel has pointed out that prolonged residence in tropical highlands produces changes in the nervous systems of the second and subsequent generations, even if it does not do so in the first.

These remarks in general agree with Caddy's work, as he considers that the European is unable to rear strong healthy children in India, and that even those which are sent home, when four or five years old, owing to the debilitating influences of the tropical climate at an important growing period, are not so fine physically as their parents.

If, however, the new-comer into the tropics desires to become acclimatized he must use some protection for his head, and in many cases for his spine and eyes; he must wear suitable clothing, live in suitable houses, work in suitable offices, dwell in sanitary surroundings, avoid alcohol and exposure to the midday sun, while roads in common use should be suitably constructed and well shaded.

It is not within the province of this work to go into detail with regard to these matters, but a few brief remarks may be made.

Suitable Head-gear.—All Europeans should wear a light helmet or topee covered with white or khaki-coloured cloth externally and ventilated. This helmet should have a broad brim lined with green and prolonged down the back of the neck, should be lined internally with red, or red and yellow, or black, and should possess an internal band attached in such a manner that the head does not touch the frame of the hat, while it allows free circulation of the air.

When persons are compelled to work under the tropical sun and to expose their backs to its rays, a thin strip of yellow and red coloured silk should be sewn into the shirt along the spine, or attached to the inner aspect of the coat by means of hooks and eyelets. Eyes should be protected with dark glasses, or with Sir William Crookes' non-actinic glass with side-pieces.

Ladies who are particular about the skin of the face should wear veils, though these are very warm.

The reasons of these requirements are, while white reflects heat very well, and absorbs very little, and is therefore excellent externally, yet it transmits the chemical rays, while red and yellow absorb them.

Clothing.—Clothing should be loose and as light as possible in weight, and of a white or khaki colour externally. Sambon some years ago devised a cloth, called 'Solaro,' khaki-coloured externally and red internally, with the object of preventing the action of the sun's rays on the body. It is made by using threads of yellow and blue twisted separately and together for the warp, while red threads are used for the weft, but these latter are brought back in the proportion of three to one, so that the front has three yellow and three blue threads to one red thread, thus producing the khaki colour. It should only be used as a coat, and should be obtained as thin as possible, and made up as lightly as possible without linings or doublings. The general opinion at the present is, however, that white is by far the best colour.

As regards underclothing, we are of the opinion that thin woollen materials are the best, but we are not in favour of openwork underclothes. At the present time the use of abdominal woollen or flannel belts (so-called 'cholera belts') is much abused; they are useful, however, to people with a tendency to intestinal disorders.

It should be remembered that when clothing is wet it is a good conductor of heat, and hence the risk of sitting down in damp clothes. Clothing should not be too heavy, nor too tight-fitting. Ladies should not wear too heavy skirts, which congest the pelvic viscera.

A silk hat and frock-coat have still to be worn by men at official functions at midday, but the custom is unfortunate, and may perhaps in time disappear.

Houses, Offices, etc.—Buildings should never be painted white or blue, but should be of a dark red colour. The amount of light admitted to a room should be restricted, and care should be taken that reflection from the ground into the room does not take place. Deep verandas, without which no building in the tropics is comfortable, are of the greatest value in controlling the light, as are tatties or tats made of grasses and wood, and jalousies.

Rooms should be capable of being cooled by punkahs or fans, and should be lit with electric light whenever possible. Ice-blocks are very useful in very warm weather or at meetings, or in sick-rooms. The walls of rooms should be painted rose-colour, not white.

Damp courses are required in the tropics, as walls are apt to absorb moisture and become very damp. Round roof-tiles and ventilated double ceilings are necessary to keep off the sun's rays.

Roads.—Roads should be protected from the glare of the sun by shade-trees—that is to say, trees with spreading branches—while plots of green grass are most valuable in towns. There is not the slightest doubt that red roads are the most comfortable for the eye and soothing to the nervous system, and that white roads are exceedingly trying to both.

Avoidance of the Midday Heat.—If possible, travelling and muscular exertion should be done in the early morning or late afternoon, and avoided in the middle of the day, when a siesta is most beneficial. The absurd custom of making social calls at 12 noon in certain parts of the tropics should be discouraged, and a more reasonable hour substituted.

Avoidance of Alcohol.—Alcohol should never be taken before the sun goes down, for it unfits the individual for work, and is the most important predisposing cause of sunstroke.

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CHAPTER IV

TROPICAL FOODS

Preliminary Remarks—Evolution—Chemical composition—Quantity—Quality—Tropical food materials—Calculation of diets—Low protein dietaries—Vitamines—Lipoids—Less known matters—References.

PRELIMINARY REMARKS.

It is not our purpose to attempt to give an account of the foods found in various tropical regions, but merely to give a brief summary of some of the more important facts known to us with regard to tropical foods and their effects upon man.

The subject owes much to the labours of McCay in India, while Wilson in Egypt has shown how this work can be extended to other parts of the tropics.

We will begin by tracing briefly the origins of foods as far as we know them.

EVOLUTION.

At the present time human food is everywhere more or less cooked, and it is rare for mankind anywhere to eat, even for a limited period, absolutely raw materials. Dr. Campbell, in a most interesting manner, has traced the evolution of man's diet. He distinguishes first of all the pre-cookery epoch, during which evolving and primeval man lived upon raw materials, unaltered by any of the chemical and physical processes involved in cooking; secondly, the cookery epoch, which may be subdivided into the pre-cibicultural and the cibicultural eras. In the former, although he cooked his food, man did not cultivate vegetal foods, nor did he rear animals for purposes of food. During this period vegetal foods would probably be used in greater quantities than before, as they are easier to obtain than hunted animals; and, also, because the processes of cookery by breaking up the cellulose, rendered them more easily digestible and absorbable, and therefore more nutritious, as well as more palatable. Just as we have already pointed out that certain tribes have remained in the status of the Stone Age almost to the present day, so certain tribes—*e.g.*, the Bushmen of Africa, the true Veddahs of Ceylon, the Andamanese of the Bay of Bengal, and the aborigines of Australia—have remained in this pre-cibicultural era. These peoples obtain their foods from all sorts of animals—*e.g.*, worms, centipedes, flies, caterpillars ants, etc.—as well as from game, while their vegetal foods are collected and stored, but they have never learned to extract any chemical substance—*e.g.*, sugar—from their vegetal foods. Probably this is one of the reasons why they prize honey so highly. In the cibicultural era man cultivated his vegetal foods, and reared domestic animals for the purposes of animal food, and here again his vegetal feeding increased in amount, as this food was the cheapest and easiest to produce. Here again rose the urgent need for salt, to which we have already drawn attention in the account of the migrations of negro tribes.

The arts of cultivation and domestication became gradually dispersed over the world, but to-day it is exceedingly difficult to trace the means by which this diffusion took place, though it is probable that much of it was due to Aryan invasions.

Primitive wheats can be found growing wild in Palestine to-day, and it is probable that the home of this cultivation was Mesopotamia. It also seems likely that the art of bread-making was known to the Chaldeans and to the Egyptians some three thousand and more years before the commencement of the present era.

According to Tibbles, rice cultivation was in existence in China some three thousand years before Christ, and was introduced into India by the Aryan invasion. From India it passed into Europe with Alexander the Great's army in 334 B.C., and from Europe it was introduced into America in the fifteenth and sixteenth centuries.

Maize, on the other hand, was first cultivated in America by the ancient inhabitants of Mexico and Peru, and was brought by the Spaniards to Europe and has gradually found its way all over the world.

Millet appears to have been cultivated from very ancient days in Africa and Asia, and even in [illegible] Stone Age it had extended into Middle and Southern Europe.

Beans were first cultivated by the Aryans, but the haricot bean comes from South America, while lentils are of prehistoric origin, and spinach was apparently cultivated by the Medes and Persians. Onions possibly originated in India, while the potato came from Chile.

Fruit-growing is not as ancient as cereal cultivation.

The domestication of animals enabled man to obtain meat without being compelled to roam over large areas in search of wild game. Man is omnivorous and desires greatly to eat meat, but when this is unobtainable or in too small a quantity to supply the needs of the population, as in the present war, he eats the foods which are available, and is thankful even though they are not those after which his stomach hankers.

The reason why man in Eastern countries eats so much rice must be sought for in the overpopulation of the Eastern Asia of long ago, when the great food difficulties began those large movements of peoples which we have noted in Chapter II.

To-day Governments place peoples on meatless days and give them food tickets, and the peoples obey willingly because they understand the reason, but it might have been extremely dangerous for a despotic monarch of Eastern Asia to have issued orders of this nature long ago. The ruling powers of those days must have invoked the aid of the religious sects, who, being feared and respected by the people, were obeyed; and to-day these religious maxims are still in force, and the people avoid animal food, although the over-population on account of which the rulers probably originated this custom has ceased to exist.

During historic days man has attempted to improve the appearance, the smell, and the taste of his food by all sorts of devices, which vary in different countries. These refinements include condiments and colouring matters, and form part of the basis of the science and art of modern cookery.

But man desires not food alone, but something to cheer and exhilarate him when he feels ill or depressed, and when he wishes to celebrate some occasion; and hence in all countries some form of stimulating liquid is to be found, be it in the form of tea, coffee, or cocoa, of malt liquors, wines or distilled spirits, and all these are of great antiquity.

Early dealers in food materials soon learned that it was profitable to adulterate their merchandise, as this could be done with impunity. Of late, legislation, aided by chemical, physical, and physiological research, is endeavouring to insure that foodstuffs shall be pure, though with regard to some foods, such as milk, the standard is far from perfection, and certainly in the tropics mixed milk can rival sewage in the numbers of its organisms.

With regard to quantity and composition of primitive foods, naturally but little is known, and this little is entirely due to McCay, who has investigated the dietary of the primitive peoples of Chota Nagpur in Bengal. Among those there are peoples who have begun to cultivate the ground, while others still live upon the food which they can gather. Thus the Dravidian Mundas and Uraons eat insects, lizards, snakes, rats, jackals, and pigs—or, in other words, anything which they can catch. Their daily dietary is composed of protein 80 grammes, carbohydrates 500 grammes, and fats 50 grammes, which provides calories 2 800.

The Todas of the Nilghiri Hills live upon milk, the meat of buffaloes and of such animals as they can kill or capture. They take no vegetal food, and hence, like the carnivora, require no salt, which is an essential to vegetal feeders in order to prevent acidosis.

The Bushmen of South Africa and the Bedouin of Arabia are meat eaters.

The necessity for food is to provide heat and energy, and to form new bodily tissues, as well as to make good the wear and tear of existing tissues; and to do this a community requires pure water and plenty of it, and good and varied foodstuffs in quantity proportional to the numbers of the population, a fact which the present war has made clear to nearly every family in the civilized regions of the earth

Dietetics are based upon chemical and physiological considerations, into which we will now inquire very briefly.

CHEMICAL COMPOSITION.

In order to meet the requirements of the body, foods must be composed of the same essential chemical substances as that body. They are therefore made up of proteins, carbohydrates, fats, mineral substances, and water, but these alone are insufficient to keep the body in health, and they must be associated with vitamines and lipoids or nitrogenous fats.

Proteins may be obtained from the muscles, bones, and organs of animals used as food, also from animal products such as milk and eggs, while the many vegetal substances, but particularly legumes, nuts, and cereals, also provide this valuable food constituent. Their primary value is as tissue formers, and their secondary value as heat-energy producers, but all proteins are not of equal value, as we shall see later.

Carbohydrates are chiefly of vegetal origin, and are principally of value as heat-energy producers.

Fats are widely distributed both in the animal and in the vegetal kingdoms, and are essentially heat-energy producers, while the **Lipoids** or nitrogenous fats are indispensable to man, though their exact use is not known.

Mineral Substances are compounds of sodium, potassium, calcium, magnesium, manganese, and iron, either with carbonic, sulphuric, phosphoric, and silicic acids, or with acetic, citric, malic, oxalic, and tartaric acids, or with chlorine or fluorine. They produce no heat or energy, but are essentials for building up the fluids and tissues of the body, in which they represent some 5 or 6 per cent. of the total weight.

Water, forming some 58·5 per cent. by weight of the human body, is an indispensable.

Vitamines are nitrogenous complexes, which are essential for the growth or the well-being of the organism.

The food materials may therefore be classified into the great tissue-forming protein, aided by salts and water, and the great heat-energy producing carbohydrate and fats, aided by protein, and essentials, the work of which is not understood—viz., vitamines and lipoids.

As the heat and energy can be expressed in terms of the calorie (or large calorie written with a capital C), which is the amount of heat necessary to raise the temperature of 1 kilogramme of water one degree centigrade, and as protein is the essential tissue-former, it follows that in calculations as to a diet two matters stand out—viz., the quantity of protein in that diet, and the number of calories which can be obtained therefrom.

Water has a food value of 1 in 1,000, and should be freely available, and salt is usually easily procurable, though we have lived in parts of the tropics in which neither were easily obtained.

Vitamines and lipoids we cannot measure, and at present we are merely concerned with their presence.

Therefore, from a practical point of view, the quantities which require calculation are the amount of protein in a diet and the number of Calories, and this brings us to the subject of quantity.

QUANTITY.

The only accurate method of determining the quantity of the various food factors of any given diet is by means of the *respiration calorimeter*, in which the work done, the heat generated, and the waste products eliminated, are expressed in terms of the Calorie, which, in energy, is the equivalent of 1·54 foot tons, or, in other words, represents that amount of mechanical energy which is required to raise 1 ton in weight 1·54 feet in height.

When the respiration calorimeter is not available, the quantity of the total food consumed by the person or persons under observation should be carefully weighed and records made. Then samples of the various constituents of this diet should be analyzed, with the view of determining the quantity of protein, carbohydrate, and fat contained therein.

With regard to the Calories produced by these various factors, Rubner's experiments upon animals enabled him to enunciate the so-called *isodynamic law*, which states that 227 grammes of protein, or of carbohydrate, yield 930 Calories on consumption in the body, and that this is the same as the heat so produced by 100 grammes of fat, and therefore 227 grammes of protein, or of carbohydrate, are *isodynamic* with 100 grammes of fat. In other words, 1 gramme of protein produces the same amount of heat as 1 gramme of carbohydrate—viz., 4·1 Calories, while 1 gramme of fat gives 9·3 Calories.

It may, perhaps, be incidentally noted that 1 gramme of alcohol produces 7·0 Calories.

Standard diets expressed in grammes have been determined for an average strong healthy man weighing some 11 stone (68-70 kilogrammes) and living under average conditions of work in the Temperate Zone. The following table gives some examples of these standards:—

Observer	*Protein.*	*Carbohydrate*	*Fat.*	*Calories.*
Ranke	100	240	100	2,324
Voit .. .	118	500	56	3,055
Rubner .	127	500	52	3,092
Moleschott	130	550	40	3,160
Atwater .	125	400	125	3,315

As these diets are on the *man value*, it is necessary to have a table showing the values of children and women in terms of this man value. Such a table as made by Greenwood and Thompson is given below:—

Atwater's Coefficients.		*Inter-Allied Food Commission.*	
Ages.	*Man Value.*	*Ages.*	*Man Value.*
0 to 5 ..	0·4	0 to 5 .	0·5
6 to 9 ..	0·5	6 to 10	0·7
10 to 13 .	0·6	11 and over:	
14 to 15:		Males ..	1·0
Males	0·8	Females	0·83
Females	0·7		
16 and over:			
Males .	1·0		
Females	0·8		
All children, combined ages	0·51	All children, combined ages.	0·68

These figures may be compared with some Indian dietaries given by McCay:—

Class of Person	*Protein.*	*Carbohydrates.*	*Fats.*	*Calories.*
Cultivators ..	52	475	25	2,390
Poor middle .	50	400	50	2,310
Middle .	70	300	90	2,350
Better	85-100	300-400	150	2,050-3,450
Bengali prison diet ..	93	693	30	3,500

In Égypt, Wilson has inquired into the food of a Bedouin, and found that large quantities of rice and milk were used, while meat was eaten once a week in the winter and only once a fortnight in the summer, and lentils eaten in the winter were rarely used in the hot weather, being replaced by extra rice. About ½ pound of butter was taken in the winter, but less in the summer. Bread consisted of a mixture of two parts of dura and one part of wheaten flour, but on desert journeys was made entirely from wheat. Onions and cheese were also used.

He investigated the diets of two Egyptian men, with the following results, which, however, are complicated by the fact that they are calculated from the amount used by the family:—

Egyptian Men	*Protein*	*Carbohydrate.*	*Fat.*	*Calories.*
Strong and healthy	89·1	628·0	47·5	3,328
Not very robust	82·0	520·0	49·0	2,870

Perhaps the best practical test is the British war ration, which, according to Delean, was inadequate in the South African War, producing loss of efficiency from neurasthenia and debility, as was afterwards proved by experimental marches performed upon it, but which, in 1913, was altered to one containing a high amount of protein, which, indeed, is required to meet the needs of tissue repair. It is as follows:—

Protein.	*Carbohydrate.*	*Fat.*	*Calories.*
175	218	515	1,855

We have already invited attention to the possible simplification of these tables, and have shown that the essentials are the protein and the Calories, and now we will see how Atwater applies this method for determining the diet of a man doing various kinds of mechanical work:—

Nature of Work.	*Protein.*	*Calories.*
Rest	100	2,700
Light work	112	3,000
Moderate work	125	3,500
Hard work	150	4,500

In Japan, Oshima found that a jinricksha-man doing hard work consumes different foods during his periods of work and rest. During work he eats large quantities of rice, and during rest quantities of fish, eggs, beef, and pork. He consumes about 20 to 30 ounces of beef or mutton per diem, which works out at 158 grammes of protein and 5,050 Calories.

Light-worked Japanese require 100 grammes of protein and about 3,000 Calories per diem.

In India, McCay determined the amount of nitrogen excreted daily in the urine, and adding to this the other metabolized nitrogen mentioned above, and converting this into terms of protein, obtained the absorbed protein, which, he calculated, was 75 per cent. of the dietary protein.

For example, the urinary nitrogen being 6 grammes, which is the equivalent of 35·5 grammes of absorbed protein, adding to this the other metabolized nitrogen and 25 per cent. for that lacking, he concludes that the average *rice-eating Bengali* of 50 kilogrammes weight only uses 55 grammes of protein per diem—or, in other words, lives on a poorer protein supply than any other race investigated.

Further, this *rice-eating Bengali* exemplifies on a large scale the results of Chittenden's experiments, and as claimed by this experimenter, should exhibit *good bodily health, great working power, and freedom from disease,* whereas he shows none of these traits, and, as a matter of fact, *the reverse is true.*

Our own experiences of Chittenden's dietary in the tropics is that the experiment, if continued sufficiently long, lowers the resistance of the body against disease; and this can scarcely be surprising, as he maintains that 0·12 gramme of nitrogen per diem per kilogramme of body weight is sufficient to keep a man in health. This is certainly not so in the tropics. And we doubt its general application to temperate and cold climates, where one would expect more food to be required

Chittenden's figures of the nitrogen metabolized per kilogramme of body weight may be compared with Voit, McCay's, and Oshima's figures as follows:—

Bengalis and Ooriyas (rice diet largely)	0·110-0·120
Chittenden	0·120-0·130
Beharis and Eastern Bengalis ..	0·140-0·160
Japanese poorer classes .	0·177
Nepalese	0·180-0·250
Sikkim Bhutias	0·250
Average European .. .	0·270
Thibetan and Bholan Bhutias. .	0·350
Nepalese Bhutias	0·420

Indeed, McCay found that Indian dandy carriers, Indian rickshaw-men, and Indian coolies performing exceedingly hard work, did so on a diet containing 175-200 grammes of protein and 6,300-6,500 Calories per diem, whereas the British Army ration mentioned above only allows 175 grammes of protein and 4,855 Calories.

It will be noted that nothing is said in these diets as to the quantity of the food digested and absorbed into the body, as it is from this alone that tissue-formation and heat-energy production can take place—or, in other words, we require to know something as to the quality as well as the quantity of the food supplied in a diet.

QUALITY.

In this section we desire to know the amount of any given food which is absorbed, and is therefore available for use in producing heat, energy, and repair.

The amount which is capable of being digested may be determined by artificial digestion of a sample, but though said to give good results, it is hardly reliable as to absorption.

A better method is to begin by giving the person to be experimented upon a dose of charcoal, and after a few hours to administer a given quantity of the food to be tested of which the protein, carbohydrate, and fat factors are known. The fæces are in due course carefully collected and weighed, and the total amount of nitrogen and of fat determined. From the nitrogen, after deducting 0·5 gramme to allow for the daily amount of excreted metabolized nitrogen, can be calculated the amount of protein in the fæces, and this deducted from the amount of protein in the food gives the quantity absorbed.

The fat is determined in the same way by ether extraction, while the carbohydrate is obtained by calculation.

Nature of Food.	*Protein*	*Carbohydrate*	*Fat*
Mixed diet :			
Total foods	92	97	95
Animal foods .	97	98	95
Vegetal foods .	84	97	90
Meat and fish .	97	98	95
Eggs ..	97	98	95
Milk, cheese, etc. ..	97	98	95
Cereals ..	85	98	90
Starches and sugars ..	[illegible]	98	—
Legumes (dried)	78	97	90
Vegetables	83	95	90
Fruits	85	90	90

Langworthy gives the table above showing the *coefficients of digestibility* or the amounts per cent. of the foods which were digested. It must be remembered that by the word 'digestibility' as used in dietetics is meant not 'apparent digestibility,' or the time a food requires to pass through the stomach, but 'actual digestibility,' which is the quantity of a given food which is absorbed, from which alone tissue formation and heat energy can take place.

Benedict, taking into account this factor, together with the work done, gives the following table:—

Nature of Work	*Total Protein*	*Ingestible Protein.*	*Calories.*
Light	100	92	2,700
Moderate	115	105	3,300
Hard ..	175	160	5,500

It will be noted that the British Army ration is below Benedict's hard-work calories by 745.

So far we have been writing as though all proteins were of equal value, but they are not, as the researches of Rubner and Thomas have shown.

The minimum quantity of protein required daily, so that a man of average weight may live without drawing upon the proteins in his tissues, is 30 *grammes of animal protein*—that is to say, protein derived from meat and eggs.

To reproduce this value, 34 *grammes of rice protein* and 102 *grammes of maize protein* are required.

This factor is called the *biological value of protein*, and so far as we know has only been studied by its authors and by Wilson in Egypt, as set forth below:

100 Grammes of Food Material.	*Available Protein*	*Biological Value of Protein.*	*Absorption Co efficient calculated on Available Protein.*
Meat ..	19·00	19·00	95
Wheaten bread	5·00	2·00	75
Millet bread .	3·40	1·36	55
Rice .	6·50	6·00	80
Lentils ..	19·39	10·70	70
Beans	18·60	10·30	70
Fresh vegetables ..	1·00	0·50	—
Dura	7·80	2·30	75
Millet	4·15	1·78	55
Milk (buffalo) . .	5·90	5·90	—
Dried dates .	1·90	0·90	—
Fûl Sudâni (shell ..	19·00	10·50	70

Wilson gives the following table of the diets in use at Egyptian prisons, with suggested modifications:—

Details.	*Available Protein*	*Biological Value of Protein.*	*Protein from Animal Sources*	*Fat*	*Available Carbohydrate Gross, less Five per Cent.*	*Energy Value in Kilo-Calories*
Hard labour diet:						
Before 1898 .	72·0	37·0	8·28	20·7	524·0	2,786·0
1898-1899	77·0	39·5	6·89	80·0	569·0	3,136·0
1900-1905 .. .	71·0	37·5	0·0	50·0	516·0	3,056·0
1905 (wheat bread)	96·0	57·8	22·5	46·0	547·0	3,058·0
1911 (millet bread)	83·0	53·34	22·5	40·0	521·0	2,987·0
Suggested	89·2	45·28	7·0	48·0	588·3	3,218·0
Ordinary labour diet						
1898-1899 .. .	68·5	31·5	0·0	56·5	520·5	2,978·5
1900-1905 .. .	57·1	25·4	2·5	48·0	460·0	2,561·0
1905 (wheat bread)	82·7	44·2	0·0	43·0	553·0	3,010·0
1911 (millet bread)	60·7	38·7	6·0	43·0	520·0	2,844·0
Suggested ..	78·175	40·05	3·0	47·8	522·7	2,861·0
Non-labour diet						
1898-1899	49·0	21·5		38·5	404·0	2,216·5
1899-1905	42·8	20·0		28·5	345·0	1,890·0
1905 (wheat bread)	70·2	35·1		37·0	499·0	2,680·0
1911 (millet bread)	59·2	31·2		37·0	480·0	2,556·0
Suggested	65·20	32·0		36·0	450·5	2,442·0
Bread diet, 1898-1911	38·0	16·0	-	12·0	375·0	1,803·0
Millet bread diet, 1911	28·0	11·0	-	12·0	354·0	1,679·0

Starling has recently drawn attention to the *fat factor* in the diet, and concludes that if the Calorie value of the total diet is sufficient there is no evidence of a physiological minimum, but the human alimentary canal has become so accustomed to fat that it requires this factor in the following ratio:—

Age in Years.	*Total Calories per Day.*		*Fat in Grammes*	*Fat Calories per Cent. of Total.*
	Gross.	*Net.*		
0 to 6	1,650	1,500	62	35
6 to 10	2,310	2,100	62	25
10 to 13 .. .	2,750	2,500	74	25
13 to 20:				
Males	3,300	3,000	88	25
Females	2,750	2,500	74	25
Adult average bodily workers:				
Males	3,300	3,000	70-88	20-25
Females	2,750	2,500	60-74	20-25
Adult sedentary workers:				
Males	2,750	2,500	60-74	20-25
Females	2,200	2,000	47-60	20-25
Adult very heavy bodily workers	3,900 to 5,000		12-100	30

Chalmers Watson found by actual analysis that the daily dietaries of eight healthy English children between four and six years of age contained protein 71 grammes, fat 67 grammes, carbohydrates 198 grammes, and yielded a total of 1,725 Calories.

A most important matter is that food must be made tasty, and should be well cooked and look nice—matters of great importance in armies.

As emphasized by Rho, in making a dietary the racial food peculiarities, which are, after all, adaptations to climate, should always be taken into consideration—*e.g.*, the beef-eating British soldier requires a different dietary from that of the soldiers of Southern countries.

TROPICAL FOOD MATERIALS.

Excluding the work of McCay and of Wilson, there is very little information available as to the chemical composition, the biological value, or the absorptions of tropical food materials.

Wheat.—This is a very important cereal in many tropical places. The grain is ground between small hand moved stones and the bran removed by sifting, while the meal contains the germ and the endosperm. Wheat and barley are often mixed, while poor samples may contain gram, maize, linseed, etc. McCay finds that the absorption of wheat in India amounts to about 80·5 per cent. of the protein contained in all the elements of the wheat grain, including the germs—everything, in fact, except the coarser parts of the bran.

In the modern steel-roller milling both bran and germ are removed and the flour is composed solely of endosperm, of which the central portion, poor in protein and rich in starch, forms the *patents*, and the remaining part *household or bakers' flo* while the flour from the whole wheat is called *Graham*, and from the entire grain—*i.e.*, with germ and semolina—is *standard*.

Rice.—Turning now to the consideration of certain articles of food in common use in the tropics, one of the most important is rice, because it is widely used throughout the East, where it is believed to be consumed by over 400,000,000 Indians, Chinese, Japanese, and Malays, and because it is very deficient in protein material, and for this reason has to be consumed in large quantities in order that a sufficiency of this important factor may be obtained. Unfortunately dry rice absorbs water very greedily, and is increased by boiling in water to five times its original bulk. Further, its progress through the stomach is slow, and therefore it not merely distends, but keeps this organ distended for some hours.

Rice is, however, well digested in the intestines, nearly all the starch being absorbed, while the protein absorbed varies from 45·76 to 84 per cent. This lack of absorption of protein leads, therefore, to a loss in the nitrogenous value of the rice, and, indeed, is the chief method of loss of its nitrogenous value, as but little disappears during cooking. The percentage of nitrogen, absorbed from a rice diet has been shown by McCay to vary directly with the quantity of the rice. Thus, in a mixed diet containing 32 ounces of rice 6·55 grammes of nitrogen, or 45·76 per cent., were absorbed; while the same diet, with only 20 ounces of rice, showed 8·40 grammes of nitrogen, or 68·33 per cent., to be absorbed. From this it will be evident that mixed diets containing large quantities of rice tend to a low standard of protein absorption.

There are two kinds of rice commonly met with, viz.:—

(*a*) The Indian, country rice, or paddy, variously described in medical papers as 'cured,' 'stale,' 'unpolished,' or 'parboiled' rice, which is prepared by soaking in water for twenty-four to forty-eight hours, and then steaming in cylinders, and finally drying by exposure to the sun. This rice is yellowish-brown in colour, and carries attached to it the outer layers of the grain, while it has not lost much of its protein in the process of preparation.

(*b*) The Burma, Rangoon, or white rice, also variously described as 'uncured,' 'milled,' or 'polished' rice, which is prepared by milling the unhusked paddy until the husk, the pericarp, and the surface layers of the seed are removed, which results in the production of a nice clean white grain, partially denuded of its outer layers and to some extent of its protein.

At the present time many authorities believe that the differences between these two methods of preparation of rice are the explanation of the etiology of beri-beri, as they believe that the latter method, by separating the subpericarpal layers from the rice, deprives it of a substance which is absolutely necessary for the health of the human body.

Maize.—With reference to this much-abused and excellent food, which has, in our opinion, been wrongfully accused of causing pellagra, we may briefly state that it is prepared for food by crushing between millstones or milling by machinery to produce maize meal, which can be made into unleavened bread (porous bread cannot be made, because of the absence of the gluten found in wheat-meal), into porridge or polenta. Often, however, it is roasted, and eaten with butter and salt.

In general, about 74 to 88 per cent. of its protein is absorbed, and, as regards India, McCay says that it is decidedly superior to all the cereals experimented upon, with the exception of wheat. Woods says that it is wholesome, cheap, and well suited to its numerous uses as a food material, and provides a greater return in protein, carbohydrates, and energy for the same outlay than any other cereal.

Millet.—The sorghums, or millets, according to McCay, show a very defective protein absorption—*e.g.*, *Sorghum vulgare* 53 per cent., and *Pennisetum typhoideum* only 49·4 per cent.

Legumes.—The legumes are extensively used in the tropics, and among them come the dals, or dhals, of India (*Cajanus indicus*, *Ervum lens* Linn., *Cicer arietinum* Linn., *Pisum sativum* Linn., *Phaseolus radiatus*, *Ph. mungo*, all belonging to the Leguminosæ), which are allied to the European pea, and all contain a high percentage of protein, whereby they occupy an important position in the food of tropical peoples. They are utilized by being ground into meal, from which unleavened bread, porridge, or sauce is prepared, or they are simply dried (parched) and eaten in this condition.

They resemble rice in absorbing a large quantity of water when cooked, and so becoming bulky, but they differ from this and other food materials in that they are less thoroughly digested. Moreover, their addition to diet lowers the percentage absorption of all the food factors, but especially that of the protein factor.

McCay considers that these dhals produce a great waste of nutriment, in that 25·42 per cent. of the nitrogen of the food appears in the fæces of Bengalis, while only 15 per cent. appears in that of Europeans on a vegetable diet. Moreover, he considers that they are a factor in the production of the bowel disorders so common among the Bengalis.

Wilson has recently performed much excellent work in investigating diets in Egypt. He gives a table of food values, of which the following is an extract:—

100 *Grammes of*—	*Available Protein.*	*Available Carbohydrate.*	*Fat*	*Calories.*	*Cost in Milliemes*
Millet bread ..	3·4	15·0	1·5	212·5	0·0577
Dura	7·8	65·5	54·0	344·3	0·82
Soya bean meal ..	32·0	28·5	2·1	269·0	0·80
Dried dates ..	1·9	47·0	0·6	253·0	2·44
Fûl Sudâni (shelled) ..	19·0	16·8	45·0	562·0	1·787

CALCULATION OF DIETS.

In the calculation of diets it appears to us that two important matters must be considered—viz., the quantity of protein and the number of Calories.

With regard to protein, having obtained from the tables of analysis the *available protein* in the food, it is necessary to determine its *biological value* and the quantity of the *absorbed protein*, and from this the Calories can be calculated. The fat and carbohydrate present no difficulties, except that it is necessary to know the quantity of the available matter which is absorbed. Having obtained the quantities absorbed, the matter is simple arithmetic.

Protein : fat : carbohydrate :: 5 : 3 : 1.

Having done this, certain facts must be considered. It is necessary to remember that the figures given for Europe will not apply to the tropics, and that as a rule they do not represent a minimum, and that no diet should be based upon a minimum.

Wilson has invited especial attention to the quantity of protein, which is not a producer of energy until the carbohydrate and fats are used up, but repairs wear and tear or is stored up as fat or carbohydrate.

The nearer the quantity of protein is to the minimum, the longer will the organism require to rebuild damaged tissue and the less will its powers of resistance be against disease. He states that excess of protein will mean increased heat production, and therefore in the tropics, where there is a cold season, two diets should be in existence—viz., one with less protein for the hot weather, and one with more protein for the cool weather or cool regions.

If this is not done, then the increased heat must be got rid of by radiation and conduction, and this can be obtained by natural or artificial breezes or by exercise, when the extra heat of muscular exertion will be dissipated by sweating.

He also draws attention to the low biological values of the vegetal proteins, which are less well absorbed than are the animal proteins, a fact which he thinks is due to the structure of the food materials rather than to the nature of the proteins.

His conclusion with regard to protein appears to us to be worth quoting.

'A minimum amount of protein is required daily, over and above which a certain excess is desirable; this minimum is different for different proteins, and is measured by the biological value of the protein. In determining, therefore, the requisite amount of protein it is essential to take into consideration the biological value of the protein components of the diet, and fix the daily quantities on this basis rather than on the nitrogen content. In determining the amount of protein the defective absorption of vegetable proteins must be allowed for.'

We would add that care should be taken that vitamines and lipoids are present in the dietary, and that the former are not destroyed entirely by cooking.

Water should be freely supplied in tropical towns—*e.g.*, Calcutta and Peshawar allow 4·15 gallons per head per diem of filtered water, but many tropical towns are not so well provided, and the minimum in the tropics for drinking purposes should be 3 to 4 pints per head per diem.

Salts are also of great importance, and usually present in the food, but with much vegetal food addition of ordinary table salt is necessary.

LOW PROTEIN DIETARIES.

In tropical lands there are many peoples who live mainly upon cooked cultivated vegetal foods, with but little admixture of animal foods, and this is due to force of circumstances rather than to any desire of the peoples, who would be glad enough to eat animal food if it could be obtained. Among these peoples the protein in the food sinks to a very low amount, with, as we shall presently see, a markedly deteriorating influence on the race.

The effects produced by this low protein standard may be illustrated by the following table, which is given by McCay to exemplify the differences in the diets of Bengalis as compared with those of Anglo-Indians and Eurasians:—

Food.	*Bengalis I*	*Bengalis II.*	*Anglo Indian. and Eurasians*
Proteids in grammes ..	67·11	43·61	80·56
Carbohydrates in grammes	518·73	200·31	376·53
Fats in grammes ..	71·55	33·02	51·75

McCay, in his excellent works quoted at the end of this chapter, has shown that when the protein standard of a tropical dietary is very low, then the physique, the capacity for work, the health, and the resistance against disease are also lowered, and he has illustrated these facts by reference to the rice-eating Bengali. Moreover, he has answered his critics in a most able manner, and has demonstrated by comparing closely-allied tribes living under identical conditions of climate, solar irradiation, sexual excesses, early marriage, etc., that it is the influence exerted by the food, and particularly by the proteins of the food, that is all-important in determining the degree of muscular power, the general physical endowment, the powers of endurance, the resistance to disease, and, most important of all, the place which a tribe or race has won for itself in manliness, courage, and soldierly instincts. It is impossible to discuss at length in this place the facts which he has adduced, but certain important results may be briefly mentioned.

Thus, he has drawn attention to the great difference in the analysis of the blood of male Bengalis in India, as compared with that of the blood of Europeans in Europe, as set forth in the following table:—

Nature of Observation.	*Male Bengalis in India.*	*Europeans in Europe.*
Erythrocytes	5,300,000	5,193,000
Leucocytes	9,000	7,500
Hæmoglobin (Haldane's method)	81	100
Colour index ..	0·71 to 0·85	0·95 to 1·1
Water	78·88	78·87
Total solids	21·12	21·13
Proteids	18·20	19·17
Salts	1·06	0·78
Blood-pressure in brachial by Riva-Rocci's sphygmomanometer	100 millimetres Hyg	110 to 130 millimetres Hyg.
Ratio of salts in the urine to those in the blood	1·2	2·0

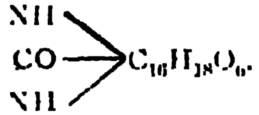
His observations show that too little protein in the food affects the growth of the Bengali boy, who grows up slender, and is defective in vigour and vitality, and in conjunction with Bannarji, Dutton, and Ghosal, he has demonstrated the differences in the constituents of the urine in male Bengalis in India, as compared with male Europeans in Europe as is shown in this table:

Constituent in the Urine.	*Male Bengalis in India*	*Male Europeans in Europe.*
Quantity	1,177 c.c.	1,200 to 1,500 c.c.
Specific gravity	1,006 to 1,024	1,015 to 1,025
Urea	5·50 to 10·68 grammes per diem	30 to 35 grammes per diem
Total nitrogen	5·0 grammes per diem	14 to 18 grammes
Chlorides ..	0·43 grammes per diem	15 grammes per diem
Phosphates .. .	0·05 to 1·4 grammes per diem	2 to 3·5 grammes per diem
N : P_2O_5 ratio .. .	5 or 6 : 1	Practically the same
Uric acid	0·18 gramme per diem	0·3 to 7 grammes per diem
Total sulphates	1·75 to 2·2 grammes	2·5 to 3 grammes
Ethereal sulphates .. .	0·15 to 0·22 gramme	—

These are most important conclusions, and we must state that our own observations in tropical practice support McCay, and are directly in opposition to Chittenden's observations. We have observed that when persons in good health have for some time carried out Chittenden's dietary, the result has often been sharp attacks of illness, indicating a lowered resistance to disease.

VITAMINES.

Eijkmánn, Gryns, Takaki, Fraser, and Stanton, have shown that the uncured, milled, polished, or white rice is deprived of its subpericarpal layers by the processes of milling or polishing, and that these layers contain some substance of importance in the prevention of beri-beri. This substance is present in the proportion of 0·1 gramme to the kilogramme of rice. Funk has isolated this substance, called ***beri-beri vitamine***, from the polishings of the rice mentioned above, and has determined its chemical composition—*i.e.*, 55·63 per cent. C, 5·29 per cent. H, and 7·68 per cent. N, which correspond best to the formula $C_{17}H_{18}O_4N(HNO_3)$—and has demonstrated its power of curing the polyneuritis induced in fowls by a rice diet, 4 milligrammes being sufficient to cure pigeons. In further researches he came to the conclusion that the beri-beri vitamine was a base belonging to the pyramidine group, and that its formula was:—



$$\left.\begin{matrix} NH \\ CO \\ NH \end{matrix}\right> C_{16}H_{18}O_6.$$

It was described as being soluble in water, alcohol, and acidulated alcohol, as being dialyzable and capable of being destroyed by heat at 130° C., while the amount present in 1 kilogramme of rice is 0·01 gramme.

According to Funk, this substance is essential for the metabolism of the nervous system, and if it is lacking in a diet it must be supplied from the body, and when this fails then symptoms of beri-beri appear.

Beri-beri is, therefore, according to general opinion, a *deficiency disease*, and is grouped with epidemic dropsy, scurvy, experimental scurvy, infantile scurvy, ship beri-beri, pellagra, and polyneuritis of birds.

All vitamines are not the same, and the *scurvy vitamine* appears to be different from that of beri-beri, being a crystalline substance destroyable at 120° C. or less, and constant in fresh potatoes, onions, cabbages, apples, lemons, limes, and lime-juice; and being less stable than that of beri-beri, is only found in the fresh condition of vegetables and fruits.

There appears also to be a *specific growth vitamine*, the composition of which is unknown. It is contained in milk, and is necessary for the growth and development of the child. If the mother suffers from beri-beri, as Andrews has shown, there will be great risk of the child dying either of beri-beri or some other complaint, owing to defective growth and development.

There is also a suggestion that pellagra may be a deficiency disease.

With regard to the distribution of vitamines, they are present in yeast, milk, cereals, and probably in muscle juice, brain, fish, legumes, and fresh vegetables. With regard to cereals, they are present in the germ and subpericarpal layers of the bran of wheat, in rice bran, and in the pericarp and outer layers of maize.

Their action upon metabolism is unknown, and it is still doubtful whether they assist anabolism as hormones.

The processes associated with the sterilization and canning of foods destroy vitamines.

Lipoids.—The best known of the lipoids is lecithin, and it is suggested that they are required to enable amino-acids, fats, and salts to enter the cells of the body, and so to form the colloidal substances thereof. It is further suggested that mice cannot live on lipoid-free food, and that perhaps vitamines are unable to enter the cells except as lipoidal compounds, but the whole subject is very nebulous.

LITTLE-KNOWN MATTERS.

All proteins contain amino-acids, but these are not combined in the same proportions, and it appears possible that a minimum thereof is necessary for the growth, if not for the maintenance in health, of the organism; but the whole subject is in its infancy, and the same holds good with regard to the salts, some of which may be necessary for proteins and others for the lipoids.

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CHAPTER V

TROPICAL DISEASES

Preliminary remarks—Evolution—Geographical discovery—Endemicity—Epidemicity—Eugenics—Incidence—Distribution—Prevention—References.

PRELIMINARY REMARKS.

BEFORE entering upon the systematic study of tropical diseases a few remarks may be made upon their evolution, the influences of geographical discovery upon their dissemination, their endemicity and epidemicity, tropical eugenics, the geography of tropical disease; with special reference to countries and not to given diseases, and finally the prevention of these diseases.

It will be obvious that, if these subjects were to be treated at all fully, they would require several volumes, each of which would be larger than the present little book; but this is not our object, which is to bring subjects to the notice of the tropical practitioner with the view that he may apply them to the diseases and peoples by whom he is surrounded, and references are given whereby he may extend his reading and knowledge far beyond the confined limits of our manual.

All tropical countries are inhabited by three different sets of inhabitants. Firstly, there are the true *indigenous natives*; secondly, there are *immigrants* from other countries; and, thirdly, there are the *descendants of an admixture* of the first two, and generally of a European with a native. Such are the Mulattoes of Central and Southern America, the Eurasians or Anglo-Indians of India, and the Burghers of Ceylon, and it is our duty to try to trace out the cause of disease and death among these peoples.

EVOLUTION.

Auckland Geddes and Adami consider that the Piltdown skull is pathological, and that its remarkable thickness and the bold outline of the temporal ridges are to be explained by the assumption that its original owner suffered from *acromegaly*.

The researches of the late highly talented Sir Armand Ruffer into *palæo-pathology* have demonstrated the existence of bilharziosis, tuberculosis, rheumatoid arthritis, and pyorrhœa alveolaris in Egyptian mummies dating some 4,000-6,000 B.C., while certainly some of the organisms of disease were present then, as he was able to demonstrate the tubercle bacillus in mummies of the Twelfth Dynasty.

But disease is much older than man, for Moodie has noted the presence of arthritis and osteomyelitis in cave bears, of pyorrhœa in early tertiary three-toed horses, and caries in Permian fish.

There can be no doubt as to the great antiquity of bacteria, and it seems possible that they performed great geological works in the early history of the world, and may be largely responsible for the formation of some of the oldest sedimentary rocks, in much the same way as Drew's *Bacillus calcis* does its work to-day in the lagoons of Florida and on the Great Bahama Reef.

When higher plants and animals evolved, the struggle for existence must have compelled minute animal and vegetal organisms to seek protection for themselves therein, and at first this protection would be used temporarily to tide over some difficulty.

This being admitted, the parasite would desire an easy method of entrance into and escape from the body of the temporary host, and hence the common infection of the alimentary canal with organisms.

So long as the chemical substances produced by the metabolism of the parasite were innocuous or helpful to the host, there would be no reaction on its part against the intruder, and the two would live together in peace, as many bacteria do at the present day in the human alimentary canal, and a condition of commensalism may be arrived at.

Other intruders, on the other hand, might give rise to irritating chemical substances which would provoke a reaction on the part of the host. And thus begins the long struggle between the invading organism and cells of the host which has produced all those complicated mechanisms which are gathered together under the term 'immunity.' The reader will notice that the whole of this struggle is *adaptation to environment*—viz., to that portion of the host's environment in which is centred the invading organism.

The parasite would naturally attempt to escape from the defensive chemical substances poured on to it by the host, and in so doing pierced more deeply into the tissues of that host; but now its escape would not be so easy as when living in some cavity freely communicating with the exterior, and hence it would be to its advantage to either kill that host, or, if it failed to do that, to enter some cavity communicating with the exterior and suitable for the parasite's existence,—*e.g.*, the enteric bacilli in the gall-bladder and the pelvis of the kidney.

All these changes of environment would cause variation in the protists (protozoan and bacterial), and, if the same environmental conditions acted long enough, then these changes would become inherited (*vide* Adami); hence the origin of the numerous parasitic protists, animal and vegetal, and hence also the preservation of characters, including those complicated phenomena associated with the reaction of the host which we call the signs and symptoms of disease and the natural recovery therefrom It appears to us that just as disease arose *de novo* in the long ago, so it has probably been arising century after century, and we see no reason why new diseases should not appear in the twentieth century of the present era in man and animals, as they did when hosts were first evolved, only the matter is more complicated owing to the evolution of methods of defence upon the part of the host.

In his most interesting and masterly book Adami has shown that a non-pathogenic organism can be made pathogenic by injecting into an animal killed non-pathogenic bacilli, and then ten or fifteen days later the live bacilli. These, when recovered from the tissues of the experimental animals, were found to have undergone considerable variation due to their altered environment, and had so changed their characters as to be very virulent to guinea-pigs. In other words, by means of a preliminary anaphylactic phenomenon a non-pathogenic microbe may become pathogenic and a new disease be evolved.

Similarly, according to some of our observations, when man is immunized artificially against typhoid and the paratyphoids, he becomes more susceptible to infections by chance intestinal organisms, which in this way give rise to new diseases.

Finally a germ accustomed to a human race which has developed a certain amount of immunity may meet with another race which lacks this immunity, and immediately a disease which is mild may develop rapidly fatal attacks and spread widely—*e.g.*, measles in the Sandwich Islanders in London long ago.

Enough has been said to show the line of thought—viz., the importance of environment, the difficulty of impressing characters, but the hereditary transmission of these characters when once evolved producing variation in the parasites, while the reaction on the part of the host tending to produce an immunity against older forms, and yet leaving, in the phenomenon of anaphylaxis, a gate open for further variation on the part of non-pathogenic organisms and the possibility of the origin of new diseases.

GEOGRAPHICAL DISCOVERY.

Just above we have mentioned the introduction of pathogenic organisms to races to which they were previously unknown, and as this is primarily due to geographical discovery, we desire to invite the reader's attention to this factor in the dissemination of tropical disease, as the discovery of new lands has eventually led to the betterment of means of communication, and hence to the easier and quicker transference of the microbes of disease.

Diseases which may have been endemic in one region for centuries may, by means of geographical discovery and by means of the present and past wars, spread to other regions where they were previously unknown; and this brings us to the consideration of endemicity and epidemicity.

ENDEMICITY.

As so much epidemiological investigation of disease has of late been undertaken, mainly due to the initiative of Manson and Sambon, we feel that a few general remarks on endemicity and epidemicity as applied to disease in general may not be amiss.

The presence of a given disease in a locality depends primarily upon the presence of conditions favourable for the action of the causal agent, and upon the presence of suitable vehicles for its conveyance into the human body, which must be non-immune to its attack. The causal agents of disease may be physical, chemical, or parasitic.

Physical causes of disease are often cosmopolitan in their distribution—as, for example, the action of gravity in producing the traumatisms brought about by falls; but though some causes, such as the rays from the sun, are also cosmopolitan, still they are unable to produce deleterious effects upon human beings unless assisted by secondary influences, such as latitude, altitude, the rotation and inclination of the world, etc., while some are restricted—as, for example, the traumatisms due to ferocious animals, which, though occasionally taking place in other parts, whither the animals have been artificially conveyed, generally only occur in the natural habitats of these creatures.

Chemical causes of disease have become largely cosmopolitan in distribution owing to improved methods of intercommunication and the manufacture of chemical principles: still, certain chemical causes have very restricted localities even to-day, because they are little known, and only affect primitive peoples living in these regions —*e.g., Gloriosa superba*, etc.

The parasitic causes of disease may be animal or vegetal. The endemicity of a given parasite depends upon (*a*) the presence of non-immune human beings, in which part of the life-cycle can be gone through, and which for convenience we will term the *human hosts*; (*b*) easy modes of escape from the human host into the exterior; (*c*) suitable means of continuing the life-cycle in the exterior—*i.e.*, in earth, water, air, on or in other animals or plants, *intermediary hosts* we will call them; (*d*) ready means of re-entry into the human host or into some other animal host in which the life-cycle is completed; (*e*) partially immune animal hosts or partially immune human hosts to act as reservoirs or carriers, to enable the parasite to complete its life-cycle without producing marked pathological changes in the host. Examples of these may be found in the malarial parasite attacking (*a*) the white man and the native child in West Africa and elsewhere, and passing by the agency of (*b*) blood-sucking into (*c*) *Anopheles costalis*, which, by the act of biting, (*d*) conveys the parasite to another non-immune host or to the partially immune adult native, who acts as a reservoir or carrier.

Another example is the passage of the plague bacillus from the rat via the flea back to the rat or man.

Other examples are the amœbæ of dysentery, which pass from man by the evacuations on to vegetal substances or into water, by which they may be reintroduced into man direct or by the agency of flies.

By a suitable non-immune host is meant a host which, while providing abundant suitable food material for the parasite, does not produce such a quantity of chemical substances antagonistic to the parasite as to seriously hamper or prevent its growth and development.

Given such conditions as those just described, a parasite should be capable of developing enormously in a given district; but there are still other factors to be considered, and the first of these is the fact that the intermediary host, if an animal, depends for its existence upon the presence of a suitable food-supply, as well as suitable means for propagating its species.

If anything untoward happens to these, the intermediary host may die out, but the problem is not quite so simple as this, because the intermediary host itself may be preyed upon by some other animal, or may be affected by disease, and so reduced in numbers.

If the intermediary host is reduced in numbers, even without being exterminated, the parasite will have difficulty in completing its life-cycle, and is therefore faced with the problem of seeking another intermediary host, or another entirely different method of leaving the human host, or of being exterminated.

The reduction in numbers of the intermediary host in a given area is one of the bases of prophylaxis in malarial fever, yellow fever, dengue fever, and sleeping sickness. Faced with these difficulties, it would appear possible that the parasite can change its intermediary, probably undergoing certain changes itself in so doing, and this would appear to be a possible explanation of the slight modifications of the various forms of spirochætes causing the relapsing fevers.

On the other hand, the malarial parasite would seem to be less capable of accommodating itself to a change of hosts, for it would appear to be only capable of completing its life-cycle in the less common anophelinæ, and not in the more common culicinæ—a most important fact in malarial prophylaxis.

Another factor to be considered is the effect of atmospheric temperature upon the parasite, for the study of the life-cycle of the malarial parasite has clearly shown that this has a marked effect upon the development of the oöcyst in the anopheles. It is also quite possible that other physical and chemical factors, concerning which we are at present ignorant, may play important parts in controlling the life of parasites.

Finally, the parasite itself may suffer from the attacks of another parasite, a condition of affairs called 'hyperparasitism,' and, thus becoming diseased, may be unable to complete its life-cycle, and so become extinct.

It will thus be seen that the problems connected with the appearance and the disappearance of a disease in a locality are extremely complex; and that next to the parasite itself the most important factor is the intermediary host, its food, its life-cycle, and its habits—in one word, its œcology.

Hence, in studying an endemic parasitic disease, or a disease thought to be possibly parasitic, it is not advisable to restrict one's researches solely to work in the hospital or the laboratory—for it must be remembered that the parasitic causes of some diseases are most probably ultramicroscopical—but to associate with the clinical and experimental methods of research epidemiological researches conducted by visiting several widely separated and, if possible, completely detached endemic areas, in order by carefully studying therein all the conditions of life and the habits of the human hosts to endeavour to find factors common to the different localities. A further study of these common factors from the point of view of possible modes of infection may indicate one or more possibilities, and then these must be put to the crucial test of experiment with a view of ascertaining definitely the accuracy of the epidemiological observations.

EPIDEMICITY.

From an endemic area diseases due to physical causes may spread by the alteration, naturally or artificially, of the physical conditions in the surrounding regions, and would draw back to the original region upon the return to normal of these conditions. Similarly, chemical causes of disease may be spread from their original restricted area by modern methods of intercommunication—*e.g.*, poisonous plants or their products may be brought from the tropics to the Temperate Zone, and *vice versa*.

In order that a parasitic disease may spread from its endemic focus several factors are necessary:-

(*a*) Carriers to convey it from one place to another. These may be either the human host, an animal host, or the intermediary host —*e.g.* fleas infected with plague.

(*b*) In order that the disease may spread in the new area there must be the suitable conditions already mentioned.

(*c*) There must also be suitable climatic conditions.

If these, and perhaps other still unknown factors, are present, the disease will be able to spread with perhaps increased virulence, first within the new area and then from one area to another, until an epidemic or pandemic is produced. With the appearance of partial immunity in the human and animal hosts, altered climatic and other conditions, as well as the æstivation or hibernation of one of the hosts, the epidemic will die down, perhaps only to reawaken after the hibernation of the host is over or with a change of climatic conditions; and this may be repeated for years, until conditions become too adverse for the life of the parasite or its host, when the epidemic dies away, and the disease again becomes restricted to its endemic areas.

The possibilities of epidemics and the presence of endemic diseases raises the question of the possibility of giving man such a start in life that he may be advantageously placed in the combat before him. The questions involved in such a possibility constitute the large and ever-increasing subject of *Eugenics*, to which we will now turn our attention.

EUGENICS.

Any attempt to improve the racial qualities, mental and physical, of the future generations will, without doubt, equip them better for the struggle for existence, including therein the fight against disease. In order to bring about an improvement two factors are open for consideration– viz., the parents and the child.

With regard to the parents, eugenics attempts to combat such racial poisons as are represented by alcohol and such social diseases as are indicated by syphilis, gonorrhœa, and tuberculosis.

In regard to *alcohol*, when taken in large quantities and for long periods it is said to act upon the germ cells, leading to the production of children possessing a lower resistance against disease. Unfortunately, as we shall see later, alcoholism is common among the natives of many tropical regions, and has already produced marked racial effects.

Alcoholism in the mother is a more serious matter than alcoholism in the father, because in the former the embryo is produced by alcohol-poisoned germ cells, while during intra-uterine life its growing cells are being constantly alcoholized, and finally the child, after birth, is either fed upon an alcoholic mother's milk or, as is more frequently the case, is reared by such hand-feeding as an alcoholic mother may give it.

As hand-feeding in the tropics requires the greatest care, it is not surprising that when reared by an alcoholic mother the child usually acquires disease at an early stage of its life-history, and often helps to swell the infant mortality rate.

Alcoholism is a great social question, and can only be combated by a sociological movement such as to-day is taking place in England and other Temperate Zone countries.

With regard to the so-called social diseases, every medical practitioner is conversant with *syphilis* and *gonorrhœa*, and all that is necessary is to invite attention to Sir Malcolm Morris's summary of the Recommendations of the Royal Commission on Venereal Disease, which include facilities for diagnosis and treatment, diffusion of knowledge with regard to the diseases, and the collection of statistics. It is particularly to be noted that they conclude that at the present time any system of compulsory personal notification would fail to secure the advantages claimed. The Commission considered that undeclared venereal disease should be a ground for the annulment of a marriage. They further considered that advertisements of patent medicines should be prohibited, and apparently they were in favour of making it penal for unqualified persons to treat venereal diseases. Venereal disease is at the present time exceedingly common in all parts of the tropics, and undoubtedly is leading to racial degeneration, and we strongly advocate that some preventive scheme should be inaugurated in all tropical countries. At the same time, we desire to record our disapproval of attempts to combat these evils by the registration and general police supervision of prostitutes as we believe such a system is bound to increase rather than diminish the disease, as it leads to secrecy; and, indeed, it has so far been a failure wherever it has been put to the test seriously.

With regard to venereal disease, there is no doubt that, although the war has increased the numbers of infections, it has nevertheless acted beneficially in bringing the seriousness of the subject home to the authorities; and, even in England, preventive measures, for male and female alike, are being widely distributed free of charge, and institutes are in existence for the diagnosis and treatment of these diseases. It is impossible to close the section without acknowledging, with honour, the great work which New Zealand has done in Europe with regard to this matter. When a country with traditions like England has awakened from its sleep of ages, a sleep largely due to its religious tendencies, it is possible for tropical countries, unhampered by these religious bands, to do even more than what we see going on around us as we write these lines in London.

Turning now to *tuberculosis*, it seems probable that the tubercle bacillus has had an opportunity of infecting every child living in the slums of the large European cities before it has attained the age of twelve years. It would further appear as though tuberculosis was either being better diagnosed or was increasing in many tropical lands.

There ought to be no slums in tropical countries, and where they exist it is the duty of the Government, forthwith, to formulate a scheme of betterment whereby in the course of years they shall be removed, and State-built State-owned, and State-regulated buildings should be provided, where the poor may live in a reasonable condition of sanitation. Further, it should be the duty of the State to take over and to bring up such illegitimate children as cannot be properly provided for, thereby not merely helping in the population and work questions, but also in the diminution of tuberculosis.

In the tropics there are two other eugenic problems to which we may invite attention, and these are *food* and *half-castes*.

With regard to food, the low protein dietary of the poorer native population of such regions as India is a great sociological problem, being connected with religious sentiment. It leads to racial degeneration, as we have already seen, but its remedy is very difficult, and must be done by a social movement on the part of the natives themselves.

In regard to *half-castes*, the number of poor Eurasians or Anglo-Indians in India is increasing, and as their children live in the slums of great cities they tend to degenerate.

After fourteen years of strenuous work Graham has shown that if these children are taken to sanatoria in the Himalaya Mountains, and placed in a new physical, mental, and moral environment, they do not show this degeneration.

This is a great discovery, and if confirmed and acted upon may produce lasting results, because, as we have already hinted, there is a belief that the third generation of children, with European parents, born and living entirely in the tropics, tend to degeneration in every way, and yet it is desirable that portions of the tropics should be permanently colonized from temperate climates if possible.

Lastly, the *infantile mortality* of most tropical countries is appallingly high, and this passes unheeded, even in places where a local dearth of labour indicates to those in authority the necessity for a steady and rapid increase in the population. This is not a book on hygiene, but perhaps as practitioners for many years in various tropical countries we may be permitted to recommend anyone anxious to reduce the death-rate of a district to study the factors which contribute to the local infantile mortality, and to combat those of greatest importance, which will often be found to be tetanus and diarrhœa, the latter being associated with the question of a pure milk supply.

Enough, perhaps too much, has now been written as regards lines of thought associated with the word eugenics as applied to the tropics, and we will now pass on to consider the incidence of disease in tropical countries.

INCIDENCE OF DISEASE.

In previous editions we gave in considerable detail the analysis of the causes of death in Ceylon, and their incidence in the various peoples inhabiting that island. Several years have passed since these figures were compiled, and as they are old we omit them, and take a general view of the distribution of disease in tropical countries.

DISTRIBUTION OF DISEASE.

Asia.

Asia Minor is not a tropical country, as it possesses cold and prolonged winters, but it also has very hot summers, during which it resembles the tropics, and becomes the home of many diseases, such as malaria, enteric fevers, dysentery, and often cholera, while diphtheria is usually present, and cerebro-spinal meningitis is by no means unknown. Goitre and cretinism exist in the Valley of the Upper Euphrates.

In *Mesopotamia* the winters are temperate, but the summers are very hot, and heat-stroke is well known, while malaria, the enteric fevers, dysentery, and cholera are present. Plague is said to have been endemic in this region for years. Typhus, smallpox, measles, whooping-cough, and, it is said, scarlet fever, occur there. Bagdad sore is almost too well known to be mentioned, while beri-beri occurred in the siege of Kut, and also among other troops.

In *Arabia*, in addition to the fevers mentioned above, ophthalmia is to be noted.

Very little is accurately known as to the diseases of *Persia*, though we possess a large manuscript written thereon many years ago. Cutaneous Leishmaniasis, leprosy, and some form of relapsing fever may be noted.

As regards *India*, in the Bombay Presidency the infantile mortality in native races is 220·08 in males and 219·07 in females per 1,000 births. In Bombay City the ratios were 557·24 and 569·66, but it is stated that these ratios are very fallacious.

The racial death-rates are:—

	1905.	1906.
Europeans	14·36	14·41
Eurasians	20·89	26·99
Natives	31·84	41·39

The year 1905 seems to have been unusually healthy; only 588,394 natives died, as compared with 1,318,783 in 1900.

The principal cause of death was plague, which accounted for 71,363, or 12·13 per cent., in 1905, as compared with 223,957, or 29·28 per cent., in 1904.

The plague deaths in Bombay for the ten years 1896-1905 are as follows:—

1896	2,086
1897	46,944
1898	86,191
1899	96,596
1900	33,196
1901	128,259
1902	184,752
1903	281,269
1904	223,957
1905	71,363
Total	1,154,613

The population in 1901 was:—

European (exclusive of cantonments)	18,804
Eurasian	6,557
Native	18,481,362

The above figures will thus give the reader some idea of the mortality caused by the plague in India.

The next important cause of death is cholera:—

1896	35,404
1897	57,109
1898	4,368
1899	8,579
1900	163,889
1901	13,600
1902	3,229
1903	1,825
1904	13,156
1905	5,396

The general term 'fever' causes a mean of 310,420 deaths in the six years 1900-1905; most of this is supposed to be malaria.

The simplest way to show the Bombay death-rate is in the ratio per 1,000 inhabtiants:—

Cholera	2·11
Smallpox	0·26
Plague	9·18
Fevers	17·43
Dysentery and diarrhœa	4·90
Injuries	0·39
Other causes	12·12
Total	46·39

Respiratory disease in 1904 caused 3·22, and in 1905 2·95, deaths per 1,000 of the populatoin.

The Bombay death-rate indicates clearly the incidence of cholera, plague, and fevers. In many parts of India—*e.g.*, Madras—kala-azar is an important death-producing factor. In Calcutta, phthisis is causing some apprehension by its increase. The importance of snake-bite as a cause of death is marked in India. Relapsing fever is also known.

Ceylon possesses a high infantile mortality, of which the principal factors are infantile diarrhœa and convulsions, and often the bad condition of the mother *before* the birth of the child, associated with improper and bad food, and lack of proper care of the child. Eugenics requires more study in that island than, so far as we know, it has received.

The deaths of women in child-birth are high, and the principal cause is puerperal fever.

Among adults diarrhœa, dysentery, and the various forms of enteric fever are important factors of the death-rate. Plague has recently visited the island, but has been well controlled; cholera is present from time to time; while systematic steps have been taken to deal with the prevalent malaria and ankylostomiasis. Cancer exists in all races, and diabetes is a prevalent disease among better-class natives, such as lawyers, doctors, and merchants. Syphilis is common, though the parasyphilitic diseases are very rare, while insanity is also relatively less than in Europe. Leprosy is endemic, and eye diseases frequent; though, thanks to the Victoria Eye Memorial Hospital, where they are skilfully treated, blindness is less frequently met with.

With reference to the Straits Settlements, the infantile mortality, after deducting immigrant deaths, is 250·29 per 1,000 births in 1905, and is racially classified as follows:

Europeans	57·32
Other nationalities	224·07
Malays	229·78
Indians	278·72
Chinese	302·03
Eurasians	307·69

The general death rate was 40·51 per 1,000 inhabitants, and its factors, phthisis, beri-beri, unclassed fevers, dysentery, cholera, malaria, cancer, anæmia, sprue, dropsy, and parasites.

In Indo-China the enteric fevers, the diarrhœas and dysenteries, liver abscesses, intestinal parasites, cholera, diphtheria, spreading ulcer, which used to be called Cochin China ulcer, scurvy, purpura hæmorrhagica, beri-beri, dengue fever, and parasites, are to be mentioned.

Much has been written on the diseases of China, where Manson and Cantlie did their work, and its diseases are beginning to be known; but of special interest are its trematode infections, its beri-beri, its plague, and its skin diseases.

Japan is now the centre of much scientific work, and no passing reference would do justice to the valuable work being performed therein; but it may be noted that it is interesting in its parasitic diseases, its tsutsu-gamushi disease, its trematode infections, its fuguismus, its rat-bite and cat-bite diseases, and its beri-beri.

The Philippine Islands are monuments of American carefulness, forethought, and hard work, and their diseases are well set forth in the valuable *Philippine Journal of Tropical Medicine*. Especially to be noted are their parasitic affections, their beri-beri, and though much remains to be done, yet much has been done with regard to malaria and smallpox, which has been reduced to insignificant proportions, while tuberculosis, cholera and plague, and the enteric fevers, are present, and the whole problem of eugenics is still in its infancy.

Australasia.

The diseases of tropical Australia, which includes Queensland, Papua, Torres Straits, Thursday Island, etc., are:—Sprue, amœbic dysentery, filariasis, malaria, beri-beri, ulcerative granuloma, frambœsia tropica, dengue fever, leprosy. The intestinal parasites are:—*Ancylostoma duodenale, Trichuris trichiura, Oxyuris vermicularis, Strongyloides stercoralis*, and *Tænia saginata*.

Under the term 'sandworm disease,' Breinl describes an inflammation of

the inner side of the sole of the foot in the Innisfail and Cairns districts, which, beginning as a small erythematous area, spreads in the form of spirals, and after a time disappears. No animal parasite could be found. It appears to us that this is a form of 'creeping eruption.' He also describes 'barcoo rot.'

Seligmann, during the eighteen months which he spent in British New Guinea and the islands of the Torres Straits in the years 1898 and 1904, gathered much information as to the incidence of disease among the Papuo-Melanesians of Papua, who are really only just emerging from the Stone Age.

He found talipes equino-varus to be common, while hare-lip, meningocele, dwarfism, albinism, and erythrism (*i.e.*, aborigines with auburn or reddish-brown hair, pinkish-brown skin, and brown eyes) occur. Albinism and erythrism showed a family distribution.

Malaria was common, and children with greatly enlarged malarial spleens were easily found. Adults with large spleens could also be seen, but this enlargement might not be malarial. Leprosy was endemic in the valley of the St. Joseph River—*i.e.*, in the Roro-Mekeo district—and could not be attributed to foreign influences. Yaws was common, but syphilis was considered to have been introduced in comparatively recent times; in fact, he is of the opinion that in Oceania the introduction of syphilis is possibly not antecedent to Captain Cook's voyages. Respiratory diseases and dysentery are very common, as are skin diseases—*e.g.*, eczema, tinea imbricata, tinea flava, keratosis pilaris, and leucoderma. With regard to new growths, he records cutaneous papillomata, fibromata, lipomata, osteomata (?), and angiomata. Malignant tumours were rare, but sarcomata were found. He describes and illustrates subcutaneous nodules freely movable over the deep fascia, over or near bony prominences, and especially about the elbow, which are probably juxta-articular nodules. He describes and illustrates a nasal ulceration somewhat similar to gangosa, variously referred to as lupus by Sir William MacGregor and cancer by the white residents of British New Guinea. He also describes a peculiar ulcerative process of the legs and other parts of the body. He draws attention to the impulsive character of the people as a crime-producing factor. Paralysis and psychoses are not common. The presence of cretinism was noted. He did not meet with tuberculosis except in natives in intimate contact with Europeans, nor with arterio sclerosis, valvular heart disease, rickets, or gout, locomotor ataxy, or general paralysis, while anæmia was rare.

Oceania.

This is interesting for its diarrhœas, dysenteries, and elephantiasis, which have been studied in detail by Baker; for its yaws, leprosy, and skin diseases, which latter are common, and of which tokelau and ringworm may be especially noted.

Syphilis is believed to have been unknown in the Sandwich Islands before the visit of Cook in 1779, while leprosy is believed to have been introduced therein in 1830 by Chinese emigrants.

Epidemic gangrenous rectitis and a similar form of stomatitis occurs according to Corny in Fiji. Cerebro spinal meningitis was introduced probably about 1876.

Tropical America.

The tropical medical schools situate in Harvard University and in other parts of the United States, the work of the American Society of Tropical Medicine and of the Canal Zone Medical Association, added to the researches of the Institute Oswaldo Cruz of Brazil, are steadily increasing our knowledge of the diseases of tropical America, among which malaria, yellow fever, the enteric fevers, the dysenteries, elephantiasis, Chagas' disease, Leishmaniasis, verruga peruviana, parasites, yaws, and certain skin diseases, stand out as pathological features, among which must be given prominence to those caused by the jigger.

Moreover, it is in tropical America that the most brilliant prophylaxis with regard to malaria and yellow fever has been conducted.

With regard to *Northern Mexico*, Aleš Hrdlička made six expeditions in the years 1898-1905 to study the physiological and medical conditions of the Amerinds residing in Northern Mexico and in the south-western portions of the United States.

He concludes that on the whole the health of these people is superior to that of whites living in larger communities, as they do not suffer so much from inherited morbid conditions, or from those connected with teething, puberty, menstruation, gestation, puerperium, menopause, and senility, nor do they suffer so much from malignant growths, but they have a weak resistance to a few contagions—*e.g.*, smallpox.

Their most common ailments are diseases of the gastro-intestinal tract, especially dysentery; of the respiratory organs, especially pneumonia, while consumption is very rare; of the eyes, especially ophthalmia due to dust, which, being neglected, leads to blindness, as does smallpox; of muscular rheumatism and arthritis. Malaria, smallpox, and pemphigus contagiosus in children are very common. Typhoid fever appears to be rare; leprosy and elephantiasis are known, as is goitre.

He very much doubts the presence of syphilis prior to Columbus, and points out that the bones in the ancient graves in California, on the north-west coast, in Peru, and other localities in South America, do not show any signs of the disease, even when thorough examinations of extensive osteological collections have been made.

In children the common cause of death is diarrhœa. He makes most interesting observations on the mites which burrow under the skin of the toes in the Huastec, who live to the east of the Otomi (Hidalgo region), and which may cause suppuration and even loss of a toe. Injuries due to spiders, centipedes, scorpions, rattlesnakes, and the gila monster are mentioned, as well as poisoning from aconite, datura, and fungi. The narcotic effects of Peyote are noted, while two plants, cul-ick-um-ek (*Donedia suffrutescens*) and hā-van tātat (*Phacelia infundibuliformis*), cause dangerous wounds when journeying through forests, leading to some form of poisoning, and in the case of the former even to death. He met with albinism and leucoderma, but pinta was unknown, though stated to occur farther south. The diseases which were rare were: anæmia, diseases of breast, circulatory organs, liver, female generative organs, and skin; while asthma, dental caries, cancer, rickets, hernia, idiocy, insanity, nervous diseases except epilepsy, scarlet fever, and fracture of bones were also rare.

With regard to the *Virgin Islands*, Butler and Hakansson have pointed out that malignant tertian and quartan malarias are present, but that the carrier anopheline has not been identified, while pellagra is quite common and ankylostomiasis is present. The lack of sanitation causes considerable morbidity and mortality, and there is a high illegitimacy rate, venereal disease rate, and infantile mortality, while the poor food conditions are held to be the cause of pellagra, and the poor sewage disposal and defective water-supplies to encourage diarrhœa, dysentery, enteric fevers, and the encouragement of mosquitoes to breed in houses causes the high filarial infection and its associate morbidity.

Ecuador has been studied by Espinosa-Tamayo, who finds *Ancylostoma duodenale* and *Necator americanus* present, as well as *Oxyuris*, *Tænia solium*, and *Hymenolepis nana*. The jigger is noted and so is *Xenopsylla cheopis* and *Clinocoris rotundatus*. Yellow fever has almost disappeared, but malaria, amœbic dysentery, enteric fevers, and tuberculosis, are rife. Chichismos caused by drinking 'chicha made from fermenting maize is said to be like pellagra.

Tropical Africa.

The outstanding features of tropical Africa are its trypanosomiases, its malarias, and its relapsing fevers, while enteric fevers and typhus are more prevalent in the north, where the schistosomiasis and pellagra also abound. Porocephalosis is likewise a feature of this country, which is the home of numerous local diseases, such as guondou, while skin complaints are extremely common.

Whether or no cerebro-spinal meningitis originated in Central Africa is an interesting speculation.

The primitive forms of medicine, the venomous animals, and the poisons are all of great interest and require much further research.

PREVENTION.

It is not our intention to write upon prophylaxis in this portion of the book, but merely to indicate that many diseases exist in the tropics which medical research has shown to be due to definite parasitic organisms spread in a very definite manner, and therefore more or less preventable.

We would venture respectfully to quote His Most Gracious Majesty King George V., who long ago said:—"*If preventable, why not prevented?*" We would further venture to ask that more regard should be paid to this memorable utterance, which we believe will echo down the rolling centuries and will be more and more appreciated as they pass.

We would, however, ask the reader to remember that to prevent disease entails hard unappreciated work, usually in the face of much opposition and in direct contrast to the comfortable life of letting things drift; but in the light of His Majesty's words this work should be taken up by his subjects.

Moreover, the present war has shown what can be done when military authorities work hand in hand with medical research, and we are of the opinion that civilian Governments should learn this lesson also.

It is, indeed, a satisfactory sign that the Secretary of State for India is reported as stating, in a remarkable speech made to a British Medical Association deputation, that a modern Government required and should take all suitable means to obtain the best and most accessible advice on various medical and sanitary problems with which every such Government is called upon to deal. If this dictum is acted upon—*i.e.*, if it passes the realm of advice—a new era will dawn in the tropics.

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CHAPTER VI

FITNESS FOR TROPICAL LIFE

Preliminary—Examination—Women—Invaliding—Natives—Life assurance —Expectation of life in tropical natives—References.

PRELIMINARY.

THE selection of European and American men for service in the tropics, the fitness of European and American women for tropical life, the question as to how long white children should remain in warm climates (Chapter LXXXVI.), the invaliding of sick persons of all races, the selection of natives for employment under Governments or in mercantile houses, and the problems of tropical life assurance, are all matters of great importance to the tropical practitioner.

He may have nothing to say in regard to the selection of persons for tropical service, but he has very considerable knowledge of their after medical history.

We are unable to allow much space in the present book for the consideration of these questions, but we will endeavour to touch upon such points as appear to us to be of importance, and to leave the elaboration of the same to the reader, and for this purpose we give references at the end of the chapter.

EXAMINATION.

We presume that every medical practitioner appointed for the purpose of selecting men for service in the tropics will go faithfully through a routine examination more or less based upon that adopted by the best type of assurance companies, and therefore we need not lay stress upon such an examination; but there are certain points to which we desire to invite especial attention.

First-Class Lives.—Every selected candidate be a first-class life and *free from any trace of albumen* in the urine.

Venereal Disease.—The examining physician should make it his duty to exclude *gonorrhœa*, not by mere question, but by actual examination, and the same is true for *syphilis*. No one should be allowed to proceed for the first time to the tropics with an uncured gonorrhœa or with an imperfectly treated syphilitic infection.

Further, we are of the opinion that it is the duty of the examiner to warn all selected candidates as to the dangers of infection with venereal disease in the tropics, and at the same time to give and to read to him *printed instructions*, similar to those provided to-day for soldiers, detailing methods for prevention of infection.

Every tropical practitioner knows how much sickness and loss of work is due, directly or indirectly, to venereal disease; and we feel that it is not too much, in the interests of the employer and the employee alike, to ask that the above should form part of the duties of every medical examiner of candidates destined for the tropics. We further submit that each health report should state clearly that these duties have been carefully carried out by the examiner.

Vaccination.—It is necessary that every selected candidate, before final appointment, should produce a certificate that he has received two injections of a vaccine prophylactic against typhoid and the paratyphoid fevers, or of a so-called tetra- or penta-vaccine containing in addition to the already mentioned three diseases, cholera or cholera and plague. Evidence of Jennerian vaccination forms part of the routine medical examination, and must not be older than seven years.

Quinine.—Every selected candidate, before final appointment, should produce a medical certificate that he is able to take a dose of 10 grains of quinine without developing serious symptoms.

Teeth. No candidate should be finally selected for the tropics until his teeth are in such a condition as to satisfy the examiner, or until he produces a dentist's certificate to the effect that they are in good order.

Alcohol.—The objections to alcoholic candidates are so well understood that the mere mention of this point is sufficient (see Chapters III., V., and LVI.).

Age.—We are convinced that no one under twenty-one years of age or over fifty years should be allowed to proceed for service for the first time in the tropics. We are also of the opinion that the nearer the minimal age is to twenty-five years the better for employer and employee alike.

Heat and Sun.—Whatever personal views the examiner may have as to the effects of heat and sun, he should nevertheless, as part of his duties, warn the selected candidate as to the possible dangers of careless exposure to the tropical sun and as to the effects of tropical heat, and should acquaint him with methods of prophylaxis. He should also give advice on clothing, as we have seen distinguished visitors arrive in the tropics in clothing suitable for an English winter. There are, of course, cold regions and cool seasons in the tropics, but the cold is not generally felt by the new arrival from the Temperate Zone.

Energy.—The selected candidate should be warned that, on first arrival, he may not feel the heat of the tropics to be excessive. On the other hand, he may feel that the climate suits him admirably, and that he is full of energy for work and play, and should be told that this state of affairs will not last for ever, and that, if he allows his energy to outrun his common sense, there will be trouble.

Moderation in all things should be indicated as the motto for a tropical life.

Duties of the Examiner.—We have insisted upon the medical examiner giving advice upon various points to the selected candidate. Our reasons for so doing are because he may be the only medical practitioner to examine the candidate before the tropics are reached.

We feel that it is in the interests of employer and employee that every opportunity should be given for the selected candidate to keep fit until he reaches the local medical officers.

Check Examination.—We are of the opinion that a check medical examination by the local medical officers immediately upon the arrival of the new official is advisable, in order to see whether entry into the tropics has induced any changes in his health, and also for the purpose of giving him local medical advice.

This check examination is very necessary, as we know that persons have arrived slightly indisposed, and have allowed these slight symptoms to become serious owing to lack of knowledge.

WOMEN.

European and American women proceeding to the tropics are usually either married or about to be married, or, because of the scarcity of white women therein, are very likely to be married fairly soon, although they may start as nurses, missionaries, etc.

We therefore consider that all women proposing to live in the tropics should be medically examined in the same way as men, and should be specially tested as to their ability to stand quinine therapy; and if this is found wanting, should be educated up to a necessary quinine standard, by regulated small doses, before being allowed to begin their new life.

Our experience makes us agree with Mrs. Scharlieb that the medical examination of women should include the bony pelvis and the organs contained therein when practical.

Often women have to live in out-stations far from medical aid, and it is little short of criminality not to take the external measurements of the pelvis, and if necessary to investigate the condition of the internal pelvic organs by means of a rectal examination. If abnormalities are discovered the woman or her husband, or both, should be warned as to the possibilities of such abnormalities.

At such an examination care should be taken to see that there is no obvious cause for dyspareunia, as it may cause trouble to the examinee and her husband. This has been brought home to us in our long experience of tropical practice.

Moreover, the woman should be warned as to the possibility of menorrhagia (or the much less common amenorrhœa), which may begin after arrival in warm climates, and should be given advice as to clothing.

The necessity of having the urine examined on the occurrence of pregnancy should be impressed upon the wife and her husband, as well as the requirements of diet, exercise, rest in the warmer hours of the day, etc.

White men, as a rule, require at regular intervals visits to temperate climates if their health, strength, and mental vigour are to be maintained unimpaired; and the same holds good, but perhaps with more force, for women, who should be allowed leave to cooler tropical regions and to the Temperate Zone as often as circumstances permit. When a woman returns to a temperate climate she should be advised as to the necessity of an immediate medical examination, as well as of the dangers of the change into cooler weather.

INVALIDING.

Two classes of cases require to be considered under this heading – viz., the *tropical resident* about to be invalided to cooler climates, and the *cool-climate resident* about to be sent to the tropics for the benefit of his health.

With regard to the first, there are two quite different aspects of the case, viz.. –

(*a*) **Invaliding for the Good of the Employer and Employee Alike.** —This is a matter of common sense, and is the kindest method of dealing with many cases.

(*b*) **Invaliding because of Health.**– Temporary invaliding or sick leave should always be advised if the patient's health requires it, but his financial status should also be taken into consideration before too drastic recommendations are made.

More difficult by far is the question of permanent invaliding from service, and in coming to a decision the medical practitioner has many points for consideration with reference to the present condition of the patient and his future prospects.

The nature of the illness, the physical and mental condition of the patient, his age, his pension or gratuity, his possibilities of future employment in cooler regions, his family, etc., have all to be considered.

Among the many difficulties which present themselves under this heading we venture to express the opinion that one attack of *blackwater fever* should not constitute *per se* a reason for permanent invaliding.

On the other hand, we are of the opinion that *mental symptoms* should constitute a reason for permanent invaliding, as the tropics are climatologically unsuited for an unstable nervous system.

As a general rule, if an endemic infection– *e.g.*, bilharziosis– is playing havoc with a patient, he should be permanently invalided from that particular area or areas, which may not mean that he should be invalided from the tropics or from the service.

NATIVES.

Natives should never be accepted for employment unless they are first-class lives. The eyes require careful attention, and colour-blindness should be looked for, especially in certain employments such as railways, steamers, ports, etc.

Particular attention should be paid to the urine, and natives know many tricks with regard to this part of a medical examination.

Schistosomiasis of any part of the body should cause rejection, and diffuse leucoderma if the candidate is to work in the sun, but it is not possible to give further details, which must be left to the common sense of the examining officer.

The invaliding, temporary or permanent, of natives from a service, particularly if a pension or a gratuity is available, requires great care, and the possibilities of malingering must be remembered. On the other hand, the effects of such apparently harmless diseases as diffuse leucoderma should be borne in mind, and injustice should, if possible, be avoided.

LIFE ASSURANCE.

Tropical life assurance is in its infancy, and so far has been mostly studied in regard to India.

Insurance offices usually regard 33° north to 30° south latitude as including the dangerous climates of the world. They usually consider those lands which lie nearest to the Equator as the most dangerous, because of the heat, the endemic diseases, the lack of sanitation, and the imperfect food-supplies.

But the advance of knowledge with regard to the prevention and treatment of tropical diseases, and the dawn of tropical sanitation, has reduced, and is reducing, the baneful effects of many of these factors. For example, the West Coast of Africa used to have an official mortality rate of 80 per thousand, and an official invaliding rate of 95 per thousand, but these had been reduced to 21·7 and 76·3 per thousand as long ago as 1903, and to-day are probably much less.

It is true that the older type of official, medical and non-medical alike, disliked spending money upon improved sanitation and upon the prevention of disease; but this type of official is slowly but surely disappearing, and the danger to-day is that official inertia may undo years of official toil.

It is therefore necessary that a high standard of sanitation and disease prevention should be set for the tropics, and that this should be maintained; and if this is done, then many of the serious objections to tropical life assurance may be removed or abated in the future, and as this is done better assurance terms should be forthcoming.

Very many tropical practitioners have had experience in the selection and rejection of tropical candidates for life insurance, but, unfortunately, there are but few records to be found based upon this work.

In 1897 and later, Cantlie, writing with regard to this matter, stated that although the person in the tropics was exposed to many deadly diseases, he was not very liable to scarlet fever, rheumatism, and pneumonia, and that, excluding malaria, his chief dangers were diseases affecting his alimentary canal and abdominal organs, and that alcohol was an even greater curse in the tropics than in temperate climates.

He states that the insurance companies deal with each case individually, and he suggests that during the first seven years of residence in a proscribed area an extra premium should be paid, but that after that period it should be reduced to one-half upon a certificate from the company's medical officer that no permanent injury to health has been incurred, and that the cost of this examination should be paid by the insurer. Further, after ten years' residence the extra premium should be reduced to one-third of the original sum, and after thirteen years no extra premium should be charged, provided always that the necessary certificate was forthcoming.

He points out that a period of danger is the first year or two after the old tropical resident takes up his permanent abode in the Temperate Zone, and he recommends that an extra premium be charged for these two years.

The next paper, published by Winter in 1909, we have been unable to peruse in the original, but he apparently lays stress on the first few years of residence in India, on the ground that Europeans are very likely to become victims to enteric and similar fevers.

Caddy in 1912 came to the conclusion that the European does not acclimatize well in the tropics, meaning by this statement that he is unable to rear healthy strong children in India, and that he becomes debilitated by residence there, requiring a change to a temperate climate every four or five years, and that after years of residence he is even more liable to sunstroke than on arrival.

Out of 1,799 cases he rejected 6 per cent. and loaded 8 per cent., making together 14 per cent., which was caused by inferior physique, obesity, glycosuria, albuminuria, consumption, consumptive family history, bad family history, syphilis, heart disease, sundry diseases (3·39 per cent.), alcoholism.

With regard to natives desiring insurance, it is true that years ago it was only the Europeanized native who sought after this; but to-day it is different, and even native women of due social standing are allowed assurance, provided that careful inquiries have been made, though years ago such an assurance was never considered.

Caddy adds to the list of causes of rejection 'elephantiasis,' and he is of the opinion that opium and hemp are very harmful, but that they are not commonly consumed by the insuring classes of India.

He considers that Rajahs, wealthy landowner Marwaris, or bankers and money-lenders, and petty merchants, are bad lives, while the best native risks are Government servants and native clerks in European offices.

As a rule the native does not consume alcohol, but if he does he should be regarded an indifferent risk.

He also states that the native of India is a shorter man than the European, and that height for height he is about the same weight, but he is very subject to glycosuria and to hydrocele.

The discussion on this paper was interesting, and in our opinion some of his views are open to criticism.

With regard to life assurance in Egypt, the only publication with which we are acquainted is by Day, who distinguishes four groups of proposers—viz., the Western European, the Southern European, the Eastern, and the Egyptian.

In general, he considers the first class to be a good risk on the same terms as in Europe, but with regard to the second he considers that they should be examined in their own homes, and each case should be judged on its own merits, and the third class is intermediate in risk between the second and fourth.

The native Egyptian appears to be a great difficulty, owing to the paucity and unreliability of the family history, while sexual excess and cigarette-smoking are considered to balance the lack of alcoholic excess. Rheumatic fever, tuberculosis, and syphilis are rife, and he is liable to many tropical diseases, including ankylostomiasis, pellagra, splenomegaly, relapsing fever, typhus fever, and the schistosomiases, so that he is not a good risk until education and sanitation improve matters; but Day says a proposer then in good health, and whose children are successfully reared and whose education has been sound, may be accepted for a whole life on European terms, but this was contested during the discussion on his paper.

The common sense of the whole matter is that there is an increased risk on the life of the European living in the tropics, and that it is most marked during the earlier years of his residence; there is a considerable risk in insuring native men, and that this is greatly increased when considering native women.

EXPECTATION OF LIFE IN TROPICAL NATIVES.

The expectation of life in India compared with the same for England may be gathered from the following table obtained from Hardy via McCay's book:—

Age.	*India.*		*England.*	
	Males.	*Females.*	*Males.*	*Females.*
0	24·6	25·5	43·7	47·2
5	37·1	30·1	52·7	54·9
10	35·5	34·4	49·0	51·1
15	32·3	31·7	44·5	46·5
20	29·2	29·3	40·3	42·4
25	26·3	27·0	36·3	38·5
35	21·1	22·4	28·9	31·2
45	16·5	17·9	22·1	24·0
55	12·2	13·2	15·7	17·2
65	8·2	8·7	10·3	11·3

The figures speak for themselves, but they were compiled years ago, and it is possible that more modern tables might show a better expectation of life.

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PART II

THE CAUSATION OF DISEASE IN THE TROPICS

PHYSICAL CAUSES
CHEMICAL CAUSES
PARASITES

SECTION A

PHYSICAL CAUSES

TEMPERATURE AND HUMIDITY
PRESSURE AND RADIATION
TRAUMATISM

CHAPTER VII

TEMPERATURE AND HUMIDITY

Preliminary—High atmospheric temperatures—Conclusions—References.

PRELIMINARY.

HAVING finished with the introductory portion of our task, we enter upon the second part of this book, which is devoted to the *causation of disease,* and is therefore essentially pathological. This subject is divided into three sections, embracing the physical, chemical, and parasitic causes of tropical diseases.

HIGH ATMOSPHERIC TEMPERATURES.

The present short chapter is confined to a brief consideration of the pathological effects of high atmospheric temperatures, which are the most important physical causes of disease in the tropics, and are only markedly evident when there is a definite amount of atmospheric humidity; and therefore we have entitled this chapter Temperature and Humidity.

To exemplify what we mean we will quote a concrete example. In a certain tropical locality there were the usual high air temperatures with relatively low humidity and cool nights until about the middle of a month, when the temperature rose to 116° F., the humidity increased, the sky became cloudy, and for twenty-four hours there was little breeze. During this period about fifty laboratory animals died, though well protected from the sun by living in large brick houses. They showed post-mortem the typical signs of heat-stroke—viz., the congestion of the meninges and brain, and the marked congestion of the lungs, which were almost black with stagnated blood. During this period there were a few deaths in the population of the place from the same cause.

Clinical experience has shown that there are two different pictures associated with the pathological effects of high air temperatures. The first picture is that of extremely high fever, and is called *heat-stroke;* while the second is depicted by collapse and low bodily temperatures, and is named *heat-syncope.*

We have investigated these two conditions experimentally. It was our practice in our journeys from Ceylon to Europe to test the effects of high air temperatures upon ourselves, and such of our fellow-passengers as took an interest therein, when passing through the Red Sea in the hot months thereof.

The air of the engine-room in steamers is laden with aqueous vapour, and certain corners can be found near the condensers with high air temperatures and practically no draught—or, in other words, with conditions analogous to those under which Haldane performed his experiments which we have mentioned in Chapter III.

When the steamer is in the hottest part of the Red Sea in a warm month, if a person, lightly clad and in good health, places himself in such a corner, with a clinical thermometer in his mouth, it will be found that at first he begins to sweat violently, and for a time remains at a normal temperature. But in due course his temperature will gradually rise and his pulse-rate increase, until temperatures of over 102° F. are reached, and the person breaks off the experiment because he feels uncomfortable, after which his temperature slowly returns to normal.

We have performed this simple experiment several times, but on one occasion, in a person who was not in very good health, the temperature, after reaching 101° F., ceased to rise; the skin became cooler, the tension of the pulse altered remarkably, and he began to look ill. The experiment was quickly stopped and stimulants administered, so that he did not suffer any serious effects, though it was some hours before he felt quite right.

These two experiments show that a high atmospheric temperature can act in two ways. In the first there was a gradual rise of the body temperature, which, if continued long enough, would probably have resulted in hyperpyrexia. In the second, after an initial rise, the heart became embarrassed, and if the heat had been continued, there appears no reason to doubt that this person would have passed into a condition of syncope.

There are, therefore, two distinct clinical entities to be considered—viz., heat-stroke, characterized by high bodily temperature; and heat-syncope, in which there are symptoms due to cardiac failure but no fever, both of which are brought about by the same cause—viz., high atmospheric temperatures associated with moderate or high humidity.

Such are our views; but it is as well for the reader to be acquainted with those of other authors, which may be briefly stated in an historical account as follows:—

High air temperatures, whether in the day time or at night, have been known since ancient times to have an effect upon human beings. The case of the child of the Shunamite woman described in the English Bible in 2 Kings iv., from verse 18 onwards, is probably the earliest on record. The child complained to his father of his head when out with the reapers, and was carried to his mother, and is reported to have died at twelve noon—became insensible—but recovered under Elisha's treatment, which appears to have been of the nature of massage. This treatment reminds one strongly of the active friction by which the miners of the Comstock Silver Mines of Nevada are said to treat successfully those of their fellows who faint when coming out of the warm mine in which the hot, steamy air has a temperature of 128° F.

It has been said that though old writers such as Dio Cassius described these conditions, the medical writers of ancient times were silent about them. This does not seem to be quite just, for Paulus Ægineta, Oribasius, and the Arabians certainly understood that there were head symptoms which they called 'siriasis' (after Sirius, the dog-star), due to excessive heat. Certainly this knowledge was lost, and Cardanus, in the sixteenth century, describes symptoms due to morbus attonitus (apoplexy) brought about by the heat and drought of the summer of 1543 in Florence. After this for a long time the disease was considered to be an apoplexy till Boerhaave, early in the eighteenth century, introduced the name 'insolatio,' and considered it to be a phrenitis—*i.e.*, meningitis.

Steinkühl (1819) thought that the congestion of the lungs caused death by asphyxia; Swift (1854) that it was due to exhaustion produced by fatigue; Hill (1857) evidently confounded pernicious malaria and heat stroke. Levick (1859) suggested that it was an acute specific fever; H. C. Wood (1863) considered that it was due to a poison developed in the blood, and called it thermic fever; while Stiles (1864) performed experiments on animals, and concluded that the disease was due to the direct effect of heat on the muscular system.

In 1869 Eulenberg and Vohl stated that the disease was due to sudden liberation of the gases in the blood; and Weikard and Richardson attributed it to clotting of blood in the vessels.

In 1870 Vallin performed several experiments by locally heating parts of the body, and concluded that there were two conditions: (1) sthenic insolation, due to coagulation of the muscle fibres of the left ventricle; (2) asthenic insolation, due to the action of heat on the nerve centres of the brain, thus disturbing the innervation of the heart.

In 1871 and 1872 Claude Bernard performed some experiments which tended to show that when a warm-blooded animal died as the result of heat, it was due to rigor in the musculature of the heart.

In 1872 H. C. Wood performed experiments which showed that sunstroke could be produced in animals as readily as in man by artificial or natural heat.

He came to the conclusion that death took place from asphyxia, and that after death the rigidity of heart and muscles was due to the coagulation of the myosin, and he further pointed out that this will take place at once in the heart if the temperature of the body reaches 115° F., and said that he considered it to be the cause of sudden deaths in soldiers in battle. Further, he pointed out that the heating of the brain of a mammal to 108° F. produces insensibility, with or without convulsions, and that when 113° F. was reached the animal died, and that, though the general symptoms of sunstroke were absent, the nervous symptoms were present. He came to the conclusion that no capillary thrombi were formed, that no poisons were generated in the blood, and that the real condition was the heat acting upon the nervous system, as a result of which there was rapid metabolism, which used up oxygen and at the same time induced brain changes, causing asphyxia. But he distinguished from the true heat-stroke:—

1. Acute meningitis or phrenitis, due to exposure to the sun, in which he disbelieved.

2. Heat exhaustion, due to working in a heated atmosphere, which he said did not differ from acute exhaustion due to other causes, and therefore was not true sunstroke.

In 1879 Jacubash classified heat accidents into: (1) sunstroke due to the action of the sun on the body, when the temperature may reach 113° to 115° F. (45° to 46° C.); (2) heat-stroke, due to exertion, and often seen in marching troops in the Temperate Zone; (3) thermic fever, which he considered to be the true heat-stroke of the tropics, due to accumulation of heat in the human body in consequence of high atmospheric temperatures without exposure to the sun or muscular exercise.

Dony (1884) considered that there were two main conditions: (1) sunstroke, due to the sun's rays acting upon the cranium and brain, only without very great rise of temperature; and (2) heat-stroke, due to intense heat acting on the whole body and after certain prodromes, resulting in a rapid rise of temperature to a great height.

In 1893 Saquel classified the diseases into (1) sunstroke, meaning the erythema due to the sun's rays; and (2) insolation, meaning the action of the sun on the nervous system, producing either congestion (mild form in the Temperate Zone) or meningitis and encephalitis (severe form in the tropics); (3) heat-stroke; and (4) thermopeliosis, a combination of insolation and heat-stroke.

In 1898 Sambon defined heat exhaustion as an ordinary syncope, while he considers that under the term 'sunstroke' there is confounded an infectious fever which he calls 'siriasis,' due to some micro-organism as yet not defined.

In the period 1898-1907 Sir Patrick Manson, in his book on tropical diseases, recognized three conditions: (1) heat exhaustion—sudden cardiac failure or fainting, brought about by exposure to high atmospheric temperature; (2) siriasis, an acute disease developing in the presence of high atmospheric temperature, and characterized by sudden incidence of hyperpyrexia, coma; and (3) sun traumatism, or direct action of the sun's rays on the tissue, causing either sudden death or a febrile condition.

In 1905 Van Brero, in Mense's 'Handbuch der Tropenkrankheiten,' recognizes (1) heat exhaustion, due to excessive heat from the sun or other source; and (2) sun traumatism, caused by the direct action of the sun's rays.

In 1907 Sir Joseph Fayrer, in Allbutt and Rolleston's 'System,' recognizes (1) a state of exhaustion leading to syncope, and (2) an overheating of the nervous centres, blood, and tissues, leading to thermic fever.

In 1908 Brook defines diathermasia as the effect of heat on the thermotaxic mechanism, and phœbism, a kind of shock due to the actinic rays from the sun.

(For the continuation of this history see Chapter LVI.)

It will thus be seen that authorities in general recognize the action of heat and the action of sun's rays as being separate, and, further, that heat may produce a syncopal condition of fever, while the sun's rays may also cause syncope and fever. Some few, including especially Sambon, suspect the presence of an acute specific fever as being concealed in the diseases above mentioned. Others, again, consider the symptoms to be toxic in origin, so that there are four theories: (1) caloric; (2) actinic; (3) microbic; (4) toxic.

CONCLUSIONS.

Personally, we believe that high atmospheric temperatures with a sufficiently high atmospheric humidity and more or less stagnation of the air can produce the clinical pictures called *heat-stroke* and *heat-syncope*, especially in people working hard at manual labour and clad in unsuitable clothing.

As to the reason why some persons should develop these symptoms, while others living under exactly similar conditions escape, we believe it to be a matter of general health and personal habits, which in the one case disturb the metabolism of the body, causing a derangement of physical or chemical heat regulation, while in the other case this mechanism is working normally.

The regulation of bodily heat can be disturbed by anything which tends to derange metabolism or heat regulation, such as overwork, lack of care in protecting the body as much as possible from heat by the means indicated in Chapter III., p. 89, alcoholism, and the effects of bodily disease.

Muscular work is especially dangerous, as under certain conditions even a couple of sets of tennis may produce a temporary increase of the bodily temperature, which may rise as high as 101°-102° F.

If in addition to the deranged heat regulation there is added cardiac weakness or lack of vaso-motor control, then ***heat-syncope*** and not heat-stroke appears.

The essential pathological change producing death from heat-stroke is the partial coagulation of the globulin found in the cells of the body. It is possible that this coagulation takes place first in voluntary and cardiac muscles, thus leading to respiratory and cardiac failure, while later marked changes are to be found in the nerve cells, especially in the medulla, leading to chromatolysis.

The clinical description of these diseases will be found in the third part of this book, in Chapter LVI.

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CHAPTER VIII

PRESSURE AND RADIATION

Preliminary—Increased pressure—Diminished pressure—Radiation—Electricity—References.

PRELIMINARY.

THE present chapter is devoted to the study of the *pathological effects* of atmospheric pressure when considerably increased or diminished, and of the rays from the sun under conditions which produce disease.

If there are pathological effects, other than those already mentioned (p. 88), as the result of rays from the moon, they are unknown. Probably they do not exist, and possibly the effects already described may be due to the fact that the moon's rays when reflected become polarized.

A passing reference will be made to the effects of lightning, as death from this cause is not infrequent in the tropics.

INCREASED PRESSURE.

The work of facilitating trade by means of roads and railways throughout the tropics necessitates the construction of bridges across deep rivers, and therefore for many years to come the effects of artificially increased atmospheric pressure will be more obvious in these regions than elsewhere.

Moreover, for centuries tropical natives have been exposed to increased pressure when diving for commercial purposes, and though generally they do not remain down long enough to suffer any bad effects, still at times these are noted.

The effects of greatly increased atmospheric pressure are usually termed 'caisson disease,' because it was observed first in connection with the special compressed air apparatus used by engineers for work under water.

In 1878 Paul Bert, as the results of his experiments upon animals, showed that the extraordinary symptoms of this disease could all be explained by increased atmospheric pressure, but it is mainly by the labours of Leonard Hill that Paul Bert's work has been confirmed and made known.

Symptoms of the disease are rarely observed until a pressure of one atmosphere (15 pounds to the square inch) has been reached, but above that point the danger rapidly increases, and at two atmospheres the risk is very considerable.

The causation is due to the fact that the blood absorbs nitrogen from the compressed air, and this gas is retained in simple solution in the blood-plasma solely by the increased pressure. If, now, this pressure be rapidly diminished, the nitrogen is liberated in the form of bubbles in the plasma, and these in their turn block the capillaries and also tend to accumulate in the heart. The other gases, oxygen and carbon dioxide, have nothing to do with the causation, for obvious reasons, because oxygen would be rapidly absorbed by the tissues, and the other gas cannot be increased in the blood affected by compressed air.

Nitrogen is also held in solution in the tissues, especially in fat, and hence fat people are more susceptible to the disease.

Time is required to saturate the blood and tissues with nitrogen, and therefore the danger increases with the length of exposure.

The actual liberation of the bubbles of nitrogen will not take place until decompression is begun. If this is rapid, then the symptoms will be severe; if slow, they may be few or absent; but it has been found that danger depends upon relative and not absolute reduction. Thus, two atmospheres may safely be reduced to one, four to two, six to three, but three atmospheres cannot be reduced to one without danger.

Decompression should therefore be based upon reduction to one-half of that at which work has been done, and after that there is a considerable pause, during which muscular exercises are performed to rid the body of the nitrogen; and, again, a half-decompression, and so on, but each interval must be considerable.

As the symptoms are due to bubbles of gas, they are extremely varied, but pain and paralysis are the most marked, and should be treated by immediate recompression, followed by slow decompression.

The medical examination of persons about to work on these lines is most necessary, and all fat persons and those with any organic lesion should be rejected.

DIMINISHED PRESSURE.

The attention of tropical workers has been drawn of late to the effects of diminished atmospheric pressure as exemplified by able accounts of the mountain sickness of the Andes.

Normal atmospheric pressure in alveolar air, which is saturated with aqueous vapour, is 760 millimetres of mercury, of which 47 are due to the pressure of the aqueous vapour, and therefore the rest is due to air gases, of which oxygen, which is present in a proportion of 14·2 per cent., is responsible for 101 and carbon dioxide for 40 millimetres.

If the oxygen percentage in inspired air falls from 20·9 to 12 per cent., hyperpnœa takes place; if to 10 per cent., cyanosis appears and increased frequency of the heart; and at 5 per cent. there is loss of consciousness.

If the atmospheric pressure is reduced to 580 millimetres, the want of oxygen begins to tell upon the breathing, and the carbon dioxide pressure in alveolar air is also diminished.

Mosso and Aggazotti, noting the favourable effects of adding CO_2 to inspired air and reduced oxygen pressure, came to the conclusion that mountain sickness was 'acapnia'—*i.e.*, primarily due to deficiency in carbon dioxide—but the real facts are that Paul Bert was right in tracing it primarily to lack of oxygen, produced gradually. Mountain sickness usually begins about 6,000 to 7,000 feet, and is more marked at heights of over 10,000, but after a sojourn of one or two weeks the effects pass away. The physiological effects of high altitudes have been studied by Haldane, Douglas, and others, at a height of 14,000 feet and a barometric pressure of 457, when it was found that though persons became ill within half an hour of arrival, their symptoms were relieved immediately by inhalation of oxygen, and acclimatization took place within eight to ten days.

The partial pressure of CO_2 in alveolar air had fallen to 27 millimetres, and the carbon dioxide ventilation had increased considerably, and therefore the alveolar oxygen pressure was raised above what it otherwise would have been—*i.e.*, 52 millimetres.

The arterial oxygen pressure was 35 millimetres above oxygen pressure in alveolar air, and accounted for the disappearance of mountain sickness and for the bright red colour of the lips. On arrival it is little above that of alveolar air, therefore acclimatization depends upon the development of the powers of the epithelium of the lung alveoli to actively secrete oxygen inwards, a power which does not exist during rest at sea-level.

The hæmoglobin is increased in a few weeks' residence to 115 to 154 per cent., as indicated by the Gowers Haldane scale; and this slow increase is associated with a slow increase in the total hæmoglobin of the body and a slight increase in the blood volume.

The red bone marrow is increased in amount (as shown by experiments on dogs by Zantz), and there is new formation of red corpuscles and a diminished alkalinity of the plasma for unknown reasons.

RADIATION.

Radiation from the sun, of heat and chemical rays, is potentially an important factor in producing pathological conditions in man residing in all climates, but more particularly in the tropics.

In temperate climates its heat effects have been especially studied by Rubner, Cramer, and Wolpert, who state that, adding half the number of degress of difference between the register of the black bulb thermometer and that of the shade thermometer to the shade temperature, one obtains a figure which corresponds to the thermic effects of the sun. This calculation in the tropics gives a temperature considerably above that of the body, but the only exact method of measuring the caloric value of radiation from the sun is the *pyrheliometer* of *Angstrom*, as used in Manila by Aron. Schmidt estimates the heat effect of the tropical sun as being equal to 2 small calories per square centimetre per minute.

Now, the animal body having a much higher coefficient of absorption of heat than has the air, is capable of absorbing these rays, and hence of becoming hotter; therefore in this way exposure to the sun tends to make the body hotter and helps in the production of the heat-stroke already considered in the last chapter.

It is, however, with the chemical rays that we are more concerned in the present section, and as yet there are but few observations on this subject in the tropics.

The earliest experiments, with a view to ascertaining definitely whether there is such a condition, were those by Scaghosi on rabbits exposed to the Sicilian sun. Their temperature rose considerably, and if the experiment was continued long enough they died, but if it was stopped they recovered. The post-mortem changes were hyperæmia of the meninges, heart, lungs, liver, and spleen. The nerve cells of the brain and spinal cord showed coagulative necrosis and chromatolysis.

The next experiments of importance on the ætiology of this condition are those of Möller on rabbits, who showed that thermal rays, with or without chemical rays, if directed on to the skin covering the skull, produced more or less intense cerebral disturbance, and sometimes even sudden death. The autopsy after intense irradiation showed the skin of the head much swollen and bloody, with gelatinous exudation in the subcutaneous tissue. The periosteum, cranial bones, and dura were discoloured, and covered with ecchymoses. The vessels of the brain surface were much dilated, and showed numerous, and in part confluent, ecchymoses.

Our own experiments on rabbits, performed yearly for several years, during the particularly hot weather in Colombo, show that if such animals are exposed to the sun at about twelve noon they die with all the symptoms, post-mortem appearances, macroscopical and microscopical, of sunstroke, in about sixty-seven minutes, whereas other rabbits similarly treated and exposed at the same time and in the same place, but protected by red glass, live. Although it is true that the red glass did absorb a proportion of the heat rays, still the rabbit was intensely hot to the touch at the end of the experiment, being kept in position under the red glass by being placed in a box painted black externally and so narrow that the sun's rays fell directly upon its shaven head and unshaven back. Nevertheless, the protected rabbits, though kept under observation for months, never seemed to be any the worse for their treatment.

We came to the conclusion that the ultra-violet rays were not the pathogenic agent in these experiments, but that the active rays were in the visible blue and violet; and in this we were much aided by Professor Browning, who supplied us with glasses spectroscopically adjusted.

Aron studied the action of the tropical sun in the Philippino Islands, and concluded—

1. Under climatic conditions rabbits and monkeys, having by nature only a limited power of physical heat regulation, die if exposed to sun, the body temperature rising to febrile heights.

2. The post-mortem findings are hæmorrhagic lesions of the meninges and (in monkeys) of the heart.

3. In animals with a poorly developed sweat-gland system the subcutaneous tissues are heated by radiation from the sun to temperatures above that compatible with life.

4. The human skin is warmed to about 3° to 4° above normal skin temperature, but an increase in bodily temperature is prevented by evaporation of sweat, which causes a fall of skin temperature.

5. Brown skin shows a smaller rise in temperature than white skin, due possibly to an earlier and better water evaporation by sweat secretion. Hence a coloured skin is a better heat regulator than a white skin.

6. The air in human hair, especially black hair, under the influence of the tropical sun, acquires temperatures far above those compatible with life.

He also states that increased body temperature probably accounts for many of the accidents called sunstroke or heat-stroke, and he thinks that an excessive and continued watery evaporation from the skin, while avoiding a rise of body temperature, may lead to collapse, unless the lost water is replaced.

We believe that it is possible that direct radiation from the sun can bring about sudden death and congestion of the meninges of the brain. The connection between sunstroke and the chemical rays requires more investigation; but, whatever this may produce, there is no doubt that if the improperly protected head is exposed to radiation from the sun, headache and a feeling of illness is often produced, and that therefore adequate protection is required.

As is well known, monkeys prefer the shade to the sun's rays, and seem to understand the danger therefrom; and yet no one is afraid of monkeys dying from the heat in laboratory outhouses, though its effect on other kinds of tropical animals, such as gerbils, is a matter of bitter experience, leading to the loss of strains of trypanosomes.

We hold, however, that there is no clinical difference between heat-stroke and sunstroke, and therefore these will be considered as one and the same disease in the clinical section of this work (see Chapter LVI., p. 1449).

ELECTRICITY.

Thunderstorms are often of extreme violence in the tropics, and death from lightning-stroke is much commoner than in the Temperate Zone; but the signs of lightning-stroke are exactly the same as those usually recorded in books on general surgery, and need not be repeated here.

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CHAPTER IX

SOME TROPICAL TRAUMATISMS

Remarks—Traumatisms brought about by animal agencies: the larger Carnivora; the smaller Carnivora; the Ungulata; the Proboscidæ; the Reptilia; the Selachii; Man—Traumatisms due to physical agencies: Foot-binding—Heavy fruits—Electric fans—Powdered glass—Bamboo hairs—References.

REMARKS.

In the tropics many accidents and injuries occur which are but rarely met with in temperate climates. These accidents and injuries may be divided into two categories—traumatisms brought about by animal agencies, and those due to physical agencies. Under the first heading come those caused by the bites or maulings of wild and domestic animals, as well as the injuries caused by man's bite. In the second division are grouped various accidents caused by electric fans, by the fall of heavy fruits from trees, and, lastly, the peculiar deformity of the foot in high-class Chinese women brought about by bandaging the feet of young female children.

There are, of course, many other traumatisms which might be worthy of note, as, for example, penetrating wounds of the abdomen by sword fish, as described by Renner, or bites by Congo fish, as privately mentioned to us by Christy; but they are either too rarely met with, or else they are too well known in the Temperate Zone to require notice here.

It will be observed that we make a distinction between the physical injury caused by the bite of one of the larger animals and the chemical injury caused by a venomous animal, and we do this advisedly, while fully recognizing that the former may introduce septic toxins, sometimes in large amount, as well as germs into the wounds so produced.

TRAUMATISMS BROUGHT ABOUT BY ANIMAL AGENCIES.

Traumatisms caused by the Larger Carnivora.—The word 'traumatism' is peculiarly suitable for this nomenclature, as it is derived from the Greek words *τραῦμα* (a wound) and *θηρίον* (a wild animal). The synonyms are **Morsus** and Rostro et Unguibus dilaceratio (Latin); *δῆγμα, δῆξις, διασπασμός*; *κἄπσις, σπαραγμός* (Greek); **Morsures**, Déchirements musculaires, Dilacérations, Dépiecement des chairs, Myalgies traumathérigènes (French). Under the definition 'Traumatisms caused by the larger Carnivora' we refer especially to the injuries inflicted by the bites, rends, and scratches produced by the teeth and claws of species belonging to the families Felidæ and Ursidæ.

In the Felidæ are *Felis leo* Linnæus, whose habitat is Africa and Asia; *F. tigris* Linnæus, habitat Asia; *F. pardus* Linnæus, habitat India; *F. leopardus*, habitat Africa; *F. onca* Linnæus, habitat South America; *F. pardalis* Linnæus, habitat South America. These cats have a general dental formula, $\frac{3.\ 1.\ 3,\ 1,}{3.\ 1.\ 2,\ 1}$ giving thirty teeth for the whole mouth, which include the most perfect types of carnassial teeth capable of producing exceedingly severe lacerations. These animals feed not merely on the fresh prey which they have recently slain, but also on its body for a day or so after its death. Their maws and claws, therefore, become exceedingly foul, being infected with micro-organisms and their toxins, and hence the great danger of septic intoxication and infection, which markedly increases the gravity of the injuries inflicted.

The other family, Ursidæ, includes the bears which are found in India and Ceylon—*e.g.*, *Ursus torquatus*, of the Himalayas, and *U. malayanus*. Their dental formula is $\frac{3.\ 1.\ 4,\ 2}{3.\ 1.\ 4,\ 3}$ = forty-two teeth in the mouth, but these do not include carnassial teeth, which, added to the facts that they are not as a rule such foul feeders and often eat vegetal foods, causes their bites to be not quite so serious from a septic point of view as those of the Felidæ. Their claws, however, may produce most serious effects of both a traumatic and of a septic nature.

The importance of the septicity of these wounds has been well appreciated from the earliest times, for in the fifth book of his 'De Medicina' Celsus remarks with regard to the bites of men, apes, dogs, and ferocious animals, 'Omnis autem fere morsus habet quoddam virus,' and on this he based his treatment. This statement has been quoted again and again in the centuries which have passed since the days of Celsus: for example, by Morgagni, when investigating the serious illness produced in a young lady by the peck of a sparrow inflicted on a finger, and by Heister, of Helmstadt, in the section on bites in his 'System of Surgery,' published in 1739.

It is of course possible for any person of any age and either sex to be the victim of wounds inflicted by these animals, but the persons most frequently injured are hunters (shikaris) and sportsmen, while the district postmen in jungle regions run great risk, as do shepherds and, to a less extent, herdsmen, and to a still less extent cultivators and villagers living in lonely places in the bush or jungle. The present writers have also encountered wild animals under unexpected circumstances during their journeys into the interior of Africa; but the risk which an ordinary traveller with his gang of porters runs is relatively small, particularly if he has some slight knowledge of the habits of these animals. The most dangerous region to travel through is tall grass, as the hunter or traveller and the wild beast may meet suddenly, and it is here that an accident is more likely to occur than in more open scrub country. Another prevalent cause of accidents is the beating by means of men on foot of jungle or bush into which a wounded animal has retreated. The especially dangerous animal under such circumstances is the tiger, and as eminent as authority as Sir Samuel Baker has especially drawn attention to this fact, and has stated that if no elephants are available then a herd of buffaloes should be driven through the jungle, as they will quickly dislodge the tiger. The possible presence in the vicinity of the mate of the attacked animal should always be borne in mind, as the omission to remember this simple fact has often led to unpleasant accidents.

The physical signs and symptoms produced by these bites and mauls may be divided into general and local. With regard to the former, immediately after being bitten or mauled the victim, if able to stand, feels giddy, turns pale, becomes unable to stand, and, if the injury is at all severe, quickly passes into a condition of shock with a weak pulse, cold extremities, pinched and drawn face, and weak voice, and may become insensible, which, indeed, is often his condition when first rescued in the severer cases. As a rule he remains in a more or less torpid condition, sleeping day and night, and suffering severely, when aroused, from thirst and pain. All these symptoms are more accentuated in Europeans than in natives.

Usually reaction sets in fairly quickly, the temperature rising to 101° to 102° F. or even more, while the pulse is generally quick, ranging about 110 to 120 beats per minute. Usually the torpor continues for some time, but delirium may intervene. The mouth and throat continue to be dry, and thirst is still a marked symptom. Locally the injured region may show rends and tears in the skin, lacerations of the muscles, tendons exposed and torn, vessels and nerves injured, and perhaps torn across, with more or less haemorrhage, bones may be exposed, bruised, broken, or dislocated, joints may be exposed, opened, and injured. Around the injured regions the parts are bluish or red in colour, and swollen, and quickly become œdematous, firm, and hot to the touch.

If the wounds are but slight, the inflammation may remain superficial, but usually the great danger is a cellulitis associated with pus formation and intermittent fever. A more serious complication is spreading or acute traumatic gangrene. Later, as the patient recovers, there is the liability of sinus formation and of stiffness in joints.

It is very important to remember that malaria can occur as a complication, and that therefore some of the intermittent temperature may at times be due to this cause. There is no difficulty with regard to the diagnosis as a rule, as there is generally a history to be obtained, while the local signs are sufficiently indicative of the condition, but the prognosis with regard to even slight wounds must at first be guarded, especially in Europeans, as it is impossible to foretell how serious the intercurrent septic infection may prove to be.

The treatment resolves itself into two distinct categories: first, the first aid when the rescue is effected; and, secondly, the usual surgical treatment.

With regard to the first aid, the usual methods for arresting hæmorrhage, combating shock, and carrying the victim are too well known to require repetition, but the thorough washing of the wound with water, even jungle water, would appear preferable to leaving the poisons from the animal's teeth and claws in the wound. We consider that a small first-aid surgical case containing antiseptics, bandages, etc., should form part of the outfit of every sportsman, and that antiseptics should be added to the water used to wash the wound.

As a rule the hæmorrhage has more or less abated by the time the man reaches a hospital, but any possible source of bleeding must be at once attended to, and the wound thoroughly washed and syringed with warm iodine lotion. Pieces of dead or sloughing tissue may be removed, but it is better to defer any serious operative treatment for twenty-four hours if possible, as it is very dangerous to perform anything of this nature in the condition of shock usually exhibited by the patient. The parts may be drawn together by a suture if necessary, but very few of these should be inserted, and as free drainage as possible allowed. Repeated and carefully applied antiseptic dressings must be carried out. Antitetanic serum should always be administered with the view of preventing possible tetanus.

As soon as there is any suspicion that cellulitis has supervened, free incisions must be made, and hot antiseptic baths, hot fomentations, or Bier's treatment must be applied.

Amputation is necessary if spreading traumatic gangrene supervenes, when it must be performed as high up the limb as reasonable, as it is useless to do repeated operations first at low and then at higher levels, while all the time the disease is spreading. Sinuses require to be scraped and plugged with antiseptic gauze.

When recovery is proceeding and the septic infections have ceased, plastic operations are necessary to close the large wounds left by the destruction of the tissues, while massage and douches may be required to prevent joints from becoming stiff.

As regards general treatment, the first requirement of the patient is usually plenty of water to drink to relieve the urgent thirst from which he suffers, and to dilute the toxins of the possible intoxication.

At first the food should be of the lightest description—broths, soups, and milk diet—and later the ordinary hospital diets may be gradually introduced.

With regard to prophylaxis, the natives often adopt simple protective remedies, such as a bell and spear, or a stick and a small axe, the latter being in use in districts infested by small bears. For a sportsman it is important to thoroughly understand the habits of the ferocious creatures which he is hunting, and especially to know what they usually do when wounded. In travelling in the African bush, a zareba with a fire is usually a good protection during the night.

Traumatisms caused by the Smaller Carnivora.—Under this heading come the traumatisms caused by members of the family Canidæ, of which *Canis lupus* Linnæus, the wolf, *C. aureus*, the jackal, and *C. familiaris*, the dog, may be quoted. Their general dental formula is $\frac{3.\ 1.\ 4,\ 2}{3.\ 1.\ 4,\ 3}$ = forty-two teeth. A wolf bite resembles that of the larger Carnivora, while jackals generally attack children, inflicting severe wounds, often of a septic nature. The jackal is often infected with hydrophobia, which he spreads to the village dogs, and in this way the disease is kept up in tropical countries. There can be no doubt that, at the present time, hydrophobia is one of the real dangers of a tropical town or village, where a large number of pariah dogs are, as a rule, allowed to run freely about the streets and make themselves as objectionable as they like. The result is that a number of children and adults are bitten every now and again, and are compelled to seek protection against possible infection by treatment at one of the now numerous Pasteur Institutes. In our opinion, some attempt should be made by muzzling dogs for a period of at least two years throughout a country, and the destruction of all dogs not so protected, to diminish this danger. We also consider that the destruction of all ownerless dogs—*i.e.*, dogs without a collar on which a name is engraved—should be conducted by a systematic organization.

The parasite of hydrophobia is described in Chapter XXII., p. 535.

One of the most important forms in which rabies attacks dogs is that called 'dumb rabies,' in which the lower jaw early becomes paralyzed; this is a form often overlooked for some time by non-medical people, and is a source of great danger.

Anyone interested in this subject must, however, consult a book on general medicine, as this is hardly the place for a description of rabies.

Rat and cat bite diseases are described in Chapter LII., p. 1356.

Traumatisms caused by the Ungulata.—Among the Herbivora there are two families which are celebrated for vicious attacks upon man, and these are the Camelidæ and the Bovidæ.

Camelus bractrianus Linnæus may at times have a bad temper, and it is often dangerous for a stranger to approach a camel, for its bite is, as a rule, a serious injury, the deep tissues being crushed and lacerated, while the bones may be crushed, broken, or dislocated, and tendons, bursæ, and joints may be laid bare or opened, and last, and by no means least, because of the possibility of gangrene and severe septic infection. The bites generally occur on the upper or lower limb, but are also well known on the head and face. The shock from such severe injuries is naturally very great, but the symptoms, signs, and treatment resemble those already mentioned under the heading of traumatisms caused by the Carnivora, and need not be repeated.

Among the Bovidæ, the buffalo is very dangerous—*e.g.*, *Buffelus indicus* in India and Ceylon, and *Bubalus brachyceros* in Central Africa—the danger being deep, penetrating wounds of the limbs, chest, or abdomen, as well as severe punctured, lacerated, and contused wounds in any part of the body.

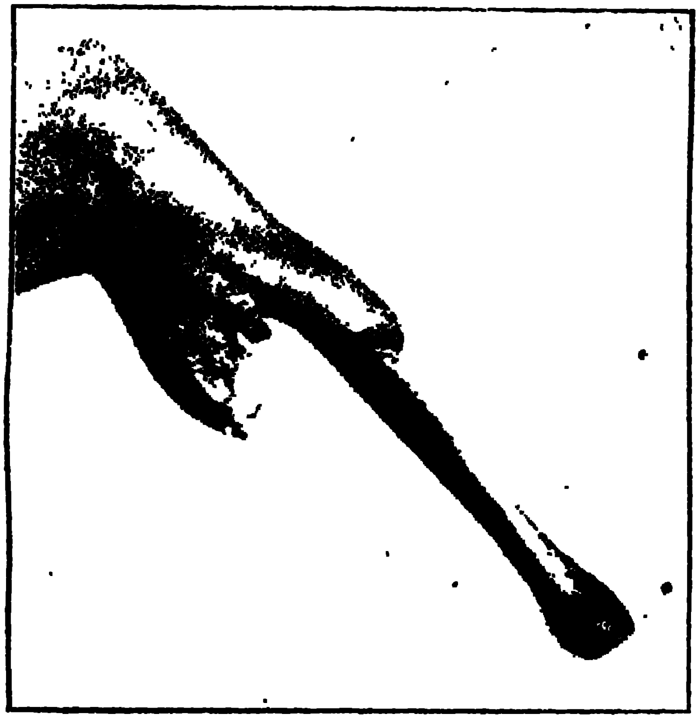

FIG. 8.—CAMEL BITE.

(From a photograph given to us by Christopherson.)

Here attention may be drawn to the fact that horses may become affected with hydrophobia, which, in animals treated as family pets, is a serious danger. The animal appears to be in great pain, and is often thought to have colic; it froths at the mouth and becomes very savage, biting articles in its stable and kicking the wall in a furious manner until weakness sets in.

Kicks may produce serious contusions and wounds, as well as injuries to internal organs.

The Rhinoceri—*Rh. indicus*, *Rh. javanicus*, *Rh. sumatrensis*, *Rh. africanus*—produce most serious punctured and lacerated wounds.

Hippopotami are common in the rivers and lakes of Africa—*e.g.*, *H. amphibius* and *H. liberiensis*. As a rule they are quite peaceful animals when left alone, but, once attacked, they become dangerous, seizing the boat or the persons in their huge jaws and crushing wood or flesh and bones into shapeless masses. They are very courageous, and nothing but death will stop the charge of one of these brutes. They will quickly stamp the life out of any victim they catch on land.

The Suidæ, or pigs, are commonly met with in tropical jungles, and are of importance because of the way in which they eat the remains of persons who have been lost in the jungle. All the soft parts are completely destroyed, while the bones are broken, so that it is impossible to say whether the unfortunate people died or were killed, whether they met with an accident or simply lost their way, whether the pigs ate them while dying or only after death.

Severe lacerated wounds can be inflicted by the tusks of an enraged boar.

Proboscidæ.—The elephants—*E. africanus* and *E. indicus*—usually kill their victim by stamping upon him until the soft parts are terribly crushed, lacerated, and bruised, while bones are broken. They also seize people by means of their trunks and dash them against surrounding objects or the ground.

Traumatism caused by the Larger Reptilia.—The crocodiles, gavials, and alligators are a constant source of danger in the tropics, especially to natives, while bathing in rivers. The names 'crocodile' and 'alligator' are often used as though they were synonyms, but this is by no means so. Some twelve species of crocodile are well known. They possess a most formidable array of teeth, expressed, as a rule, by the formula $\frac{18}{15}$, of which the third and ninth in the upper jaw are longer than the others, and are respectively lodged between the second and third and the eighth and ninth teeth in the lower jaw, in which the first, fourth, and eleventh teeth are the strongest. The muzzle of the crocodile is longer than that of the alligator. The muzzle of the alligator is relatively short and broad.

The muzzle of the gavial is very long. The two species of importance are *Gavialis schlegeli* of Java and Borneo and *G. gangeticus* of the Ganges. The latter has a dental formula $\frac{28\ 29}{25\ 26}$ teeth.

The following list, modified from Ditmar, gives the names and habitats of these formidable reptiles:—

A. Snout extremely long and slender—
  Gavialis gangeticus, India; *Tomistoma schlegeli*, Borneo and Sumatra.
B. Snout very sharp, slender, and triangular—
  Crocodilus cataphractus, West Africa; *C. johnstoni*, Australia; *C. intermedius*, Orinoco.
C. Snout moderately sharp and triangular—
  Crocodilus americanus, Mexico, Central and South America; *C. siamensis*, Siam and Java; *C. niloticus*, Africa; *C. porosus*, India and Malaysia.
D. Snout oval, bluntly triangular—
  Crocodilus robustus, Madagascar; *C. thombifer*, Cuba; *C. morelatti*, Guatemala and Honduras.

E. Snout short and broad—
Crocodilus palustris, India and Malaysia; *Osteolæmus tetraspis*, West Africa.

F. Canine teeth of lower jaw fit into a pit in upper jaw—
I. Snout as in D: *Caiman trigonotus*, Upper Amazon; *C. sclerops*, Central and Southern America; *C. palpelrosus*, Tropical South America. II. Snout very broad and rounded: *C. latcrostris*, Tropical South America; *C. niger*, Tropical South America; *Alligator mississipiensis*, U.S.A.: *A. sinensis*, China.

The celebrated man-eating species are—
Crocodilus niloticus, the Nile crocodile; *C. porosus*, the salt-water crocodile.

The American species are said to be inoffensive, as there are no records of attacks upon man.

Another important anatomical feature of these reptiles is the length and strength of the tail, by means of which they can strike a man standing on the low bank of a river such a powerful blow that he may be knocked into the water.

Accidents are commonly met with while people are crossing streams, or bathing therein, or while women are washing clothes or filling vessels with water at a river or lake. Anyone sitting on a steamer or other craft on a lake or river with his feet hanging over the side, or leaning over with his hand in the water, simply provides bait for any crocodile in the vicinity.

As a rule, if the victim is rescued, it is found that a portion of a limb has been bitten off, but we have met with a case in which only a large portion of the pectoralis major was removed. In this case the victim attributed his escape to driving his thumbs into the crocodile's eyes The wound healed excellently, though of course there was practically no pectoralis major left on the side in question, and in its place an area of scar tissue. Crocodile bites, in our experience, are not nearly so liable to septic infection as the bites of the Carnivora.

Traumatisms caused by the Larger Selachii.—By far the greatest number of sharks live in the seas of warm climates, and are well known because of the great danger of their bite, which is often fatal. The greatest risk is to bathers or fishermen, but it is a curious fact that divers for pearls appear to incur little risk. It is probable that the noise of the large number of people employed in this work frightens the sharks, which keep away.

Carcharias gangeticus was for a number of years a source of great danger to the crowds at the bathing ghats of Calcutta. Sir Joseph Fayrer says that they used to feed upon the partially burned bodies which were formerly thrown into the river, but when this custom was discontinued they began to attack the people at the bathing ghats, especially in the months of April and May, when the river contains much salt water. He says that they would dash into the crowd at the bathing ghat and inflict dangerous and, at times, mortal wounds, though they seldom were able to get away with their victim because of the numerous people at the ghat.

The patient is brought to the hospital suffering from the effects of shock and hæmorrhage, with a limb either snapped off or partially torn off, or with larger or smaller lacerated wounds, in which the bone may or may not be exposed and grooved by the sharks' teeth, and with blood dripping from the ragged surfaces of the wound. Usually the patient is in a state of extreme prostration, covered with a cold sweat, and having a hardly perceptible pulse.

More rarely there are only a few triangular or irregular lacerated wounds, showing that the shark did not obtain a proper hold of the victim.

The great danger is death, either immediately or in a few hours, from shock or hæmorrhage. If this is avoided, the wounds appear to heal readily if the patient is otherwise in fair health, but of course amputation is often necessary.

Man.—The bites inflicted by the Kru men on the West Coast of Africa in quarrels are, or were, of not uncommon occurrence, and it was also fairly common to meet with injuries on the knuckles caused by scratches from their teeth.

These wounds were usually considered to be serious, for, although the teeth of the African appear to be in excellent condition of repair and cleanliness, still the slightest scratch may lead to exceedingly severe inflammations, as the present writers well know. The most careful antiseptic treatment must be applied at once.

TRAUMATISMS DUE TO PHYSICAL AGENCIES.

Foot-binding.—The bandaging of the feet of young female children began in the imperial harem of the T'ang Dynasty in China some 1,400 years after Confucius, the idea probably being to reproduce as nearly as possible a club-foot. As a matter of fact, the result of pressure of the short, heavy bandage commonly used, neatly and tightly applied to the growing feet of young girls aged three to four years, is to produce a very small foot in the condition of a pes cavus, with the outer three toes in a varoid and the inner two toes in a valgoid position.

On examining one of these feet it is noted that it is very short, and that the plantar surface has a deep groove dividing this aspect of the foot into posterior and anterior portions. The posterior portion contains the os calcis, which, when examined radioscopically, presents a very different appearance from and position to that in a normal foot.

Notwithstanding objections to the contrary, we are of the opinion that the person walks upon the posterior aspect of the os calcis, and we further draw attention to the great alteration in the lines of pressure and stress, as compared with those in a normal os calcis. The anterior portion consists of the four small toes bent under the foot, so that the dorsal aspect is placed ventrally, while toes themselves are much atrophied. By radiographs it is seen that the heads of the metatarsals are approximated towards the os calcis. The first toe is only compressed. The weight of the body is then supported by the posterior aspect of the os calcis and by the distal end of the first metatarsal, and the plantar aspect of the great toe, while the dorsal aspect of the other toes may assist a little. The distance from the end of the os calcis to the big toe may be only three inches.

Such a compressed, deformed, stunted foot may easily become the site of disease. In the first instance, there is danger of gangrene, necrosis (especially of the phalanges), and synovitis of the knee-joint during the active bandaging, while the immediate result may be total lameness. As a later complication, tuberculosis of the bones of the deformed foot is liable to occur

Fortunately this horrible proceeding, like many other horrible fashions, is dying a natural death under the influence of increased feminine education and common sense first produced among European women, and by them introduced into China. Naturally no cure can be effected in a foot which has become fully deformed.

Heavy Fruits. The fruits of the coconut (*Cocos nucifera* Linnæus) and of the jak-tree (*Artocarpus integrifolia* Linnæus) are heavy and fairly hard, and injuries may be caused by the fall of one of these fruits from the tree on to the head or other part of the body. When the blow is received by the head, the symptoms produced may be those of concussion or compression, or there may be signs of fracture of the vault or base of the skull.

Electrical Fans.—In the more civilized tropical towns it is common to use small, movable, quickly running electric fans in order to obtain a cooling breeze. These are brought into use specially in the bedroom and dressing-room, but are also frequently seen in the dining-room, and sometimes in the office. Being easily movable, they are apt to have their position slightly altered when running at full speed, and in doing this quite a number of accidents have taken place. Sometimes during the condition between sleeping and waking, people, stretching out their arms while still in bed, catch their fingers in the fans. The most common traumatism is for the fingers to be caught by the blades, and to sustain contused and lacerated wounds, the danger of which is tetanus, as the blades of the fan are generally thickly covered with the dust brought by the current of air.

Another and far less serious but most awkward accident sometimes happens in a lady's dressing-room. The fan is placed on or near the dressing-table, and is so arranged that the back of the fan is towards the person at the dressing-table. The current of air passes from the person towards the back of the fan. If the lady has long hair and is dressing it, the current of air may carry it into the back of the fan and between the blades, which, still revolving, causes the hair to be twisted into a tangle. Usually the lady or her attendant has sufficient nerve to switch off the fan, and no very serious injury is done, but it is difficult to extract the hair from the tangle in the fan.

Powdered Glass.—In certain parts of the tropics, especially in the East, powdered glass is used for suicidal and homicidal purposes. The injury caused is, of course, purely mechanical, and the more finely it is powdered, the less likely it is to cause serious injury, owing to mucus surrounding the particles. The glass is administered in food—*e.g.*, bread, spinach, sweetmeat, etc. The symptoms are those of irritant poisoning—retching, violent vomiting, spasms, convulsions, and racking pain. The most evident post-mortem feature is acute gastritis. The mucosa is covered with a layer of thick mucus, under which it is found to be hyperæmic and lacerated. In this mucus or on the mucosa the minute pieces of glass may be found. No other pathological signs need be present. The treatment is to administer any bulky food at hand, and then, if vomiting has ceased, to give an emetic, and finally a laxative.

Bamboo Hairs.—*Dendrocalamus strictus* Nees. We have met with a case from Malaya in which the fine hairs shaved off the bamboo sheaths were administered in food with the intent to kill. They produced a severe form of enteritis very like chronic dysentery. We are therefore in a position to confirm Ridley's earlier statements that these hairs act as mechanical irritants.

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SECTION B

CHEMICAL CAUSES

POISONS
ARROW POISONS
POISONS USED IN FISHING, HUNTING, AND TRADE
POISONOUS FOOD
VENOMOUS ANIMALS

POISONS

I. CRIMINAL POISONING.
  1. Homicide
  2. Suicide.
  3. Infanticide
  4. Abortion.
  5. Robbery.
  6. Pseudotherapy.
  7. Mimicry.
  8. Aphrodisiac

II. ACCIDENTAL POISONING.

III. STIMULANT AND SEDATIVE POISONING.

IV. ORDEAL POISONING.

CHAPTER X

POISONS

Preliminary—Definition—Classification—Criminal poisoning—Accidental poisoning—Stimulant and sedative poisoning—Poisons used in trial by ordeal—References.

PRELIMINARY.

THE chemical causes of tropical disease or the tropical intoxications are numerous, and it is impossible in a book of this size to do more than give an account, in condensed form, of the more common, and to provide means, by the references, whereby the reader may extend his information if he so desires.

In the present work we shall divide these chemical causes into Poisons and Venomous Animals; and as we begin the study of these matters in the present chapter, it is as well to state what we mean by a poison.

DEFINITION.

A poison is any chemical substance which, when introduced in sufficient quantity into, or brought in contact with, the living organism, is capable of producing a variation in the structure, the chemical composition, or the functions, of the whole or any part of that organism, which exceeds the limits of physiological variation.

Such a definition includes a large number of substances, and therefore some arrangement is necessary in order that they may be considered systematically.

CLASSIFICATION.

Poisons have been classified into mineral, vegetal, and animal, or according to their action on the human economy; but we have departed from these proposals, and have attempted to arrange them according to the purposes for which they are used, as we consider that this method will be of greater service to the tropical practitioner.

With this end in view, we divide them into the chemical substances which occur in—

I. Criminal Poisoning.
II. Accidental Poisoning.
III. Stimulant and Sedative Poisoning.
IV. Trial by Ordeal.

We leave to future chapters the consideration of poisons used in war, fishing, hunting, and trade, as well as poisonous food and the effects of venomous animals.

I. CRIMINAL POISONING.

Criminal poisoning has been in existence from the earliest and most primitive ages, and as it requires a highly and specially trained chemist with a well-equipped and up-to date laboratory to detect many of the tropical vegetal poisons, the reader will not be surprised to note that criminal poisoning is more frequently met with in the tropics than in the Temperate Zone.

It seems to us that it is more commonly met with in the East than in Africa, and we are inclined to think that the reason for this is that in Africa only the fetish-man knows how to present virulent poisons in acceptable forms to his victims, whereas persons with an elementary knowledge of poisons are common in the East.

The poisons of different tropical countries vary according to custom and tradition, and also according to the plants which happen to grow in the vicinity. It is said that arsenic in the East is the cause of as many criminal poisonings as all the organic poisons put together. This may be so, but we are not certain that anyone is qualified to make this statement, as it came as a great surprise to us to find that in Ceylon a number of the poisonings at one time attributable to arsenic were found by advanced chemical research under an exceedingly able chemist to be due to *Cerbera odollam.*

We are therefore of the opinion that every tropical country requires a well-equipped toxicological laboratory, with well-trained research chemists, whose business, *inter alia*, should be to make themselves acquainted with the poisons of the land in which they are residing, with the view to discovering tests whereby these poisons may be detected and so justice done in criminal cases. This is important, for the native soon learns that methods of bringing the criminal to justice exist, and therefore becomes less inclined to use this method for the removal of his enemy.

The poisons used criminally against man may be divided into (*a*) Inorganic Poisons, (*b*) Organic Poisons.

Inorganic Poisons.

The most common poison is *arsenic* in some form, and the next is *perchloride of mercury*, followed closely by the *mineral acids*. Salts of copper have been used for homicidal purposes, but generally poisoning from this source is accidental, and due to the use of copper cooking utensils, while the preparations of antimony are seldom used.

Organic Poisons.

These may be derived from animal or vegetal sources, but the latter are far more *en evidence*, and are largely derived from plants belonging to the natural orders Apocynaceæ, Loganiaceæ, Euphorbiaceæ, Liliaceæ, and Leguminosæ.

It would doubtless be more scientific to classify these poisons by the natural orders to which the poisonous plants belong, but, following our original proposals, we divide them as follows:—

1. Poisons used for homicidal purposes.
2. Poisons used for suicidal purposes.
3. Poisons used for purposes of infanticide.
4. Poisons used for procuring abortion.
5. Poisons used with the intent to rob.
6. Poisons used with the intent to cure disease.
7. Poisons used with the intent to simulate injuries.
8. Aphrodisiacs.

1. *Homicide*.

Animal and vegetal substances are used for this purpose, but of the former the best known is *viperine venom*, which is said to cause gastritis, gastro-intestinal hæmorrhages, and even death. It is known to Ceylon natives that the venom of *Vipera russellii* Shaw, locally called the *tic polonga*, is supposed to be poisonous when administered by the mouth, and we were informed that this was usually given in toddy, an alcoholic drink prepared from the coconut and from the Palmyra palm. We once met with a case in which we suspected the possibility of this being used, but an experiment in which the recent venom administered orally by means of toddy to a monkey proving a complete failure, we were left in doubt as to the possibility of such poisoning.

The venom of the Colubridæ is harmless when taken by the mouth, provided that there are no cracks or abrasions. Its virulence is destroyed by saliva and by pancreatic juice.

Vegetal substances are sufficiently numerous, but unfortunately, as far as we know, few are on record. The table given on p. 164 is an imperfect list.

With reference to the table, a few notes, arranged in alphabetical order, may with advantage be given:

Aconite.—*Aconite* (Ranunculaceæ) is so poisonous that in India it is known as 'bish' or 'bikh,' which means 'the poison,' which generally refers to *Aconitum ferox* Wall (Himalayas), *A. napellus* L. (Himalayas), *A. luridume* Aorte (Sikkim), *A. lycoctonum* L. (Kashmir); whilst *A. heterophyllum* Wall and *A. palmatum* Don are said to be less poisonous.

The root is the principal source of the poison, which, however, also exists in the leaves and stem.

Aconite is used for homicidal purposes, as a cattle poison, and may at times be taken accidentally. The fatal dose is said to be 30 grains of the root, and the fatal period usually three to six hours.

The symptoms are tingling of the lips, tongue, mouth, and fauces, followed by numbness and anæsthesia, burning pains in the stomach,

Country.	Natural Order.	Genus and Species.
India and Ceylon.	*Ranunculaceæ* De Candolle, 1818	*Aconitum* Tournefort with *A. ferox* Wall and *A. napellus* Linnæus in the Himalayas, *A. luridum* Aorte in Sikkim, and *A. lycoctonum* Linnæus in Kashmir.
	Apocynaceæ Lindley, 1836	*Cerbera* Linnæus, 1753, with *C. odollam* Gærtner and *C. thevetia* Linnæus. *Nerium* Linnæus has *N. odorum* Solander, 1729. *Urechites* is represented by *U. suberecta* Mucker.
	Liliaceæ Linnæus, 17[illegible].	*Gloriosa* Linnæus with species *G. superba* Linnæus.
	Euphorbiaceæ A. de Jussieu, 1824	*Jatropha* Kunth with one species, *J. curcas* Linnæus, 1753
	Loganiaceæ Auctores	*Strychnos* Linnæus with *S. nux vomica* Linnæus, *S. [illegible]* Bergmann *S. colubrina* Linnæus.
Dutch Indies	*Leguminosæ* de Jussieu, 1789.	*Millettia* Wight and Arnott with *M. sericea* Wight and Arnott.
Pacific Islands	*Myrtaceæ* R. Brown, 1814	*Barringtonia* Forskal with *B. speciosa* Linnæus and *B. raratonga*.
	Apocynaceæ Lindley, 1836	*Cerbera* Linnæus with *C. lactaria* Hamilton.
Brazil.	*Sapindaceæ* de Jussieu, 1811	*Paullinia* Linnæus with *P. pinnata* Linnæus.
	Euphorbiaceæ A. de Jussieu, 1824	*Hura* Linnæus with *H. crepitans* Linnæus.
	Loganiaceæ Auctores.	*Spigelia* Linnæus with *S. anthelmia* Linnæus. *Thevetia* Linnæus with *T. ahouai* Linnæus.
British Guiana	*Sapindaceæ* de Jussieu, 1811.	*[illegible]* Linnæus, 1753, with species not mentioned
West Africa.	*Solanaceæ* Lindley, 1836.	*Hyoscyamus* Tournefort with *H. falezlez* Cosson.
	Iridaceæ Lindley, 1836	*Moræa* Linnæus with *M. collina* Waldtulpe.
	Cactaceæ Lindley, 1836.	The 'Oro' of Sierra Leone.
South Africa.	*Iridaceæ* Lindley, 1836.	*Moræa* Linnæus with *M. collina* Waldtulpe.
	Zygophyllaceæ Lindley, 1836.	*Melianthus* Linnæus with *M. major* Linnæus and other species.

and vomiting, muscular and cardiac weakness, and finally death takes place from failure of the heart or respiration.

Barringtonia Forster, 1776 (Myrtaceæ), with the species *B. speciosa* Linnæus and *B. raratonga*, is said to be used for criminal poisoning in Oceania.

Cerbera odollam.—*C. odollam* Gaertner (Apocynaceæ) is a very common plant in Ceylon, and is similar to *C. thevetia*. Its correct name is probably *C. manghas* Linnæus, 1753. Its chemical properties have not yet been properly worked out, and it is said that it *probably* contains the same poisonous principle as *C. thevetia*—viz., thevetin. The symptoms are nearly the same—*i.e.*, gastro-intestinal irritation, followed by cardiac poisoning. These symptoms are easily mistaken for arsenical poisoning. The treatment is the same as for irritant poisoning in general.

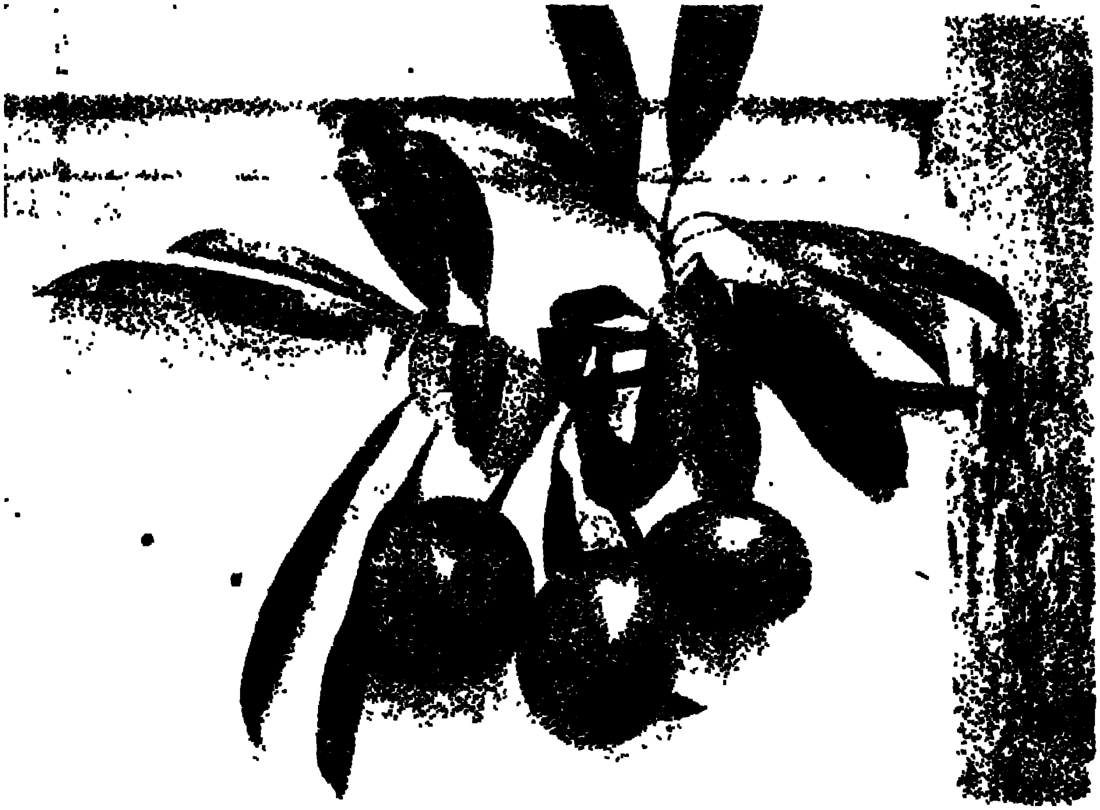

FIG. 9.—*Cerbera odollam* GAERTNER.

Cerbera thevetia. *C. thevetia*, the common yellow oleander of India, is a shrub about 6 to 12 feet in height, with yellow bell-shaped flowers and globular green fruit. It is highly poisonous, its action being due to a glucoside, thevetin, which exists in the milky juice pervading all parts of the plant. It is supposed that three seeds are sufficient to kill a man in twelve to fifteen hours, the symptoms being gastro-intestinal irritation, headache, dizziness, and pain in the throat. The pulse is very soft and slow—thirty to forty beats a minute, which Windsor says is characteristic; later it becomes weak, very rapid, and irregular. Death results from cardiac failure. The treatment is the same as for ordinary irritant poisoning.

Gloriosa superba. *G. superba* (Liliaceæ) is a well-known poison in India and Ceylon, while in Burma it is said to be used for suicidal purposes. Its active principle, superbine, is said to be allied to, or identical with, the scillitine of squills, and therefore the action of *G. superba* is not unlike that of squills The symptoms, which may appear in half an hour, are retching, violent vomiting, spasms, with contortions of the body and racking pains, with short intervals of relief from time to time Death may take place in four hours. The post-mortem reveals congestion of the brain and membranes, with extravasations of blood, congestion of the lungs, liver, and kidneys and inflammation of the mucous membrane of the stomach.

The treatment is that for irritant poisoning in general.

Hyoscyamus falezlez.— The Tuaregs are said to use *H. falezlez* to kill travellers.

Jatropha curcas *J. curcas* Linnaeus (Euphorbiaceæ), the jura-tree of India, has a seed which is called the 'physic nut,' from which the oil can be expressed which is an irritant to the skin and a purgative.

The symptoms of poisoning are vomiting, purging, abdominal pain, derangements of the special senses, muscular twitchings, and loss of memory. The treatment, after getting rid of as much of the poison as possible, is lime-juice and stimulants.

Melianthus (Melianthaceæ).- Various species of Melianthus are said to be very poisonous by Grey, who suspects the possibility of their use by South African Bushmen.

Melicocca (Sapindaceæ) occurs in British Guiana, where it is called Kinnup. In a two-year-old child it caused convulsive twitching of the hands and feet, fixed gaze, vivid flush on skin, distension of abdomen, suppression of urine, rise of temperature to 101° F. The poisoning was said to resemble that produced by belladonna. Other species are said to stupefy fish and also to be used as arrow poisons.

We may perhaps mention here that in this order are many excellent and edible fruits; thus, *Melicocca bijuga*, a West Indian tree, is cultivated in Brazil because of its agreeable, slightly acid berries, but, on the other hand, the leaves and branches of other species are poisonous.

Milletia sericea (Leguminosæ) is a poison of the Dutch Indies, causing severe diarrhœa, collapse, and death.

Morea collina.—*M. collina* (Iridaceæ), the wild tulip of South Africa, is said by Grey to have been used by a Bushwoman to poison a number of people, two of whom died.

The symptoms were severe vomiting and a feeling of constriction across the chest, feeble and intermitting heart, and a tendency to coma for hours before death. The post-mortem showed no rigor and no inflammation of the stomach. The heart musculature was flaccid, and the right side full of blood.

Nerium odorum, synonym *N. indicum* Mill. 1768 (Apocynaceæ), is the white oleander, and grows commonly in India, where it is a well-known poison. It is rarely used for homicidal purposes, but more generally for suicide, abortion, and accidental poisoning.

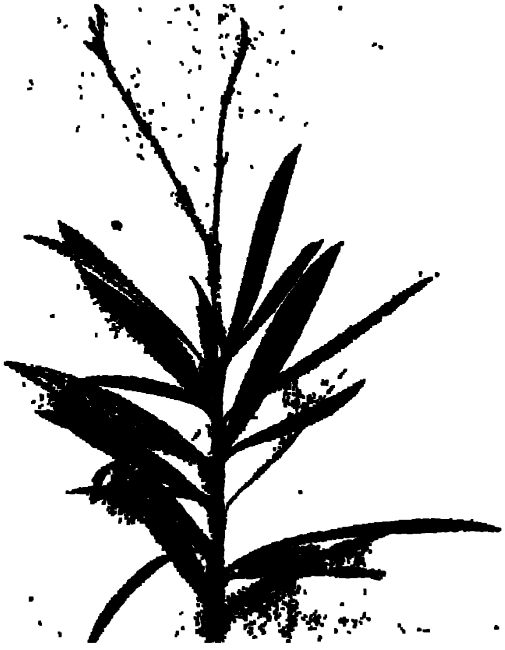
FIG. 11.—*Nerium odorum* SOLANDER.

The root is the portion used, but all parts are poisonous. The active principles are neriodorin, a powerful cardiac poison acting something like digitalis; karabin, a cardiac poison, with also a strychnine-like action on the spinal cord.

The symptoms are therefore (1) those of gastric irritation—viz., vomiting, pain in the stomach, frothing at the mouth from salivation, but as a rule without diarrhœa; (2) cardiac symptoms, producing at first a slow pulse, which finally becomes quick and weak—the respirations are rapid from the first; (3) strychnine-like symptoms of twitching of the muscles, tetanic spasms, with cramps and, at times, lockjaw.

Towards the end the patient becomes drowsy, then insensible, and finally dies from cardiac failure. The post-mortem reveals dilatation of the right side of the heart, which is full of blood, while the left side is empty, with subendocardial hæmorrhage, congestion of the liver, spleen, kidneys, and lungs, mucosa of the stomach and small intestine, while the large intestine and brain are normal. The patient must be treated on the same lines as for digitalis and strychnine poisoning.

The Oro.--The oro (a cactus) of Sierra Leone is a gastro-intestinal irritant, causing vomiting, diarrhœa, collapse [illegible] death.

Paullinia pinnata (Sapindaceæ) is said by Rho to be used by negro slaves in Brazil to poison their masters, and to depend upon an alkaloid, timboin, for its action. Adverting to our remarks on Melicocca, we may note that the seeds of *P. sorbilis* are the source of the 'Guarana' bread of Brazilian aborigines, used when travelling and as a remedy, being said to be a stomachic, febrifuge and aphrodisiac.

Sablier crepitans Linnæus, also named *Hura crepitans* (Euphorbiaceæ), grows in the Antilles, and has been imported into tropical Africa. Its fruit is purgative, and is believed to be used frequently for criminal purposes, being said to produce violent vomiting and purging, with tenesmus, constriction of the throat, and syncope. Ruiz, however, has thrown doubt on the possibility of its really being the cause of these criminal poisonings. It is to be noted that the same symptoms are produced by *Croton tiglium* Linnæus (Euphorbiaceæ), which is found in India, Cochin China, tropical America, and Africa.

Spigelia anthelmia Linnæus (Loganiaceæ) has the reputation of being very poisonous, and has been used criminally in tropical America, in Brazil, and the Antilles, where it is still used as an anth[illegible]c. It is said to produce somnolence convulsions, and death.

Strychnos.- Strychnos (Loganiaceæ) is a genus with several poisonous species, among which may be mentioned:

Strychnos nux vomica Linnæus.
Strychnos ignatii Bergmann.
Strychnos colubrina Linnæus.

Poisoning by the alkaloid strychnine is frequently met with in India, but is usually accidental. The symptoms of strychnine poisoning are bitter taste in the mouth, tetanic spasms, opisthotonus, risus sardonicus, and death from asphyxia or collapse. There are no characteristic post-mortem appearances, except congestion of the brain and spinal cord. The treatment is to empty the stomach by emetics, and to administer chloroform or chloral hydrate, and, when asphyxia threatens, to perform artificial respiration.

Thevetia ahovai.—*T. ahovai* (Apocynaceæ) is allied to the oleanders mentioned above, and has an alkaloid, thevetosin, said to cause gastric irritation and difficulty of breathing.

Urechite suberecta (Apocynaceæ) is the Savannah flower of Jamaica and other West Indian Islands, which was so celebrated in the days of the 'Obeah Man,' and about which so many tales were told. The truth is that there are two glucosides, urechitin and urechitoson, of which the former is like digitalis, and hence it has an accumulative action in small doses, which, if given to a person for a long time, will not cause any deterioration of health, but will cause, eventually, sudden death owing to the action on the heart. A full lethal dose, on the other hand, will kill in a few hours or a day or so.

2. *Suicide.*

Of all the poisons used for suicidal purposes, opium is by far the most usual, though *Nerium odorum*, *Cerbera odollam*, and *Gloriosa superba* are also at times employed, the former especially by women in India. Rarer poisons are *Calotropis procera*, *Cerbera thevetia*, aconite, prussic acid, and veratrine (meeta bish). The action of all these poisons is described either in ordinary works on toxicology or has already been mentioned.

3. *Infanticide.*

Infanticide exists in the tropics in two forms the first irrespective of sex, and said to be due in India (Waddell) to the high-caste Hindu prohibiting remarriage of widows; and, secondly, female infanticides, to prevent too many daughters growing up. A few of the more commonly used drugs may be briefly mentioned.

Opium is used in India by smearing the mother's nipples with the drug. There is little necessity here to describe the action of opium. All that need be said is to warn the practitioner that ayahs (native nurses) are apt to soothe a baby to sleep by dipping the finger in laudanum, and giving it to the baby to suck. Such treatment is highly deleterious to the child, and the intensely contracted pupils should make the practitioner suspect its use in an obscure case of illness.

Calotropis gigantea Robert Brown and *C. procera* Robert Brown (Asclepiadaceæ), called 'mador' in Hindustani and 'erukam' in Tamil, have been used in India for infanticide and abortion, rarely for suicide, and more rarely for homicide. The symptoms are vomiting, profuse salivation, severe tetanic spasms, extremely slow and stertorous breathing, and dilatation of the pupils. The active principle is a yellow bitter resin, but there is no alkaloid. The treatment is the same as for irritant poisoning.

Tobacco is also used as an infant poison.

4. *Abortion.*

Criminal abortion is very common in the tropics. In India it is said to be common among Hindu widows, because they are not allowed to remarry.

The drugs commonly used are:-

(*a*) *Reputed Emmenagogues.*—
Nerium odorum Solander.
Cerbera thevetia Linnaeus.
Carica papaya Linnaeus (seeds).
Daucus carota Linnaeus (carrot seeds).

(*b*) *Purgatives* (*Cucurbitaceæ*).—
Cucumis trigonus Roxburgh.
Momordica charanta Linnaeus.
Momordica cymbalaria Fenzl.

(*c*) *Irritants.*- Several inorganic irritants are used—arsenic, lead, mercury, copper, and quicklime. Browning informs us that copper sulphate has been used of late in Ceylon for this purpose, as well as tartar emetic, corrosive sublimate, large doses of quinine, and very large doses of Epsom salts and an aloes (socotrine) iron pill, in which the quantity of the aloes is very considerable.

Plumbago rosea Linnæus.
Plumbago zeylanica Linnæus.
Calotropis procera R. Brown.
Piper nigrum Linnæus (black pepper).
Ananas Tournefort, 1735 (unripe pine-apple)
Moringa pterygosperma Gaertner (bark).
Lasiosiphon speciosus Decaisne.

(*d*) *Supposed Ecbolics.*—
Bambusa sp.? juice of bamboo-leaves. The fruit is used.
Randia dumetorum Linnæus.
Cuscuta reflexa Roxburgh. (A decoction is used which also acts as an irritant.)
Seeds of *Celastrus paniculatus* Wight.
Seeds of *Anethum graveolens* Linnæus.

Plumbago zeylanica Linnæus and *P. rosea* Linnæus are evergreen shrubs about 2 to 5 feet high, in the root of which there is an active principle, plumbagin, which acts externally as a vesicant, and internally as an irritant and narcotic. It is used as a paste, or spread on wool on an abortion-stick.

The abortifacients which were commonly used in Ceylon were *Gloriosa superba* L., violent purgatives (including large doses of magnesium sulphate), and the twigs of the castor-oil plant, the last named being a mechanical irritant.

5. *Stupefying with Intent to Rob.*

Two drugs are much used in India and Ceylon for the purpose of stupefying with intent to rob—viz., *Datura fastuosa* Linnæus and *Cannabis sativa* Linnæus.

Datura fastuosa (Solanaceæ).—Poisoning by datura is common in India, having been used by the Thugs. The seeds are usually mixed with food or drink, and the symptoms, which develop rapidly, depend upon the dose, being generally those of a cerebral poison. First there is delirium, and later coma, but in both conditions the pupils are widely dilated. The delirium is peculiar; for example, the people affected may be found searching their bedding most vigorously for some lost article. When death occurs, it is due to cardiac failure. The fatal dose is not actually known, but may be about 10 to 15 grains of the seeds. Waddell puts the mortality at about 18½ per cent. The post mortem characteristics are wide dilatation of the pupils, congestion of the brain, meninges, and the lungs and other viscera.

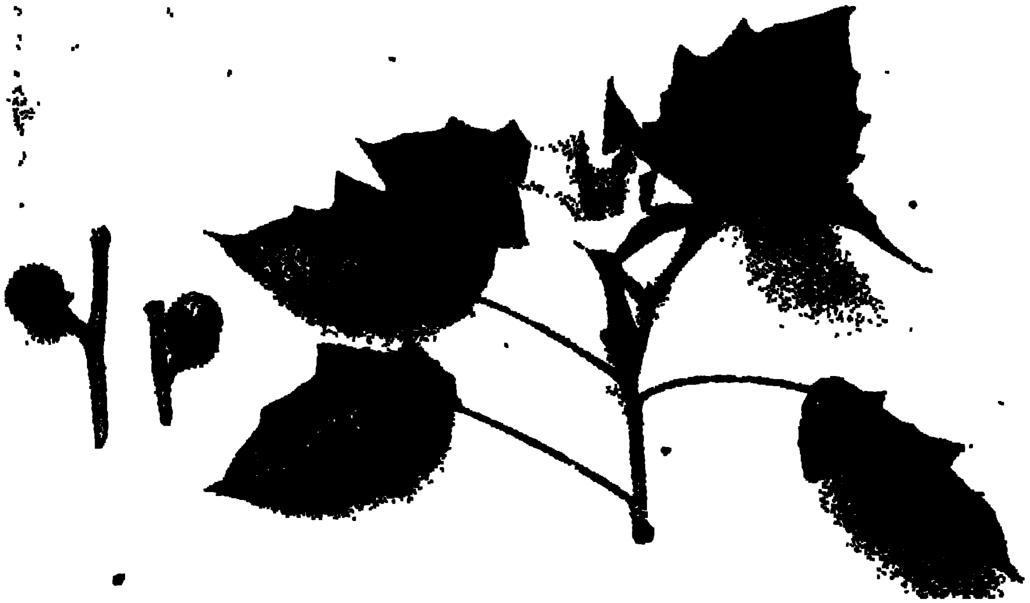

FIG. 12. *Datura fastuosa* LINNÆUS.

6. *Poisons used with Intent to Cure Disease.*

Decoctions of bark *Trianthema pentandra* Linnæus are used in the Sudan for the purpose of curing gonorrhœa; unfortunately, sometimes this remedy is worse than the disease, causing enteritis and death.

7. *Poisons used to Simulate Injuries.*

Plumbago rosea Linnæus (Plumbaginaceæ) and ***Anacardium occidentale*** Linnæus (Anacardiaceæ) are used to simulate bruises and other injuries in order to get innocent people into trouble.

8. *Aphrodisiacs.*

The aphrodisiacs, which are much in demand by tropical natives, may be divided into those of animal and those of vegetal origin.

Those of animal origin are *Meloe vesicatorius* (*Cantharis vesicatoria, Lytta vesicatoria, Musca hispaniola* are synonyms), which is well known, and *Mylabris cichorii*, a beetle called Pān-mao by the Chinese and containing 1 per cent. of cantharidine. In China and the Far East generally the testicles, spinal cords, etc., of animals, pounded and mixed with rice water, are eaten as aphrodisiacs.

Those of vegetal origin are numerous, and include *Panax quinquefolium* Linnæus (Araliaceæ), the powdered root of which, called by the Chinese Jenn-Chenn, is used; *Populus spinosa* (Amentaceæ), the Sèn-iâng hoâ of the Chinese, of which the buds are used; *Psorala corylifolia* Roxburgh (Leguminosæ), the fruit of which is used by the Chinese and Annamese; *Psorala glandulosa* Linnæus in Chili; *Amomum zingiber*, the ginger (Zingiberaceæ); *Caryophyllus aromaticus* Linnæus (*Jambosa aromatica* Miquel Myrtaceæ); *Pausinystalia yohimba* Karl Schumann, the celebrated yohimbehe or yumbehoa bark, from which the alkaloid yohimbine hydrochloride, used in 1 per cent. solution, dose 5 to 15 minims, or tablets with $\frac{1}{12}$ grain taken one three times a day, may be mentioned. The last is sometimes named *Corynanthe yohimbi*, but this is merely a synonym *P. trillesii* Pierre is also considered to contain yohimbine.* These trees grow in the Kameruns and the Congo.

Cordiceps sinensis is the mushroom called Tch'oungtis'aô by the Chinese, and is used as an aphrodisiac.

II. ACCIDENTAL POISONING.

Accidental poisoning happens fairly frequently; therefore a few examples may be given.

Certain common articles of food are poisonous until properly prepared; e.g., tapioca is the starch obtained from the root of *Manihot utilissima* Pohl 1821 (*Jatropha manihot* Linnæus—Euphorbiaceæ), commonly called the cassava, of which there are two varieties, the sweet and the bitter. The latter contains hydrocyanic acid in its milky juice, and is, therefore, poisonous until it is roasted, when the volatile acid is driven off, and the bitter cassava can then be used for food after squeezing out the juice and cooking the root. Waddell reports two cases of death from accidental poisoning by this root in 1898 in Madras.

Arisæma.—Vogt has reported the accidental poisoning of a Chinese woman by an unknown species of the genus *Arisæma* Martius, belonging to the family *Araceæ* Schott, 1832. She ate a small piece of the tuber, and in ten minutes became stuporous, and despite prompt and vigorous treatment, which included the washing out of the stomach, her abdomen became distended and she suffered from paralysis of the limbs, but eventually recovered.

The members of the Araceæ are well known to be poisonous, and *Diffenbachia sequina*, the dumb cane, which grows in the

West Indies and South America, will cause a painful swelling of the tongue if chewed.

The emanations from the flowers of *Arum dracunculus* cause dizziness, headache, and vomiting in some people.

Blighia.—The succulent aril of the akee tree, which belongs to the genus *Blighia* Koenig, synonym *Cupania* Plumer (Sapindaceæ) and called *B. sapida*, is used as an article of food in the West Indies.

It is, however, known that if eaten in an unsound condition it is poisonous, and recently Scott has shown that this is the cause of the *vomiting sickness* of Jamaica, as will be detailed in Chapter LXXII., p. 1695 of this book.

Capsicums (*C. annuum* Linnaeus, 1775 Solanaceæ), if taken in large quantities, may cause burning in the mouth and throat, vomiting, colic, diarrhœa, and even death. *C. frutescens* Linnaeus, 1753, may also be mentioned.

Cinnamomum zeylanicum Nees. Lewin states that cinnamon bark may be poisonous, while nutmegs (*Myristica fragrans* Houtt) are well known to be poisonous if taken in large doses.

Calotropis gigantea R. Brown (Asclepiadaceæ) has been known to cause fatal effects by administration non-maliciously of two dessertspoonfuls of its milk in a quantity of cow's milk. This plant is variously named 'mudar' in Bengal, 'vercumby' by Tamils, and 'warra' by the Sinhalese.

Chailletia toxicaria Don (Chailletiaceæ; native name 'magberi' or 'manuchi'), the powdered fruit of which is used for killing rats, has been described by Renner in Sierra Leone as the cause of poisoning in a Mendi carrier.

The symptoms were mainly vomiting, diarrhœa, trembling, general weakness, and inability to walk because the legs were paralyzed, the tendon reflexes having disappeared. Hyperæsthesia was present over the inner side of the thighs and legs, and pressure on the calf muscle gave severe pain. The bladder, rectum, and pupils were normal. The man recovered in about two months.

Renner remarks that this case is probably the clue to attacks of sudden paralysis of the lower limbs in young persons (twenty to forty years) of both sexes in Sierra Leone. When death ensues, it is from paralysis of the muscles of respiration.

Dioscorea.—Guerreras and de la Paz say that this genus, as well as *Jatropha*, *Anamista*, *Strychnos*, and *Datura* are the cause of poisoning in the Philippine Islands.

Fungi.—The presence of *poisonous* as well as *edible fungi* should be remembered in the tropics; although there is no literature known to us on the subject, still we have had the matter forcibly brought to our notice.

The fruit of ***Hippomane mancinella*** Linnaeus (Euphorbiaceæ), the manchineel tree of the Grenadine Islands, which has a delicious fragrance, is said to have been the cause of many sailors meeting their deaths, for it looks like an apple. The active principle is not known.

The symptoms are severe pain in the mouth and stomach, followed by collapse. The lips and tongue become swollen and blistered, the abdomen tender, the pupils widely dilated, while bullæ appear on the skin.

The treatment consists of stimulants and intramuscular injections of ether, with mouth-washes. Internally opium, bromides, chlorate of potash, bicarbonate of soda, or bismuth, made into an emulsion, may be given.

Fontainea pancheri, Heckel, 1870 (Euphorbiaceæ), is a tree growing in New Caledonia, the ingestion of the fruit of which causes symptoms analogous to those produced by *Hippomane mancinella*.

Illicium Guerreras and de la Paz have also drawn attention to poisoning from a decoction of sanki, which is the fruit *Illicium religiosum* v. Siebold, which belongs to the genus *Illicium* Linnaeus, of the family *Magnoliaceæ* De Candolle, 1818. Montel in Indo-China has also found it to be poisonous. The symptoms appear to resemble cholera, but diagnosis has to be made from strychnine poisoning, tetanus, and cerebro-spinal meningitis. The symptoms were vomiting, diarrhœa, thirst, unconsciousness, convulsions, cramps, profuse sweating, oliguria and anuria, small rapid pulse, cold extremities, paresis of the lower limbs, and exhaustion. The head is retracted, the eyeballs bulge, and the face becomes cyanotic when the respiration stops. In China and Japan it and its related species *I. anisatum*, the star anise, which is harmless, are called badiane.

The seeds of *Ricinus communis* Linnaeus (Euphorbiaceæ), the castor-oil plant, are poisonous, causing burning in the throat and abdomen, vomiting, purging (may be absent), and collapse. The fatal dose appears to be three seeds, and to kill in about forty-six hours. Post-mortem the principal feature is gastro-intestinal inflammation.

The treatment is emetics, stimulants, and hypodermics of morphia.

III. STIMULANT AND SEDATIVE POISONING.

Many drugs are employed all over the world to stimulate or to deaden the nervous system. These stimulants and sedatives have been used by man from time immemorable to whip up a flagging nervous system, or to deaden the effects of mental or bodily suffering.

Used judiciously and in a proper manner there can be no doubt that they alleviate human suffering, but if used injudiciously or immoderately, and especially if they are constantly taken, they become 'habit poisons,' and as such affect the cells of the body injuriously, and by so doing some of them become true 'racial poisons,' and as such have been mentioned in the section on Eugenics (see p. 118).

It is not our intent to write, except in the briefest manner, upon these poisons, as their effects are fully considered in special works and are also contained in all the ordinary textbooks dealing with general medicine. Notwithstanding this, we feel that a few remarks dealing with these drugs in the tropics are necessary.

Alcohol.—We have already referred to our belief that this is a personal and a racial poison, and we would warn our readers not to be misled by statistics on this point, and if they wish further information to refer to Adami on Karl Pearson (*vide* references). Alcoholism is unfortunately on the increase among tropical natives, and is doing great harm in the form of indigenous stimulants such as arrack, which is almost directly the cause of a large percentage of the violent crime in Ceylon, as was shown by the fact that the accident wards of the hospitals were nearly empty in the proscribed regions during the period of a social prohibition.

More dangerous, in our opinion, are the imported cheaper alcoholic drinks, such as the cheap whiskies, gins, and rums, which, being cheap, are drunk in quantity and greatly deteriorate native races. These bad effects are not due to fusel oil, which is not present in these cheap forms of spirit, which in many ways are the purest form of alcohol to be obtained, and hence their effect is truly due to alcohol and to alcohol only, and their real danger is simply because they are cheap. *Methyl alcohol* is a direct poison to man, a fact but little understood at the present time.

Opium is eaten in Persia, India, and Africa, and smoked in Malaya, Indo-China, and China, but for the latter process it has to be specially prepared. On the Eastern mind opium is said to have two possible effects: either it produces a sense of absolute blank, or it produces fancy dreams and visions. The effects of chronic morphinism are loss of appetite, emaciation, and exhaustion, and hence inability to think or work.

It is, however, probable that the effects of opium are not as bad as those of alcohol, and, used in moderation, it may not be more harmful than the use of tobacco.

Cocaine has been used much of late in India as an intoxicant or stimulant, to counteract the effects or in lieu, of opium, owing to the restrictions on the sale of opium. Unfortunately, children have begun habitually to use the drug. The cocaine is chewed with betel and chunam (slaked lime), and produces at first loss of sensation in the tongue and lips, followed by dryness of the mouth and fauces. The temperature does not rise, but the pulse becomes full and quick, and at this stage the inebriate likes to be left alone, and firmly closes his lips lest the saliva should flow out. His ears become hot and red, his cheeks pale, and the tip of his nose cold. Perspiration breaks out, and the maximum amount of the so-called hilarity or exaltation, due to overstimulation of the nervous system, now appears, but is speedily followed by depression, which induces the victim to take another dose. The teeth and tongue of the confirmed cocaine-eater turn jet-black, probably due to some chemical change produced by the action of lime and saliva on cocaine. Pernicious symptoms in the form of emaciation accompanied by insomnia, digestive disturbance, diarrhœa, deafness, diminution of urine, delusions and hallucinations, and even at times acute mania, may appear.

Indian hemp (*Cannabis sativa*) is used in India, Arabia, Persia, and elsewhere as a narcotic. It must be remembered that *C. sativa* grown in India has quite different properties from the same plant grown in Europe. In India there are four varieties sold: bhang, consisting of the dried leaves and stalks reduced to a powder; ganja, the flowering tops; charas, the resin from the leaves; and majun, a sweetmeat prepared with hemp. In Central Asia the resin is called haschisch.

Its action on man is first to produce a pleasurable excitement and later narcotism. In moderate doses it temporarily increases the feeling of strength and power. As an intoxicant it is much used, being eaten or smoked, and is said to be one potent cause of insanity in India. Waddell says that about 38·4 per cent. of Bengal lunacy can be traced to this source. It is asserted to be one of the causes of the strange phenomenon called 'running amok,' but this will be dealt with in detail later on, under diseases of the nervous system.

Kawa is an intoxicating drink prepared from the root of *Piper methysticum* Forster (Piperaceæ), which grows throughout Polynesia.

According to Lewin, kawa contains starch, flour, two inactive substances—kawain and yangonin—and 2 per cent. of resin, which is believed to be the active principle. But this resin, by treatment with ether, can be resolved into two separate substances, one of which has a weak, and the other a strong action on man. The drink causes a feeling of *bien etre*, but too much has an evil effect, with symptoms of inco-ordination and headache, and a desire for sleep, and may induce liver disease, dermatitis, and general debility. Taken in moderation it is said to be harmless, and also to be a cure for gonorrhœa, and, as such, was introduced into Europe.

Peyotl (pellote) is a narcotic used in Mexico, and derived from the cactus, *Anhalonium lewinii* Henn. It causes sleep with hallucinations.

Coriaria species—*C. ruscifolia* Linnaeus, the poison-foot of New Zealand, and *C. myrtifolia* Linnaeus (a native of Europe)—are considered to be intoxicant or poisonous, according to the dose. The symptoms are coma, convulsions, and dilated pupils. From *C. ruscifolia* the Maoris are said to prepare a wine and jelly.

Pituri (*Duboisia hopwoodi* F. Mueller—Solanaceæ) is a shrub growing in Australia and New Caledonia. In the former it is found in the neighbourhood of Carlo or Mungerebar on the Upper Mulligan, and from this in scattered patches eastwards. At Carlo live the Ulaolinga tribes, from whom the other tribes purchase the pituri by barter with spears, boomerangs, etc. About the beginning of March the pituri leaf is gathered and is sold in the form of half-green, half-yellow tea mixed with plenty of chips. The preparation is complex: it is first roasted in ashes, then wetted with water, then teased with the fingers, and all larger pieces removed. Then leaves of a species of wattle or gigeon are heated over a fire and finally burnt, the ashes being retained and mixed with the moist pituri on a 'pituri plate'—*i.e.*, a smooth surface—and finally manipulated by the fingers into small rolls, 2½ inches long by ¼ inch thick. These rolls are chewed by the natives, and are in great demand as a narcotic. Reserve rolls are carried at the top of the ear. The Australian native names are: 'Măja' (Walookera), 'ne-em-pa' (Yaroinga), 'un-da-kor-a' (Undekerebina), 'pi-tu-ri' (Ulaolinga), 'ti-rum-bol-a' (Karanga), 'ta-rem-bó-la' (Pitta-Pitta), 'moda' (Kalkadoon). The alkaloid piturine is identical with hyoscyamine.

Betel.—The chewing of betel is an extremely common practice in the East, where the leaves of *Chavica betle* (piper betel) are chewed with slices of the nut of *Areca oberacea* (Pinang or areca-nut palm) and mixed with lime. Betel stimulates the salivary glands and, it is said, those of the digestive organs. It diminishes the perspiration, and should be spat out and should not be swallowed. The irritation may be the cause of the commonest cancer of old people in these parts. In the young it may possibly be the cause of heart and nerve diseases.

Kola.—The kola nut so much used as a stimulant by the African native is the produce of several species of the genus *Sterculia* Linnæus, of which the principal are *St. tomentosa* Thunberg and *St. acuminata* Beaver, while *St. nitida* Vent, *St. ballayi*, *St. verticellata* Thorne, and *St sphærocarpa* may also be noted. This nut has been known since the days of Leo Africanus in 1556, when it was known in the Sudan as 'goro.'

It is supposed to be a nervous system and cardiac stimulant, it raises the blood-pressure and increases muscular power, and certainly with kola nut and water a Haussa can travel far and work hard, as we know personally.

Analyses have been made and a glucoside, 'kolamin,' has been obtained by Hilger and Knebel.

Guaraná.—This substance, which is made into oblong or round cakes, is sold in Brazil as guarana bread, being considered an indispensable requisite for travellers. It is made from the seeds of *Paullinia sorbilis* Martius (Sapindaceæ), which are pounded and sweetened. It is said to contain a white crystalline substance which Theodore Martius called 'guaranene.' The Brazilians consider guarana to be a stomachic, a febrifuge, and an aphrodisiac.

Maté.—Paraguay tea is called 'maté' from the cup out of which it is drunk, or better 'yerba,' meaning herb or plant. St. Hilaire was the first to find and name the *Ilex paraguariensis*, which Lambert in 1824 changed to *paraguayensis*, and this is accepted because St. Hilaire cancelled his original name. It is prepared by slightly scorching the leaves, which are then broken down and subjected to a strong pressure. A handful of this pressed foliage is infused in a small spouted vessel called a ' maté.' It is then sucked hot through the spout or bombilla, which is perforated on its lower side with small holes, which, while allowing the escape of the liquid, prevent the pieces of leaf following. It is drunk freshly infused, and is said to be an aperient and diuretic, and to become a habit with those who drink it.

Maté is much used in Paraguay, Uruguay, the Argentine, and Southern Brazil, but in the last-named *Ilex gongonha* Martius, and *Ilex theæzans* Martius are employed.

Coffee.—The deleterious effects of excessive tea-drinking are well known and need not be repeated, but it may perhaps be as well to invite attention to the excessive amount of Turkish coffee which is drunk in the Middle East.

Other Poisons.—In Malacca the leaves of *Mitragyna speciosa* Korth (Rubiaceæ) are said to be used in place of opium. From the leaves of *Bassia latifolia* Roxburgh and *B. longifolia* Linnæus (Sapotaceæ) intoxicating drinks are made. *Hyoscyamus muticus* is used as an intoxicant by the Baluches, and makes them dance like lunatics.

The juice of the fruit of *Anacardium occidentale* (Anacardiaceæ) is used after distillation in Goa as a drink.

IV. POISONS USED IN TRIAL BY ORDEAL.

POISONS D'ÉPREUVE (FRENCH).

Curious customs exist in savage lands of trial by ordeal, in which the patient is given a drug and then ordered to perform some act. Waddell records the history of an old Hindu woman who was supposed to be a witch. She was tried by ordeal, being given a poisonous drug (datura) in treacle, as it is a native belief that a witch can withstand poison. The result of the ordeal was that the poor woman died.

In Africa the greater part of these poisons belong to the Loganiaceæ, Apocynaceæ, Leguminosæ, and Solanaceæ, but the plant employed varies in the different regions, and many are still undetermined—*e.g.*, M'Faug may be a strophanthus, while M'Boundou is undetermined.

Rho gives an account of trial in West Africa by ' imbundi,' the sliced root bark of *Strychnos icaja* (Baillon), which is said to contain strychnine. The accused, after drinking a concoction of the root, is made to jump over a stick, and is pronounced guilty unless he is able to do this, or to pass urine on to a banana-leaf, both of which feats are usually impossible.

Christison mentions the Calabar bean of West Africa, *Physostigma venenosum* Balfour (Leguminosæ), as being used in trial by ordeal, the belief being that the innocent vomit and are safe, while the guilty retain the poison and die. Its antidote is atropine, administered hypodermically.

Erythrophlæum judiciale Procter; *Tanghinia venenifera* Poiret. (which contains a toxic base with an action like digitalin), and *Menabea venenata* Baillon, are used in Madagascar, and *Adenium somalense* Poiret in Somaliland, for purposes of trial by ordeal.

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CHAPTER XI

ARROW POISONS

Preliminary - Africa - Asia - Philippine Island - Australasia - America - References.

PRELIMINARY.

FROM time immemorable peoples have used poisons to accentuate wound made by weapons, especially arrows. In 1857 Fontau discovered some arrow points in the Pyrenees which were grooved to receive poisons. These discoveries are said to date as far back as the Old Stone Age.

The arrows of primitive peoples produce wounds which are by no means usually fatal, and therefore, in attacking big game or in warfare, it is obvious that some poison which will insure the death of the victim fairly quickly will be valuable.

Usually these poisons, or the more potent of them, are only known to the fetish priests or chiefs, and are generally mixed with all sorts of animal extracts, the whole being made into a paste, and painted on the arrow heads.

If a special poison is prepared, as a rule some sort of precaution is also taken, so that the owner of the arrow may not be accidentally wounded. Thus, the Fra-Fra people, when preparing against the invasion of their country, obtained a very potent poison, which, however, they handled with great caution, though they boasted that they had an antidote. They kept these arrows, as a rule, in special quivers, and each arrow had a tiny stick tied to its shaft, so that it could be carefully lifted out of the quiver. Moreover, a tuft of red material was tied to the base of each of these sticks, so that there could be no mistake as to which were the specially poisoned arrows.

Arrow poisons may be classified into those of animal origin and those of vegetal origin. The most common animal arrow poisons are snake-venom, scorpions, spiders, red ants, and beetles, crushed and mixed with vegetal poisons. The Bushmen of South Africa and the natives of Togoland make an arrow-poison by burning and powdering the heads of adders and vipers, regardless of the fact that the burning must destroy the venom. The Bushmen of the Kalahari Desert make a poison from the larvæ of *Diamphidia simplex* Paringuey, which is thought to be really a toxin due to some micro organism growing in the decomposing larva. But animal poisons are not nearly so common as vegetal poisons.

The most important natural orders containing vegetal arrow-poisons are, firstly, the Apocynaceæ, which contains the genera Acocanthera, Strophanthus, and Adenium, all of which are common African poisons; secondly, the Loganiaceæ, with the genus Strychnos, which is of great importance in Asian poisons; thirdly, the Urticaceæ, with the important ipoh poison of Sumatra, Borneo, and Indo-China; and fourthly, the less important orders of the Ranunculaceæ, containing *Aconitum ferox* (Wall), used in India, the Leguminosæ, and the Euphorbiaceæ, containing some African poisons.

The actions of arrow-poisons are very varied, and may be classified into-

1. An action on the heart and muscles like that of digitalis.
2. An action on the peripheral nerve endings like that of curari.
3. An action on the nervous system and heart like that of aconite.
4. An action on the nervous system like that of strychnine.
5. An action resembling snake-venoms.

The general treatment of a poisoned arrow wound is as follows:

1. *Tie a tight band on the heart side of the wound*, if on a limb, to prevent absorption of the poison

2. *Remove the arrow as quickly as possible*

The difficulty in withdrawing the arrow-head is the presence of barbs, which can be prevented from doing mischief by thrusting the head through the skin on the far side of the limb there is no necessity to fear about the bloodvessels, for they will slip away from the arrow then cutting the shaft off, and drawing the head through on the far side, and the shaft on the near If it is in the body, a good plan is to enlarge the wound and pass down some sort of a cannula e.g., a hollow bamboo over the head, and then withdraw the whole arrow

3. *Wash the wound with permanganate of potash.*

Having withdrawn the arrow, wash the wound out thoroughly with a 3 per cent solution of permanganate of potash (if this cannot be done, cup the wound or suck it), in order to neutralize any snake-venom, and, indeed, any other poison capable of being oxidized.

4. *Keep the heart acting*

Give stimulants e.g., hypodermics of strychnine after the arrow is removed and the wound washed

5. *After-treatment.*

Treat the hurt as a poisoned wound A dose of antitetanic serum would be good, if available

Some of the principal arrow poisons require to be described in more detail.

Africa. The natural order Apocynaceæ contains, as already stated, several genera of plants which provide celebrated arrow-poisons much used by native peoples in Africa.

These genera are Acocanthera, Strophanthus, and Adenium.

Acocanthera Arrow-Poison.—The genus Acocanthera supplies the most important arrow-poisons of East, Central, West, and South Africa. The poison, which is called waba, wabajo, or ouabaio, was first fully described by Burton in 1856. It is prepared from the tree *A. schimperi* (Dec) in Abyssinia and throughout the greater part of East Africa, being used by the Wataita, the Wakamba, and probably other tribes. The special Fra-Fra arrow-poison of the Gold Coast is probably derived from some species of Acocanthera. In Erythræa and Yemen *A. deflersii* Schweinfurth is used, and in Somaliland *A. ouabaio* Cathelineau. These trees are 4 to 5 metres in height, with dark green foliage, white or red flowers, and violet-red fruit. The poison is usually prepared by making a decoction of the wood, and evaporating it down until it becomes a thick tar-like extract, which contains the active principle. This principle, which is a glucoside called ouabain, acocantherin, or wabain, is a powerful cardiac poison. In addition, the natives generally add snakes' heads and gall-bladders to the tar-like mass; but it is doubtful whether these really increase its virulence, though it must be admitted that sometimes there are symptoms analogous to snake-poisoning.

The thick extract of the wood containing any other additions, which individual peculiarity may consider necessary, is now painted upon the arrow-heads.

The action of the freshly prepared poison is very rapid, death taking place in a few minutes through stoppage of the heart, after a preliminary quickening of the respirations and convulsions. Sometimes pain is complained of in the lumbar region. The symptoms can be readily prevented by a 3 per cent. solution of permanganate of potassium The native remedy is believed to consist in eating some of the poison.

Another important Acocanthera poison is *A. venenata* Thunberg, which is employed by the South African Bushmen, and is said to be made from a decoction of the bark. The symptoms are rigors, without convulsions, and loss of muscular power, followed by death in a few minutes

Strophanthus Arrow-Poison.—Livingstone was probably the first to draw attention to a Strophanthus arrow-poison called kombi, used in Central Africa *Strophanthus hispidus* De Candolle is a very common plant in many parts of West and Central Africa, and is a common arrow-poison, but not nearly so deadly as that of Acocanthera. The other varieties used are *S. glabris*, *S. kambe*, *S. lanosus*, *S. ciabé*, *S. barika*.

The poison is obtained by cooking the seeds in water, and adding snakes' heads and leaves and roots of other plants. The injured man falls to the ground, and his breathing and pulse become gradually slower and slower, until the heart-beats suddenly cease, and death ensues, preceded by a convulsion in about ten to fifteen minutes. The heart stops in systole, and will not contract on stimulation. Strophanthus is used on the Congo, Lake Nyassa, Zambesi, Gaboon, Guinea Coast, Gold Coast, Cameroons, and Senegambia as an arrow-poison.

Adenium Arrow-Poison.—There are two species of Adenium used in Africa—viz., *A. boehmianum* Schinz and *A. somalense* Oliver.

A. boehmianum, which is a shrub about 1½ to 2 metres in height, is used by the Ovambo of German South-West Africa to prepare an arrow-poison called echuja. The thickest branches or roots are cut across and held over a fire, when the thick, viscid sap exudes in threads, and is collected by winding it round small pieces of wood. The arrow heads are now moistened by spitting upon them, and then smeared with the sap.

The active principle is echujin, which is a very virulent cardiac poison. The Somaliland species is equally virulent.

Erythrophlœum judiciale Proct.—Its active principle is an alkaloid, erythrophloein, which causes dyspnœa, first slowing and then quickening of the heart, and finally death from stoppage of breathing. It is used by the Pigmies of Central Africa; but the principal Pigmy arrow-poison is a mixture of this with strychnine, which will kill an elephant. Prompt treatment, however, is said to be able to save a man's life when wounded by one of these arrows.

Munchi Arrow-Poison. The Munchi arrow-poison, which is used by the Backorana clan in Northern Nyeni, is said to be nearly always fatal to man in about half an hour. The method of preparation is not known, but the poison is plastered in a thick layer on the long point of the barb. It is brittle, of a dark brown colour, with slightly aromatic odour, and is insoluble in cold or warm water, in normal saline or acidulated solution, but dissolves easily in alkalis—*e.g.*, 1 per cent. Na_2CO_3 solution. It has no alkaloidal properties, and does not reduce copper sulphate in alkaline solution. No fluorescence occurs with H_2SO_4, and there is only slight reducing power after prolonged boiling with mixed acids. It acts by paralyzing the heart and the striated skeletal muscles, but no distinct action on the muscle plasm can be detected. The toxic substance is thought to belong to the class of resinous acids.

Euphorbia candelabrum.—This is supposed to be one of the ingredients of the poison '*uciunga*' (meaning poison), used by the Wafiomi, Wagogo, of late German East Africa. The other ingredients are not known. According to Brieger, the active principle is exactly the same as in Acocanthera. Rho says the Wakamba use a similar poison.

Less important African arrow poisons are:—

(*a*) *Used by the Monbattu Dwarfs*—

1. Erythrophlœum guineense G. Don., belonging to the Leguminosæ, of which the bark is used.
2. Palisota barteri Bentham.
3. Combretum grandiflorum G. Don.
4. Strychnos icaja Baillon.

(b) Used by the Hottentots and South African Bushmen—

5. Hæmanthus toxicarius (Linnæus).
6. Euphorbia cereiformis (Linnæus).
7. Euphorbia virosa (Wight).
8. Euphorbia heptagona (Linnæus).
9. Euphorbia arborescens (Boissier).
10. Hyænanche globosa (Lamb).

Nigerian Arrow-Poisons.—Parsons finds that the common arrow-poisons are either strophanthus or strychnos.

Asia.—The best known of these poisons are those used in Malaya Sumatra, and Borneo, and prepared from the following:—

Ranunculaceæ—

Aconite (various species).

Urticaceæ—

Antiaris toxicaria Leschenault

Leguminosæ—

Derris elliptica Bentham.

Loganiaceæ—

Strychnos tieuté Leschenault.
Strychnos wallichiana Bentham.
Strychnos maingayi Clarke.

Rubiaceæ—

Lasianthus flavescens Korthals.

Dioscoreaceæ—

Dioscorea hirsuta Blume.

Aroideæ—

Amorphophallus campanulatus Blume

Apocynaceæ—

Tabernæmontana malaccensis Hooker.

Aconite.—The Mishmi arrow-poison of North-East India is derived from some species of aconite, perhaps *A. ferox* or *A. heterophylloide.*

Aconitum ferox Wall, belonging to the natural order of the Ranunculaceæ, is used by the Himalayan tribes from Assam to Kashmir as an arrow-poison, and several Sepoys have been mortally wounded in expeditions.

The poison is applied as a paste to the arrow, and is said to be mixed with septic blood to increase its effects (Waddell). It is also said to be used along the French and Chinese frontiers of the Indian Empire, and by the Ainos in Japan, but the latter are believed to mix it with tobacco.

Antiaris toxicaria.—*A. toxicaria* (Lesch) is a tree growing in Malaya, the sap of which provides the arrow-poison known as ipuh, ipo, ipoh, ternek, kyass, poön, upas, etc. It is used by the Sakais of Malacca, the Battaks of Sumatra, the Dyaks of Borneo, and the Mois of Cochin China. Brandwood's dart-poison, dajaksch, from Borneo, appears to be from the juice of *A. toxicaria.*

The earlier travellers in Malaya gave wonderful accounts of the upas-tree and its action, which were purely imaginary. Delisle and Magendie appear to have been the first to make experiments with the poison in 1810, and they were followed by Brodie in 1811, who showed that the heart-beats became weak and irregular before respiration or the mental faculties were impaired.

There appears to have arisen a confusion between the juice of *A. toxicaria* and *Strychnos tieuté*, which explains the finding by Hedbon and Welting of strychnine in upas antiar. Pelletier and Caventou, the discoverers of quinine, studied the chemistry of the poison, and in 1838 Mulder isolated the active principle as a crystalline body, which he called antiarin, which in 1868 De Vrij and Ludwig showed to be a glucoside.

Kiliani in 1896 investigated antiarin, and found its formula to be $C_{27}H_{12}O_{10}$. The physiological action of the poison has been investigated by a large number of observers, notably by Hedbon, Kiliani, and Seligmann, the last named observer giving a most excellent account of ipoh as used by the Kenyahs of the Baram district of Sarawak.

The poison is prepared from the inspissated juice of the tree, and is either used alone or is mixed with *S. tieuté*, snakes' heads, or other substances. The whole concoction is made into a paste with water, and applied to the heads of the arrows, which are then dried before a slow fire.

The poison acts on the ventricles of the heart, behaving like digitalis, and, in addition, causes paralysis of the cerebral nervous system and passing clonic spasms of the voluntary muscles.

Croton tiglium. Fraser considers that this is one of the Abors' arrow-poison, while the other is probably aconite, possible *A. ferox* and *A. heterophyllum*.

The Strychnos Arrow-Poisons. *Strychnos tieuté* Leschenault is the upas tieuté of Borneo, *S. wallichiana* Bentham is the ipoh aker, and *S. maingayi* the aker lampong of the natives of Malacca.

The poisons obtained from these plants are said to contain strychnine and curari. The symptoms are said to be paralysis of the muscles, abolition of the reflexes, and stoppage of the heart and respiration. The urine contains a substance which reduces Fehling's solution.

Manbhum Arrow Poisons. Anderson thinks that these poisons may possibly be manufactured in the following ways:—

1. By dipping the arrow-heads into rotten fish or meat, or into the highly decomposed human body, or into animal secretions equally decomposed.
2. By coating them with nux vomica and sulphide of arsenic.
3. By coating them with snake venom.
4. By dipping them in mud, so that they acquire the organism of tetanus.

Less important Asian arrow poisons are: *Guatteria veneficiorum* Mart, *Cocculus toxiferus* Mart, *C. amazonum* Mart, which are also used in India as arrow-poisons, the active principle being curari.

Philippine Islands.—The arrow-poison used by the Negritos of the Philippine Islands is *Rabelaisia philippinensis* Planch., which causes paralysis of the extremities, dyspnœa, convulsions, and cessation of the heart's action.

Australasia.—Le Dantec, quoted by Vaughan and Novy, says that the poisonous arrows of the natives of the New Hebrides are prepared by smearing the points, which are usually made from human bones, with, first, a vegetable resin, and then with slime taken from marshy places.

America.—The important American arrow-poisons used in the valleys of the Amazon and Orinoco belong to the Loganiaceæ, and are *Strychnos toxifera* Schomb., *S. crevauxii* Planchon, *S. castelnaeana* Baillon.

The active principle is curari, and, it is said, curin. Curari, or ourari, was first brought to Europe by Sir Walter Raleigh in 1595. The drug paralyses the motor end-plates, and causes death from failure of the respiration.

Less important American arrow-poisons are:—

(*a*) *Paullinia pinnata* (Linnaeus), used by native Indians of Brazil.
(*b*) *Piscidia erythrina* (Linnaeus), used in Brazil and Central America.

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CHAPTER XII

POISONS USED IN FISHING, HUNTING, AND TRADE

Preliminary—Fish poisons—Poisons used in hunting—Cattle poisoning—Rat poisoning—Locust poisoning—Poisoning of birds—Trade poisoning—References.

PRELIMINARY.

In this chapter we consider in the briefest possible manner the use of poisons to kill fish, big game, cattle, rats, birds, and trade poisoning.

FISH POISONS.

Every now and again we have been appealed to for the purpose of explaining why a large number of fish have been found dead in a river or lake, and certainly in those which we have been able to investigate personally the causal agent has been poisoning of the waters.

It is a common practice all over the world to throw pieces of bark or leaves of trees and shrubs on to the water, in order to stupefy fish, and thus enable them to be easily caught.

The number of plants used for this purpose is very great, and though we have not thought it necessary to give a detailed list in this book, still, we consider that it is useful to give a few examples, as a knowledge of the subject is at times required.

The plants used in Ceylon for the purpose of intoxicating or killing fish are given in the following list supplied to us by Mr. Drieberg:—

1. *Anarmirta paniculata* (*A. cocculus* Wight and Arnott).
2. *Barringtonia acutangula* Gaertner.
3. *Euphorbia tirucalli* Linnæus.
4. *Lasiosiphon eriocephalus* Decaisne.
5. *Mæsa indica* Wall.
6. *Mundulea suberosa* Bentham.
7. *Randia dumetorum* Lamarck.
8. *Strychnos nux vomica* Linnæus.
9. *Walsura piscidia* Roxburgh.
10. *Derris uliginosa* Bentham.

Hydnocarpus venenatus Gaertner is also said to be used, and to be poisonous on account of the hydrocyanic acid it contains.

In India the following are used:

Anamirta cocculus Wight (Menispermaceæ).
Dolichandrone falcata Seemann (Bignoniaceæ).

In Java and Sumatra:—

Pittosporum densiflorum Putterlick (Pittosporeæ).
Tephrosia toxicaria Persoon
Tephrosia piscatoria Persoon.

In the Philippine Islands:

Sapindus rarak De Candolle (Sapindaceæ).
Harpulia arborea Radlkofer (Sapindaceæ)

In the Dutch East Indies:

Derris elliptica Bentham (Leguminosæ).
Pachyrhizus angulatus Richard

Both of these plants contain a non-nitrogenous substance, called respectively derrid and pachyrhizid, highly poisonous to fish. Derris-root will kill fish in a dilution of 1 to 25,000 of water, and derrid in 1 to 5,000,000

In the Comoro Islands

Tephrosia vogelii Hooker (Leguminosæ)

In the West Indies:

Piscidia erythrina Linnæus.

This plant, called the Jamaica dogwood, is used by throwing the leaves and entire branches into the water, when the active principle, piscidin, dissolves out and paralyzes the fish, which are easily caught floating on the surface

In Guyana:

Tapura guyanensis Aublet.
Ichthyothere cunabi Martius

In South America:—

Grewia asiatica Linnæus
Dichapetalum toxicarium Baillon.
Serjania ichthyoctona Radlk (the Timba of the Amazon).
Serjania lethalis St. Hillaire (the Timba of the Amazon).
Serjania piscatoria Radlk (the Timba of the Amazon).
Hydrocotyle javanica Ehrenberg.
Clibadium asperum De Candolle.
Jacquinia armillaris Linnæus

In Africa:—

Kiggelia africana Linnæus
Paulowilhelmia speciosa R. Brown.
Tephrosia vogelii Hooker.

In Sardinia:—

Œnanthe crocata Linnæus.
Daphne guidium Linnæus.

POISONS USED IN HUNTING.

In India the root of *Arum montanum* Roxburgh is said to be used to poison tigers, while aconite is employed for the same purpose against elephants, especially *A. ferox* Wall. In San Salvador the 'Cangoura,' *Rourea oblongifolia* Hooker, is employed.

CATTLE POISONING.

Cattle poisoning is a frequent method of revenge in India, and the drugs most commonly used are: Arsenious oxide, arsenious oxide with sulphite, arsenious oxide with oxides of lead, sulphides of arsenic only, oxides of lead only, sulphate of copper, nux vomica, *Cocculus indicus*, mercury, and sulphate of iron.

But, in addition, *Abrus precatorius* Linnaeus, *Cerbera thevetia* Linnaeus, *Calotropis procera* R. Brown, aconite, chopped hair, and snake-venom have been used. The list of Ceylon plants poisonous to man and cattle will be given below. It is important to remember that rinderpest and dysentery resemble arsenical poisoning, while poisoning with nux vomica may resemble tetanus.

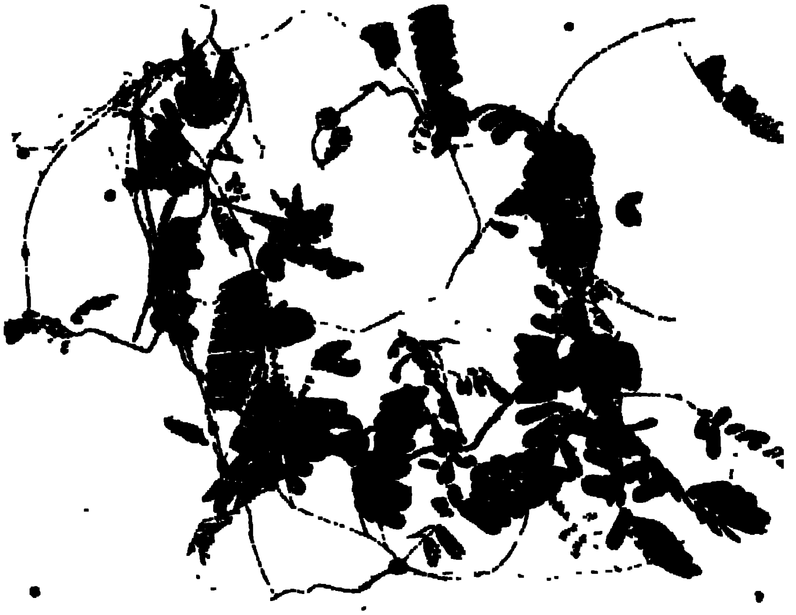

FIG. 13. *Abrus precatorius* LINNAEUS.

Grey says that *Lessertia annularis*, the Cneuta of the Karroo of South Africa, produces cerebro-spinal paralysis in sheep and goats, like *Gastrolobium*, the poison-pea of Australia. Only *Abrus precatorius* need be discussed here.

Abrus precatorius Linnaeus.—The juice of this plant, which belongs to the Leguminosae, is most irritating, and if injected under the skin of cattle proves rapidly fatal, by producing general depression, drowsiness, fall of temperature, and haemorrhagic lesions somewhat like those of snake-venom.

The decorticated seeds are made into a paste, which is worked into sharp-pointed little needles, and hardened in the sun. Two of these are inserted by their bases into a wooden handle, and then driven with great force into the animal's flesh.

The active principle is abrin, a tox-albumin resembling snake-venom, which causes thrombosis and death in from eighteen to twenty-four hours.

Ornithoglossum glaucum Salisbury, 1806.—This plant is the cause of accidental cattle poisoning in South Africa.

Much has been written of late years with regard to stock poisoning in Australia and elsewhere, but it is rather outside the work of this book to deal further with this matter, to which we give references at the end of this chapter. We, however, give a list, which we owe to the kindness of Mr. Drieberg, of Ceylon plants known to be poisonous to cattle:

1. *Ammannia baccifera* Linneus.
2. *Anamirta paniculata* (*A. cocculus*) Wight and Arnott.
3. *Arisaema curvatum* Thwaites.
4. *Chrozophora plicata* A. de Jussieu.
5. *Croton tiglium* Linnaeus.
6. *Diospyros montana* Roxburgh.
7. *Elaeodendron glaucum* Persoon.
8. *Euphorbia tirucalli* Linneus.
9. *Excoecaria agallocha* Linneus.
10. *Datura fastuosa* Linneus.
11. *Lagenaria vulgaris* Seringe.
12. *Lasiosiphon eriocephalus* Decaisne
13. *Lobelia nicotianaefolia* Heyne.
14. *Manihot utilissima* Pohl.
15. *Paspalum scrobiculatum* Linnaeus
16. *Plumbago zeylanica* Linnaeus.
17. *Rauwolfia serpentina* Bentham.
18. *Rhododendron arboreum* Smith.
19. *Ricinus communis* Linnaeus.
20. *Sapium insigne* Trimen.
21. *Tylophora fasciculata* Buch-Ham.
22. *Withania somnifera* Dunald.

RAT POISONING.

This is generally carried out by means of yellow phosphorus or arsenic.

The phosphorus is mixed with glucose to prevent spontaneous combustion, and then made into a paste with a fatty base such as lard; but it is advisable to vary, from time to time, the fatty base, as rats are very knowing and begin to suspect that something is wrong.

The poison is then spread on bread or made into bread pills, but it is often advised that people who do this should have their hands smeared with an ointment containing oil of aniseed, with which all utensils used for the poison should also be smeared.

Arsenic is often preferable to phosphorus, which is difficult to obtain and dangerous to work with. It should be treated in the same way as phosphorus, but it is as well to find the minimal lethal dose for the local rat before commencing rat poisoning on a large scale, and also to be ready with an antidote in case any person indulges in a dose.

Many rat poisons are known to natives, especially *Tylophora fasciculata* Buch-Ham (Asclepiadeæ), *Chailletia toxicaria* Don (Dichapetalaceæ), both of which are used in Africa, and *Dianella nemorosa* Linnaeus (Liliaceæ) in Malacca.

LOCUST POISONING.

Arsenic has been used with success by Mr. King, Government entomologist in the Sudan, and others as a poison for killing locusts in the 'hopper stage.' The arsenic is prepared in concentrated form in treacle and is diluted locally. Into the solution so made chopped fodder is placed, and, after soaking, is spread out for the hoppers to eat in desert parts. Spraying has also been used in cultivated areas. Mustard and the usual iron antidote are handy in case anyone takes a dose of the poison.

POISONING OF BIRDS.

Attempts have been made from time to time to diminish the sparrow pest in cultivated areas by poisons *e.g.*, strychnine—but with doubtful success.

Palicourea marcgravii (*Rubiaceæ*) St. Hilaire is said to be used for poisoning pigeons.

TRADE POISONING.

The trade poisonings are more fully dealt with in the chapter on *Dermatitis venenata*, but we may mention the following here:—

Vanilla Poisoning.

Vanillismus is poisoning by the dried fruit of *Vanilla planifolia* (Andrews), which causes colic, vomiting, and pains in the head and muscles. Men working with it may suffer from conjunctivitis, fits of sneezing, and a skin eruption called vanilla itch, characterized by swelling, followed in a few days by scaling. There is, however, great doubt as to what is the real cause of these symptoms. Probably some of them are due to a mite in the vanilla.

Lacquer Poisoning.

Lacquer is obtained from a brown treacle-like balsam, which exudes when incisions are made into the lacquer-tree, *Rhus vernicifera* De Candolle.

The disease is acquired in two ways: either by direct contact with the lacquer, or through the fumes arising from it by evaporation, but only as long as the lacquer is not dry, for the poison, whatever it is, disappears on drying.

The symptoms, which develop in a few hours, are fever, with tension and œdema of the skin of the face, limbs, and generative organs, nasal and conjunctival catarrh, while a papular eruption appears on the œdematous skin of the legs and forearms.

The treatment consists in washing the skin thoroughly with soap and water, and applying soothing applications, such as cold lotions, or *Lotio Plumbi subacetatis*.

As prophylaxis the Chinese rub the hands and face with rapeseed oil in which a ham has been boiled, and wear a linen mask for the face and a leather apron for the body. After work the exposed parts are rubbed with a decoction of chestnut, pine bark, saltpetre, and amaranth.

The above precautions are taken in China, but in Japan no such prophylaxis exists.

NOTE.—Camel poisoning caused by the hydrocyanic acid contained in immature dura is well known in the Sudan.

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CHAPTER XIII

POISONOUS FOOD

Preliminary— Animal food poisoning—Products normally present—Fuguismus—Post-mortem decomposition—Vegetal food poisoning—Lathyrismus—Lolismus—Paspalismus—Atriplicismus—Fabismus—Fagopyrismus—References

PRELIMINARY.

FOOD poisoning, technically called bromatoxismus, may be divided into two classes:—

1. Animal food poisoning.
2. Vegetal food poisoning.

1. ANIMAL FOOD POISONING.

Animal food poisoning is called zootrophotoxismus, and may be due to—

(*a*) Products normally present in certain animals, but poisonous to man.
(*b*) Poisonous food having been eaten by an animal prior to its being killed for food.
(*c*) Products abnormally produced in the living animal.
(*d*) Post-mortem decomposition.

But of these we need only concern ourselves with the first and the last.

Products Normally Present.—Poisoning by products normally present in the animal is called 'siguatera,' and is generally due to fish, though it may also be caused by Molluscs, Crustaceans, and Cœlenterates.

The most dangerous fish are those living among coral reefs, and particularly those which are bright-coloured. It is possible that the poisonous properties may be due not so much to the fish itself as to the fact that it has eaten decomposing food, such as dead medusæ, corals, etc.

Fretz and Branch have noted fish poisoning in 1915 in St. Christopher and Nevis, and think that it is due to the *Barracouda* (*Sphyræna*), while McNaughton reports similar poisoning from the Gilbert and Ellice Islands.

Certain species of the genus Clupea (Cuvier), particularly *C. thrissa* (Osbeck) are noted as being very poisonous, but there is considerable doubt about this matter, as no scientific work has been done on the subject. The symptoms are gastro-intestinal irritation, which may lead to collapse and death. Another fish which is only poisonous at certain seasons is a so-called sardine *Clupea*

FIG. 14.—*Clupea longiceps* (*Sardinella neohowii*).

longiceps (*Sardinella neohowii* Val), found off the coasts of Ceylon, and which, according to Tennent, caused much sickness years ago.

Other poisonous fish are *Tetrodon hispidus*, the 'muki-muki' or death-fish of Hawaii, and the file fishes, of which *Stephanolepsis*

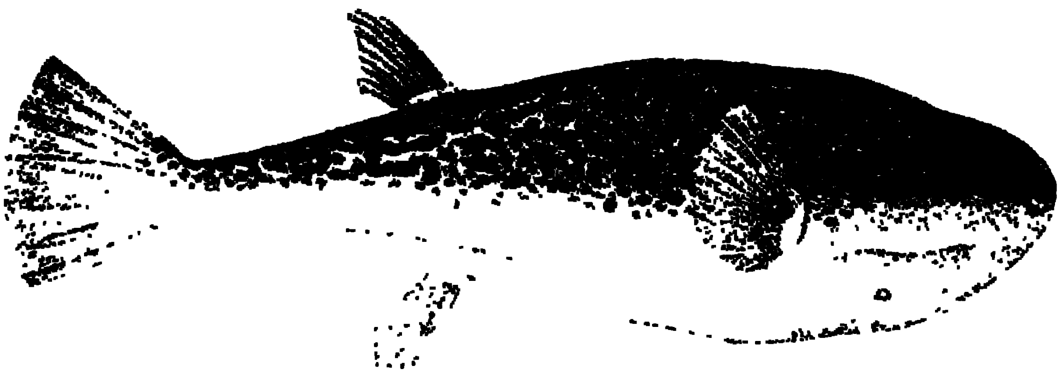

FIG. 15.—*Tetrodon vermicularis* SCHLEGEL.
(From Savtschenko's 'Atlas of Poisonous Fish')

hispidus L. may be mentioned as an example. Poisoning with Tetrodon has, however, been more accurately studied, and may be referred to at greater length under the term Fuguismus.

Fuguismus.

The Japanese term 'fugu' includes several species of fish belonging to the genus Tetrodon, of which the important species are *T. vermicularis*, *T. rubripes*, *T. lævigatus*, *T. chrysops*, *T. rivulatus*, *T. lunaris*, *T. pardalis*, *T. porphyreus*, *T. poicelonotus*, *T. stellatus*, and *T. sticonotus*, which are said by Scheube to be often used for suicidal purposes. *T. pennantii* has also been found to be the cause of poisoning in a case in Burmah.

The poison appears to lie in the ovaries and testicles, which, according to Tabara, contain—1. Tetrodin—a crystalline base; 2. Tetrodonic acid—a white, waxy body. Both are poisonous, but the acid is said to be more so than the base.

The symptoms, which begin in three to fifteen minutes after eating one roe, are, according to Scheube, an unpleasant sensation in the stomach, abdominal pains, burning in the fauces, nausea, severe headache, collapse, and fainting. Death may occur in a few hours from paralysis of the heart or respirations. The mortality is high, being said to be more than 68 per cent.

The treatment is to empty the stomach with an emetic and to give stimulants, especially hypodermics of strychnine.

Post-Mortem Decomposition.

Post-mortem changes are much more rapid in the tropics than in the Temperate Zone, and, therefore, food is quickly apt to become poisonous. Meat is especially liable to become infected with saprophytic or pathogenic micro-organisms, especially *Bacillus paratyphosus* B (Schotmüller) and the bacillus of Gaertner, more rarely *B. paratyphosus* A (Schotmüller). These micro-organisms give rise to ptomaines, which cause symptoms of irritant poisoning (kreotoxismus), which may be so severe as to resemble those of cholera. The treatment is to remove the poison by emetics if necessary and purgatives, in the meanwhile keeping up the heart's action by means of warm applications, stimulants, and cardiac tonics. When collapse sets in, saline hypodermic injections should be given. As soon as the acute symptoms subside, the bowel should be disinfected with small doses of calomel, salol, or naphthol.

2. VEGETAL FOOD POISONING.

Sitotoxismus, or vegetal food poisoning, is caused by many kinds of vegetal food, and ought to be well known, but, unfortunately, is by no means on a scientific basis in the tropics.

Ergotism, well known in the temperate regions, is not important in the tropics; but, on the other hand, there is lathyrism, believed to be due to *Lathyrus sativus*, and other species of the same genus—loliismus, due to *Lolium temulentum*; and paspalismus, due to *Paspalum scrobiculatum*—which are known to occur in India. Less known is atriplicismus, which is described in China.

Kirke has drawn attention to poisoning by *Cystisus cadjan*, by which he probably means *Dolichus catjana* (Linné), named *Vigna catjang* (Walp.) by Dragendorff, and also by *Dolichos filosa* (Klein), which is the same as *Vigna filosa* (Savi), both of which are used as foods. With regard to the former, the native name of which is urhur or toar, he says it mainly affects the poorer classes, as they do not remove the outer skin before eating it. The symptoms in the order of appearance are as follows:—Urticaria, sense of heat in the stomach, redness of the lining membrane of the mouth, apparent elongation of the teeth (by this must be meant shrinking of the gums), discoloration, bronzing of the skin, sponginess of the nails, burning of the hands and feet, a dry, harsh, cracked condition of the cuticle of the hands and feet, and deep longitudinal cracks in the heels. Rheumatic pains, with thickening of the periosteum, especially of the shins, and changes in the joints are also noticed.

Dolichos filosa, called 'oordh dal,' is said by Kirke to be poisonous only if eaten with the husks, when it causes colic, indigestion, and as secondary results rheumatic pains, harshness and dryness of the skin, with cracks. It is said to be a staple article of food among all classes, except the highest and the lowest.

Lathyrismus.

Synonyms.- Platterbsenkrankheit (Ger.); Meurd Djilben (Algeria); Latirismo (It.).

Definition.- Lathyrismus is an intoxication caused by the ingestion of *Lathyrus sativus* Linnaeus and other species of the same genus, and characterized by symptoms of spastic paraplegia.

History.- It is believed that Hippocrates was acquainted with the disease, because he mentions that people at Ainos who fed continually on pulse suffered from weakness in the legs. In 1671 the Grand-Duke of Würtemberg issued an edict forbidding the eating of bread made from vetch-seeds, as it had been noticed that those who ate such bread suffered from a peculiar stiffness of their legs, although they seldom died. In 1784 an epidemic was recorded in Tuscany, when, through scarcity of food, the people were compelled to eat chick-peas. Tozzetti, while studying this epidemic, came to the conclusion that only the people who had for at least three months eaten bread made of two parts chick pea to one part of rye or wheat became ill. He then planted some of the chick-pea seeds, and, when they grew up, identified them as *Lathyrus sativus* (L.). In 1824 Desparanches came to the conclusion that the seat of the lesion was in the lumbar cord. In 1833 the disease was first recognized in India in the Saugor territories, where, on account of three successive famines in 1829-31, the people were compelled to eat vetches, which are called kesari dal, or teori. Outbreaks took place in Sind, Chota Nagpur, the Central Provinces, and in the Himalayas. It apparently became very prevalent, for Irving says that in one district 6 per cent., and in another 3·19 per cent., of the inhabitants were affected. It still exists in India.

Climatology. The disease depends upon social rather than climatic conditions, for people will not eat the vetches unless compelled by famine. It is known in India, Algiers, Italy, and France.

Ætiology. There appears to be a consensus of opinion that the disease is due to eating bread composed largely of flour obtained from seeds of some species of Lathyrus belonging to the natural order Leguminosæ. The species most commonly suspected is *Lathyrus sativus* Linné, which grows in India; but *L. cicera* L. (red vetch), *L. clymenum* L. (Spanish vetch), *L. tuberosus*, and *L. aphaca* have all been regarded as possible causes. It is, however, by no means evident what substance or substances in these plants cause the symptoms. Teilleux obtained a resin which caused tetanic spasms and paralysis of the posterior limbs in rabbits. Bourlier obtained an extract which killed birds and frogs. Asher obtained from *L. cicera* a volatile alkaloid, which he called lathyrin, which was doughy in consistence, alkaline, insoluble in water, slightly soluble in ether, soluble in chloroform, and which on evaporation formed needles; but he did not perform any experiments with the substance, the action of which is therefore unknown. It is believed by some that Lathyrus is not poisonous unless the seeds are decomposed or contain some parasitic growth, while others hold that the symptoms are not due to Lathyrus at all, but to *Agrostemma githago* (the corn-cockle) or *Lolium temulentum* (the darnel). In 1883 Astier separated out an alkaloid, *lathyrin*, which Stockman in 1917 showed to be the poisonous principle, which is present in only small amount and only in the seed itself.

Animals are by no means immune from the baneful effects of the plants, for ducks become paralyzed and may die after eating the seeds; while pigs and horses also su the latter showing acute or chronic symptoms which are said more [illegible] less to correspond to lathyrismus. On the other hand, bulloc and buffaloes are considered to be immune.

The great predisposing c e in man is scarcity of food, whether due to famine or poverty, th of which compel the unfortunate people to eat vetches instead of ordinary food. If the disease is brought about by fa it may assume epidemic proportions; if by poverty, it may be simply endemic. Young people are more liable to be poisoned than old persons, and men more than women, perhaps because they eat more food.

Morbid Anatomy.—The pathology and morbid anatomy need investigation. When this is done, it is probable that some lesion of the pyramidal tracts—*i.e.*, of the upper motor neurones—will be found.

Symptomatology.—The incubation period is not known, and the disease comes on so insidiously that the patient often attributes it to a chill which he may have experienced a day or so previously.

Prodromata are often said to be absent, though it is more probable that digestive disturbances, colicky pains, and diarrhœa do occur, but pass unnoticed.

One of the first symptoms to arise is pain in the back and weakness in the legs, which increase until symptoms of spastic paraplegia appear. The patient now complains of girdle sensations, and walks with difficulty. The gait is characteristic, for the feet are turned slightly inwards, and are dragged or raised with difficulty from the ground. The joints appear so weak that it is difficult to proceed any distance without falling, while the body has a peculiar up and down motion. There is no ataxy, and no vasomotor phenomena, but the legs waste very much. The arms are not, as a rule, involved, though the hands may tremble. The superficial and deep reflexes are increased, and ankle clonus is present. The electrical excitability of the affected muscles is diminished, but the reaction of degeneration is absent. Incontinence of urine and impotence are early and common symptoms. The mind is unaffected.

The disease does not itself end fatally, but a definite improvement is seldom seen except in incipient cases.

Diagnosis.—Lathyrism must be distinguished from ergotism by the absence of gangrene, from beri-beri by the absence of implication of the peripheral nerves and the heart, and the absence of dropsy.

Prognosis.—The disease itself is not fatal.

Treatment.—Mild cases may be considerably benefited by being given good food and warm clothing, together with counter-irritation to the spine, and bromide of potassium internally in 15-grain doses three times a day. Strychnine is harmful.

Prophylaxis.—The only possible prophylaxis is the distribution of good food to the poor in times of famine.

Loliismus.

Loliismus is an intoxication caused by the ingestion of the seeds of *Lolium temulentum* Linnæus in bread.

History.—Loliismus has been known since Roman times, and is said by Orfila to have occurred in Genoa during the blockade of the year 1800. Kingsley of Roscrea described an outbreak in 1854, in which thirty persons suffered severely. Similar cases have been reported in India from the Punjaub, where the herb is called 'mostaki,' and from the North-West Provinces, where it is called 'moschni.'

Ætiology.—The exact method by which *Lolium temulentum* causes disease is not known. Dr. Cordier experimented on himself by taking 6 drachms of the seeds early one morning, and asserts that the result was inability to think, indistinct vision, torpor, debility, and drowsiness, followed by efforts to vomit, and later by tremors of the limbs, great depression, difficulty of speech, and vomiting. Bley separated a bitter principle, which he called loliin, but the action of this does not appear to have been investigated properly. Freeman states that the seeds owe their poisonous properties to an associated symbiotic fungus, which he carefully describes, and says that it is probably identical with that found in other species of Lolium. He says that it is a disputed point how far ergot and other fungi may be concerned in the production of the disease.

Climatology.—It occurs in the Punjaub and the North-West Provinces of India, and in Europe.

Pathology and Morbid Anatomy.—Not known.

Symptomatology.—The affected persons become very giddy, and stagger about as though drunk, and at the same time suffer from violent tremblings in the arms, legs, and tongue, impairment of vision with dilated pupils, green vision, great prostration, and in some cases vomiting. Sometimes there is a sense of burning heat in the mouth and throat, and a small irregular pulse.

Diagnosis.—The diagnosis may be effected by considering the symptoms and examining the bread, when the starch granules of Lolium may be seen.

Prognosis.—The disease does not end fatally.

Treatment.—Castor oil must be given to remove the poison, and at the same time stimulants must be used to counteract the collapse.

Prophylaxis.—Bread should not be made with the seeds of *Lolium temulentum.*

Paspalismus.

Paspalismus is an intoxication caused by eating bread made from flour derived in part from the seeds of *Paspalum scrobiculatum* Linnæus.

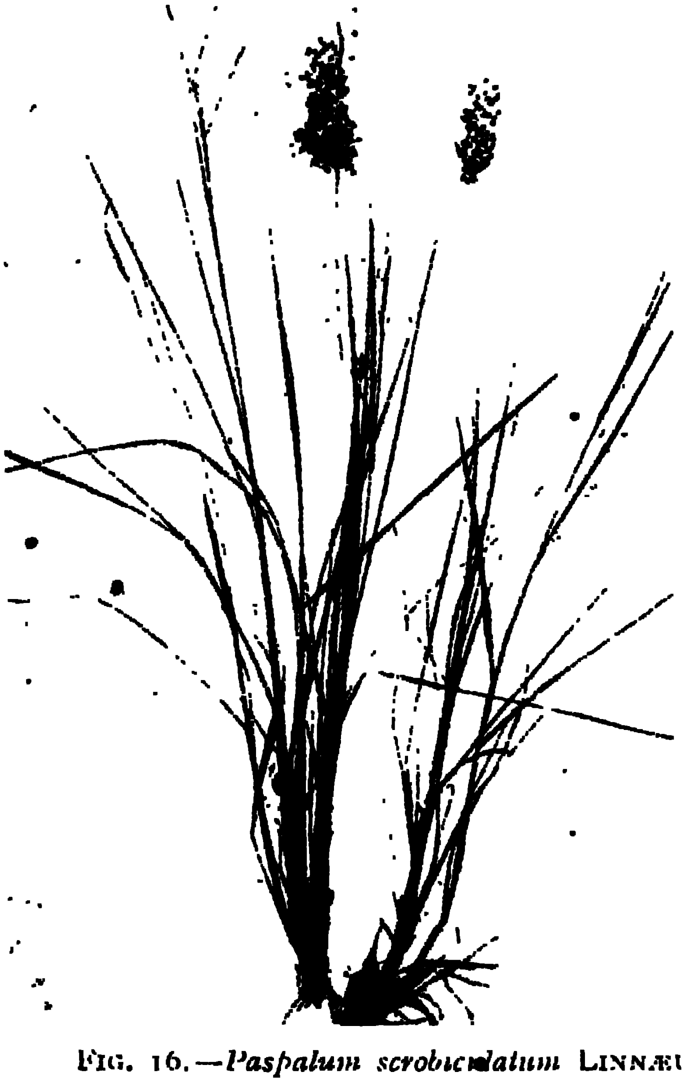

FIG. 16.—*Paspalum scrobiculatum* LINNÆUS.
Seeds show separately at the top of the illustration.

History.—Poisoning by *Paspalum scrobiculatum* occurs in India, where it was reported as far back as 1879, and probably was known earlier.

Ætiology.—Some authorities doubt the genuineness of this disease, for, as Waddell points out, the symptoms are so like loliismus that it is quite possible that some mistake may be made as to the causation.

Diagnosis.—This is made by noting the period of the year and by tracing the history of the ingestion of beans or the smelling of the flowers, and also by the family and geographical incidence.

From malaria it is diagnosed by the absence of the parasites and the negative reaction as regards complement deviation with malarial antigen

From quinine hæmoglobinuria it may be recognized by the absence of a history of the drug being taken.

Treatment. Apparently there is little known under this heading, which obviously calls for the administration of calcium salts (see Chapter XLI., p. 1213)

Prophylaxis.—Avoid eating raw or cooked fresh beans in Sardinia, and avoid the scent of the flowers. As the attacks recur it would be interesting if someone would try the administration of calcium salts to susceptible people living in Sardinia during the dangerous period of the year.

Fagopyrismus.

White animals fed upon buckwheat and exposed to the sun develop erythematous lesions of the skin and nervous symptoms.

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CHAPTER XIV

VENOMOUS ANIMALS: PROTOZOA TO ARTHROPODA

Protozoa—Cœlenterata—Echinodermata—Platyhelmia—Nemathelminthes—Arthropoda—Arachnida—Scorpionidea—Aranea—Acarina—Chilopoda—Hexapoda—Anopleura—Hemiptera—Hymenoptera—Lepidoptera—Diptera—Coleoptera—Mollusca—References.

VENOMOUS ANIMALS.

Many species belonging to the various classes and orders of the animal kingdom possess glands which secrete chemical substances injurious to man and the higher animals. The exact nature of these chemical substances is but little understood at present, though of late years much advance has been made in the knowledge of their action, which seems to be of a nature similar to that of bacterial toxins.

It will be best to consider these venomous animals in the order of their zoological classification.

PROTOZOA.

Rosenau and his collaborators have succeeded in producing a malarial paroxysm in a healthy man by injecting blood-serum taken from a malarial patient during the cold stage of the fever, and previously filtered through a Pasteur-Chamberland filter. Casagrandi and De Blasi have also described a hæmolytic toxin, concerning which more will be said when malaria is discussed.

Laveran and Mesnil have shown that *Sarcocystis tenella* produces a toxin, sarcocystin, of which 0·1 milligramme will kill 1 kilogramme of rabbit with choleraic symptoms, while a less dose will produce fatal cachexia. It is, however, less toxic to other animals.

CŒLENTERATA.

The Cœlenterata include anemones, corals, and jelly-fishes, which are capable of stinging by means of certain special cells called cnidoblasts, which enclose nematocysts—*i.e.*, little sacs—the invaginated neck of which is continued into a long, hollow, spirally coiled filament, surrounded with poisonous fluid. When stimulated, these cysts explode, and the filament is ejected and pierces the skin of the animal attacked, and so introduces the poison.

Zoantharia.- Stings from anemones cause itching and burning and skin eruptions. In its worst form this is exhibited in *la maladie des plongeurs* (*pêcheurs d'éponges*) of the Mediterranean. According to Dr. Skévos Zervos, the first symptoms are itching and intense burning in the place where contact with the anemone has taken place. A papule then appears, surrounded by an area which at first is red, but may become blue and finally black, and may spread over the surrounding skin to a distance proportional to the virulence of the poisoning. The skin sloughs, and leaves a suppurating ulcer. Dr. Zervos has produced the symptoms of this disease in a dog by rubbing an actinia, held in forceps, along its abdomen.

C. Richet has separated two poisonous principles from *Anemone sulcatus*, viz., thalassin and congestine. Thalassin is not very toxic, producing cutaneous redness, intense congestion of mucous membranes, pruritus, and sneezing. Congestine is much more virulent than thalassin, for a dose of 2 milligrammes per kilogramme will kill a dog in twenty-four hours. Thalassin is, however, antagonistic to congestine, for a dog inoculated with the former will resist an otherwise mortal dose of the latter.

The application of fat to the skin is said to be a preventative to the venomous action of the anemone.

Millepora. Jones has described an acute erythema, with severe pain, followed by papules, pustules, and desquamation, as the result of stings by the hydroids of the hydrocoralline millepores (*Millepora alcicornis*, *M. complanata*, and *M. verrucosa*) in Malaya, where the corals are known as ' Karang gatal,' or itchy corals.

Trachymedusæ. The jelly-fishes of European waters, such as *Rhizostoma pulmo* of the Mediterranean and *R. cuvieri* of the English Channel, are well known to cause local redness, swelling, and urticarial eruptions.

The jelly-fishes of the tropics produce the same symptoms, but with greater severity. The pain is agonizing, and there is collapse, with local swelling and redness.

The treatment is to give stimulants internally, and to apply alkalis, such as dilute ammonia, to the affected area. Usually recovery is quick, and there are no after-effects.

Meyer describes a case of poisoning due to the well-known *Physalia pelagica* (the Portuguese man-of-war), in which there was severe inflammation and fever. A similar case caused by *Cyanea capillata* has been recorded by Forbes.

Porter and Richet obtained a liquid from Physalia containing an active principle, hypnotoxin, which, when injected into animals, caused somnolence and finally death, due to cessation of respiration.

ECHINODERMATA.

The Echinodermata possess poison glands which supply a venom to certain modified spines, but this only affects small animals.

The Cuvierian organs of certain Polynesian species of the holothurians (allied to *Holothuria argus*) are said to cause inflammation of the skin, and, if any of the secretion gets into the eye, even blindness.

The spines of the common sea urchin of the Red Sea are poisonous, causing painful wounds, which require a long time to heal.

PLATYHELMIA.

Dibothriocephalus latus, which causes a profound anaemia, is suspected to secrete some form of poison, and, indeed, this theory is supported by certain experiments of Schaumann and Tallquist. These investigators found that if the worms were subjected to tryptic digestion, and then mixed with food and given to dogs by the mouth, or extracted with normal salt solution and injected hypodermically, an exhaustion which ended in death was sometimes produced. In one case there was a great reduction of the red blood-corpuscles. Rabbits, however, were not affected.

Tænia saginata has been investigated by Messineo and Calamida, who consider that they have found evidence of the presence of a poison which can be obtained by pulverizing the tænia with sand and extracting with normal saline solution This extract was then filtered and injected into animals, but the symptoms were not characteristic. Picou and Ramond consider that the extracts they obtained showed a decided bactericidal action.

On the other hand, the rupture of an echinococcus cyst is well known to produce symptoms of poisoning, but the chemical nature of the poison is not known. The symptoms in man are urticaria, if the dose is small; peritonitis and severe cardiac symptoms, leading to fatal collapse, if the dose is large. Injected into animals, the liquid acts as a cardiac poison causing death by stoppage of the heart in diastole, together with various other symptoms, such as a fall of the blood-pressure and temperature.

NEMATHELMINTHES.

Ascarides produce a volatile body with a peculiar and disagreeable odour, very irritating to the mucous membranes, especially to the conjunctiva. This odour is most noticeable in making post mortems upon persons suffering severely from these worms. Arthus and Chanson have injected rabbits with the liquid squeezed out of living human ascarides, and produced collapse and death within ten minutes of a dose of 2 c.c.

Cattaneo obtained a substance toxic to guinea-pigs by allowing ascarides to live in sterile broth. Cao, Jammes, Mandoul, and Boycott, however, failed to obtain any evidence of the toxicity of ascarides.

With regard to *Ancylostoma duodenale*, there has been much discussion as to whether it produces a toxin or not. The experiments of Whipple and Preti seem to establish the presence of a hæmolytic principle in the alimentary canal of the worm, and those of Loeb and Smith of a principle inhibiting the coagulation of the blood and secreted by the cephalic glands, but these substances appear to be of importance to the worm for the purposes of digestion, and not to be of sufficient strength to act upon the host. According to Alessandrini, however, the cephalic glands secrete a true toxin. The evidence which has been gathered together points also to the possibility of the toxicity of the ankylostomes being partly due to the absorption of bacteria or their products into the circulation of the host through lesions in the intestinal mucosæ caused by the bites of the worms.

ARTHROPODA.

The Phylum Arthropoda includes a number of types, which are characterized by their capability of stinging. The forms which we are about to describe occur in Class III., Arachnida, Class V., Chilopoda, and Class VI. Hexapoda, of the classification given in Chapter XXVIII.

CLASS III. THE ARACHNIDA.

As the definition and classification of this class is given in Chapter XXVIII., we have only to consider the recognition of the three orders with which we are concerned here.—

I. Abdomen segmented—
    Tail stout and armed at the end with a sting. (Scorpionidea.)
II. Abdomen unsegmented—
    (*a*) Abdomen connected with the cephalothorax by a short narrow stalk. (Aranea.)
    (*b*) Abdomen fused with the cephalothorax. (Acarina.)

1. Scorpionidea.

Scorpions abound in the tropics, where they grow to a large size, and are much feared because of the poisonous properties of their sting. The method of striking is to bring the tail forward over the body of the scorpion, so that the curved spine on the last segment (telson) of the tail penetrates into the skin and inflicts the wound. On either side of this curved barb is an opening through which the duct from a poison gland discharges the venom.

It is probable that the poison of different kinds of scorpions differ qualitatively and quantitatively, but on this subject little is known. Certainly the sting of the small European scorpion (*Euscorpius europæus*) has but slight action, causing only local pain, redness, and swelling, while the larger one of South Europe (*Buthus occitanus*) causes severe pain and phlegmonous swelling of the whole extremity, and such remote symptoms as vomiting, faintness, tremors, and cramps in muscles, while the larger tropical species kill not merely children, but even adults. According to Cararoz, as many as 200 persons die annually from scorpion-sting in the neighbourhood of Durango in Mexico. In Africa scorpion-stings are of frequent occurrence, but death is rare.

Historical.—Maupertuis in 1731 and Redi in 1779 appear to have been the first to study the effects of scorpion-venom by experiments, though the ancients were well acquainted with the sting and its effects, and had woven wonderful legends as to the origin of these animals. Redi experimented upon a pigeon and a dog, but the real study of the venom began with Guyon 1864, Paul Bert 1865, Delange 1866, and Valentin in 1876, and was followed up by Joyeaux-Laffine in 1883 and many others. A full literature is given in Faust's 'Die Tierischen Gifte.'

Classification.—This is unsettled, but Pocock gives the following:—

I. Pentagonal cephalothoracic sternum—
  (*a*) Single pedal spur. (Pandinoidæ Thorell, 1876.)
  (*b*) Two pedal spurs. (Vejovidæ Thorell, 1876.)

II. Triangular cephalothoracic sternum—
  With two pedal spurs, of which the anterior is bifurcated. (Buthidæ Simon, 1879.)

III. Short, wide, antero-posteriorly compressed cephalothoracic sternum—
  Two pedal spurs. (Bothriuridæ Simon, 1880.)

Geographical.—Scorpions occur all over the world, but the largest and most dreaded are found in the tropics. They live under stones, under the bark of trees, in sand, and also in houses, which they leave at dusk. Some of the best known are:—

1. *Euscorpius carpathicus* Linnaeus, Vejovidæ (3 to 3·5 centimetres long): Italy, Tyrol, South France.

2. *Buthus occitanus* Amoreux, Buthidæ (8·5 centimetres long): Italy, Greece, Spain, North Africa.

3. *Buthus afer* Linnaeus, 1764 (16 centimetres long): Africa, Asia.

4. *Buthus quinquestriatus* Hemprich and Ehrenberg, 1828: Upper Egypt and the Sudan.

5. *Scorpio maurus* Linnæus, 1758 Egypt, Tunis.

6 *Prionurus citrinus* Hye, 1828. Desert near Cairo and Alexandria.

7. *Prionurus amoureuxi* Savigny: Sudan.

8. *Androctonus funestus* Hemprich and Ehrenberg, 1828 (9 centimetres long): North and Middle Africa.

9. *Heterometrus indus* Geer. 1778: Ceylon.

Anatomical.—The body of the scorpion is divided into a cephalothorax or prosoma, behind which comes an abdomen subdivisible into a broader portion, or mesosoma, and a narrower, metasoma, with five segments, which is popularly called the tail. At the end of this metasoma there is a postanal curved spine, called the telson, inside which lies the paired poison gland. The appendages of the scorpion are: 1. Small three-jointed chelicerae, which are used for holding prey. 2. Large six-jointed pedipalpi, which are used for seizing prey. 3-6. Four pairs of seven-jointed walking legs.

Scorpions seize their prey with the pedipalpi, hold them close to the mouth by means of the chelicerae, and sting them, if necessary, by bringing the metasoma forwards over the mesosoma and cephalothorax, and inserting the tip of the telson well into the animal's body, and allowing it to remain there until the poison has had time to act. The telson consists of two portions—a broad swollen part (the ampulla) and a narrow portion (the spine), near the extremity of which are two small openings for the escape of the venom. The two poison glands lie inside the ampulla, one on each side of the middle line. Each gland is covered with a sheet of muscle on its mesial and dorsal aspects. This muscle, which is called by Wilson 'the compressor,' is inserted by its edge mesially along the ventral inner surface of the wall of the telson, and by a broader insertion laterally. The compressor muscle squeezes the poison out of the gland, along the duct, and through the opening in the spine into the victim. The epithelium of the gland shows three distinct types of cells: the mucous cell, the fine oxyphile granular cell, and the cell with very large granules.

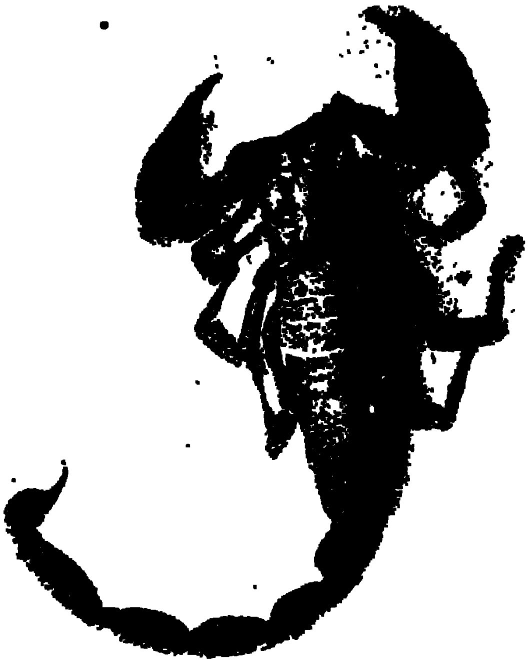

FIG. 17.—*Heterometrus indus* (B

(A scorpion commonly found in Ceylon.)

The Venom.—Scorpion-venom is a clear, faintly acid fluid of a somewhat thick or oily consistence, and possessed of an extremely faint yellowish colour. It contains no structural elements, but crystals form in it if evaporation takes place. On an average it contains about 28 per cent. of solids.

Wilson gives the following figures for the venom of *Buthus quinquestriatus*:—

Specific gravity	1·092
Solids	20·3 per cent.
Ash	8·4 "

Proteids form part of the solids, and it is believed that the active principle is either a nucleo-proteid, acid albumin, or a primary proteose. The effects described by various authors would, however, indicate the presence of toxins, one resembling the neurotoxin of snake-venom, and another a hæmolysin, for Kyes has described a typical lecithide producing hæmolysis like the lecithides of cobra-venom. Calmette has also shown that the venom of *Buthus occitanus* is neutralized by cobra antivenene. There would, therefore, appear to be some resemblance between scorpion-venom (or, at all events, the venom of *Buthus occitanus*) and cobra-venom. It is, however, impossible to make any definite statements, as the condition of our knowledge with regard to this poison is most unsatisfactory.

Iwano says that the poison is a protein, of which there are two kinds, one soluble in water and the other in dilute acids, and from these crystalline bodies can be prepared. Lecithin and cholesterin are also present in the venoms, which can be destroyed by pepsin and trypsin, permanganate of potash, and calcium hypochlorite. It seems to be very like snake-venom, and it is time that researches on modern lines were made.

Joyeux-Laffine thought that the venom first increased reflex action, and then caused paralysis of the nervous system, and that death was due to a curari-like poisoning of the end-plates of the respiratory muscles; but Valentin found these were quite intact, and that the muscles contracted well when their nerves were stimulated by electrical or mechanical stimuli.

As regards the action on the blood, coagulation, hæmorrhage due to change in the capillary walls, and hæmolysis have been observed, as well as agglutination of the red corpuscles, which are said to form viscous masses, and thus to block the bloodvessels by embolism.

These observations were made by Jousset de Bellesme on *Lilla viridis*, a frog remarkable for its lack of pigment, and therefore specially suitable for such a purpose. If confirmed, they would show the presence of fibrin ferment, hæmorrhagins, hæmolysins, and agglutinins in scorpion-venom, and would make it resemble very closely snake-venoms. Sanarelli, however, was not able to observe any change in the red cells beyond hæmolysis, which he saw in the blood of fishes, amphibia, and birds.

In conclusion, we may therefore assume the presence of a neurotoxin acting on the central nervous system, and the presence of hæmolysins, until further experiments give us more exact information.

Minimum Lethal Dose.—The minimum lethal doses for dry *Buthus afer* venom is, according to Calmette, 0·05 milligramme for white mice, and 0·5 milligramme for rabbits.

That the venom must be very toxic for small animals is shown by the fact that the minimum lethal dose for a guinea-pig is 0·1 milligramme per kilogramme, which gives a toxic value of 10,000,000 for *Buthus quinquestriatus*; but, as may be imagined, the toxicity of different venoms varies considerably, and the difference may be not merely quantitative, but qualitative.

Effects of the Venom.—It must be remembered that the venom is not merely a means of defence for the scorpion, but it is also the method by which it kills its prey, which usually consists of small animals; and, further, that, in order to be toxic, the venom must be injected subcutaneously or intravenously, for by the mouth it is harmless.

When experiments are performed on animals, the following symptoms appear:

1. Local irritation and pain.
2. Muscular twitchings, chiefly of the head and neck.
3. Jumping movements.
4. Lachrymation.
5. Increased orbital, nasal, and salivary secretions.
6. Muscular spasms, especially of the hind-limbs, but also in all muscles.
7. Erection of the hairs.
8. Passage of liquid faeces (often absent).
9. Erection of penis and emission of semen.

The venom of *Scorpio maurus* causes death in small birds within two minutes to half an hour from failure of the respiration. If the venom of a scorpion is placed on the conjunctiva of a rabbit, violent ophthalmia results.

In man, the symptoms depend upon the size and nature of the scorpion. Thus, the sting of the small (3½ centimetres) *Euscorpius europæus* causes only pain, redness, and local swelling, whereas the larger tropical scorpions cause very intense pain of a burning character radiating from the skin, associated often with violent convulsions, mental disturbance, and hallucinations, profuse perspiration, and secretion of saliva, and perhaps vomiting. The pulse is weak and quick, and the respirations hurried and shallow. These symptoms gradually diminish in three to eight hours, and by about nineteen to twenty-four hours the person is usually normal. This, however, is not always so, for death may ensue due to collapse or stoppage of the respiration, effects which are more likely to happen in small children than in adults. Thus, Wilson states that the mortality in children under five is 60 per cent. for *Buthus quinquestriatus*, but the mortality diminishes as the age increases. Of course this is simply due to the greater dilution of the poison in the body of the adult.

In addition to the above symptoms, some authors have described trismus, but it is probably due to infection with the bacillus of tetanus. The erection of the penis noted in experiments on animals has been seen in man by Delange and Guyon in Algeria. A paralysis of the lingual and hypoglossal nerves has been noted by Posada-Arango. Lymphangitis and adenitis are described as part of the local effect of the sting.

The above symptoms would indicate the action of a neurotoxin acting upon the nervous system, and causing first of all increased reflex action and convulsions, and later paralysis of the medullary nuclei; for if Valentin's observations are correct, there are no paralyses of the motor nerve-endings.

Effect on the Scorpion.—At the present time it is not believed that a scorpion commits suicide when in difficulties by stinging itself in the head with its own sting, because, though not absolutely immune to its own venom, it possesses a high degree of immunity against it. Accidental but not intentional wounding of an individual by its own sting is said to be known.

Immunity.—A natural immunity exists in the jerboa (*Jaculus jaculus* L.) and in the desert rat (*Gerbillus pyramidum* Geoffr.), and a partial immunity in the zerilla (*Ictonyx libyca* Ehrenberg).

According to Balfour, fakirs at times possess an acquired immunity, but this has not so far been obtained in any animal. Calmette has reported that the serum of a horse immunized against cobra-venom can neutralize the venom of *Buthus occitanus*—a fact which Metchnikoff has confirmed; but Nicolle and Catouillard have found this serum useless against the venom of the Tunis scorpion (*Scorpio maurus*).

Diagnosis. The history of the case and the single puncture on the affected part makes the diagnosis generally easy.

Prognosis. [illegible] is st[illegible]g, the prognosis is good, as death is known to be rare, but not so in children. The prognosis, therefore, varies with the age, and can be judged by the following table from Bray, quoted by Wilson, which gives the deaths at Omdurman in 1902 as follows:—

Under one year	5
One to five years	9
Five to fifteen years	7
Total	21

Deaths of adults, however, are known, but generally take place in a few days, not quickly.

Treatment.—In the treatment, the first thing to do is to give a full dose of the serum, and then to apply a proximal ligature and to treat the wound with permanganate of potash, as described under the heading of Snake-Bite.

Washing and bathing with a weak solution of ammonia may also be tried, and stimulants should be given.

Colonel Duke recommends that 5 to 10 minims of a 5 per cent. solution of cocaine be injected subcutaneously close to the sting in an adult, and 1 to 5 minims in infants and children. Eucaine or stovaine might be preferable, and can be imported from any chemist in sterile capsules ready for hypodermic injection. Simpson recommends the local application of a paste of ipecacuanha.

2. Aranea.

The Aranea, or spiders, are found all over the world, but by far the largest are in the tropics, and their peculiarly repulsive appearance has given rise to numerous fables, both ancient and modern, with regard to their poisonous properties.

Historical.—The study of spider-stings may be said to be modern, and to begin with Blackwell in 1855, but it was Kobert in 1893 who gave the fundamental data concerning these poisons. He maintains that, in addition to the secretion of the poison gland, there is a toxalbumin which permeates every portion of the body of the animal, and in some species of animals is mixed with the venom. He considers that the secretion of the poison gland only gives rise to local symptoms, and that the general symptoms are due to this toxalbumin, and that it is because of this admixture in *Latrodectus* that the bite may cause severe symptoms and even death in human beings. The common European garden spider (*Epeira diadema*) only causes local irritation, because the toxalbumin, though present in the body, is not mixed with the poison of the poison gland. He also describes a hæmolytic action in both *Epeira* and *Latrodectus*.

Sachs has contributed a paper in which he carefully studies this hæmolysin, which he calls arachnolysin, and Wilson has recently written an excellent monograph on the spider-bites.

Classification.—Spiders are divided into two suborders as follows:

I. Spinning organs situate far anterior to the anus. Eleven tergal plates on the dorsal surface. (Mesothelæ.)

II. Spinning organs situate just in front of the anus. No tergal plates visible. (Opisthothelæ.)

The Opisthothelæ are the only forms which concern us, and they are divided into tribes as follows:—

A. Only anterior pair of spinning organs present. (Megalomorphæ.)

B. Two pairs of viramous spinning organs present. (Arachnomorphæ.)

The Megalomorphæ include

I. Without large maxillary process on the base of the palp—
    1. Feet furnished with apical tufts or pads of hair. (Aviculariidæ.)
    2. Feet not so furnished. (Ctenizidæ.)

II. With large maxillary process on the base of the palp. (Atypidæ.)

The bird-eating spiders 'Mygale' come under the Aviculariidæ.

The Arachnomorphæ include:—

The Epeiridæ with *Epeira diadema*, the Theridiidæ with *Latrodectus*, the Lycosidæ with the Tarantula spider.

Geographical.—All genera of spiders appear to be poisonous, but the most important are: *Latrodectus mactans*, Chili; *L. scelio*, the katipo of New Zealand; *Theraphosa avicularia* L., South America; *T. blondi* Latr.; *T. javanensis* Walck.; *Chiracanthium nutrix* Walck.; *Theridium tredecim guttatum* F., France and Italy;

T. ugubre Koch, Kara kist of Russia; *Segestria perfida* St.; *Chætopelina olivacea; Lycosa tarantula* L.; *L. singoriensis* Laxman; *Epeira diadema* Walck.

Anatomical.—The body of the spider is sharply divided into cephalothorax and abdomen. The pairs of appendages are six in number:—(1) The two-jointed cheliceræ; (2) the six-jointed leg-like pedipalpi; (3-6) the seven-jointed legs. The poison gland usually lies in the basal joint of the chelicera, ensheathed in connective tissue, inside which there are two spirally arranged layers of non-striped muscle surrounding a basement membrane which bears two to three layers of polyhedral cells, surrounding the lumen of the acinus. From the gland the duct runs forwards into the distal hook-shaped joint, upon the apex of which it opens.

The Venom.—The venom, which is useful to the spider, enabling it to kill the small animals upon which it lives, is an oily, translucent, lemon-yellow-coloured liquid, with an acid reaction and a hot, bitter taste. It has proteid reactions, and gives the xanthoproteic reaction. It is difficult to obtain it in any quantity. Wilson recommends triturating the gland with distilled water (0·5 c.c. being used for each gland), and then filtering, when an extract suitable for experimental purposes is obtained. These extracts are rendered harmless by heating to 90° C., and the active principles are said not to dialyze. The chemical peculiarities and the active principles of the venom are little known. Kobert, as has already been pointed out, considers that there are two poisons:—(1) A toxin secreted by the poison gland, and only causing local symptoms; (2) a toxalbumin distributed through the body (not originating from the poison gland), and causing general symptoms The first exists alone in *Lycosa tarantula, L. singoriensis.* The second largely predominates in *Latrodectus*.

Kobert and Sachs have found and studied a hæmolysin, arachnolysin, in the venom of several kinds of spiders, and Sachs has been able to immunize a guinea-pig against this toxin, and produce an active serum. Arachnolysin acts upon the red cells of man, rabbit, ox, mouse, and goose, but not on those of the horse, dog, sheep, and guinea-pig.

Spider-venom is also said to increase the coagulability of the blood. The venom of *Theridium lugubre* is believed to act injuriously on the isolated frog's heart, even when diluted to 1 in 100,000, but it is not known whether this is due to action directly upon the heart-muscle or upon the local nervous apparatus. The walls of the capillaries are also said to be damaged by spider-venom, and to allow an increased amount of transudation, and hence the hæmorrhages and œdema seen about the wound. It is asserted that the venom acts deleteriously upon the mucous membrane of the stomach and intestines, causing redness and swelling, and even hæmorrhages, which perhaps are due to some attempt at excretion of the poison by these organs. It is also thought that the venom acts upon the central nervous system, but whether the cramps and convulsions are really due to action of the poison upon the nerve cells, or merely to the altered blood conditions, has not been decided.

The reader is particularly asked to compare these actions on the nervous system (neurotoxin ?), on the mucosa of the stomach, on the capillary wall, on the blood and red cells, with the venoms of the scorpion and of the snakes, which they strongly resemble.

Acquired immunity can be produced in animals by injections of non-lethal quantities of venom.

Minimum Lethal Dose. The minimum lethal dose for cats is 0·20 to 0·35 milligramme of the dry venom per kilogramme of the body-weight. Dogs are less sensitive, and hedgehogs still less, while frogs require fifty times the quantity of poison which will affect warm-blooded animals.

Effects of the Venom. In general, the symptoms of spider-bite rather resemble those of the scorpion, and are divisible into (1) local, (2) general. Local inflammation is generally present, but may be absent, and severe pain is felt at the site of the wound. The general symptoms are those of collapse coming on gradually, with sometimes convulsions, or rarely a typhoidal condition ensues, which may remain for weeks. Many other symptoms may also be noted, such as nausea, rigors, cold sweats, dyspnœa, fever, delirium, paralysis, and coma terminating in death. Inflammation of the stomach and intestines, coagulation of the blood, and local hæmorrhages and œdema, are the principal features of a post-mortem examination. The symptoms of the bites of the different spiders will now be briefly described.

Bite of Latrodectus mactans.—The symptoms of this bite are local pain, which does not appear till some little time after the bite, but becomes agonizing, and may last for a couple of days. In addition, tetanoid symptoms may set in, but usually end in recovery in about ten days.

Bite of Latrodectus scelio. This is the katipo spider of New Zealand. The symptoms begin in about thirty minutes with the formation of a white vesicle surrounded by a red halo, and severe pain at the site of the bite. The general symptoms include, first, stiffness of the muscles about the mouth and jaw, so that it is difficult to open the mouth or to speak, and impossible to swallow. The pulse becomes very slow (12 to 14 to the minute), and there is extreme pallor of the face and body, with coldness of the extremities, which are quite flaccid. Respiration becomes slower and slower, and death may take place at this stage, or an illness lasting about six weeks, and somewhat resembling typhoid, may ensue, which may end either in death or recovery.

Bite of Theridium lugubre.—This bite is characterized by smarting pains, no redness or swelling, cold sweats, restlessness, dizziness, mental anxiety, depression, vomiting, cyanosis, convulsions, status typhosus, and, unless improvement sets in, death in three days.

Bite of Theraphosa avicularia.—The Theraphosæ come under the commoner heading of Mygale, and cause prolonged inflammation and extensive cicatrization. *Theraphosa javanensis* is reported to kill men.

Bite of Chætopelina olivacea. The local symptoms are great pain, redness, swelling, but whether a general effect (curari-like poisoning of the voluntary muscles and death from stoppage of respiration) takes place is very doubtful.

Bite of Lycosa tarantula.—The bite of this spider produces wheals surrounded by a red areola, but no general symptoms result, and tarantismus only exists in popular imagination. The tarantula dance was probably introduced as a cure, with the purpose of keeping the patient on the move, so that he should perspire, and thus get rid of the poison. The tradition of the Middle Ages was that the bite caused the dance frenzy, *Chorea saltatoria*, or tarantismus, which was supposed to lead to such violent exertion that death resulted unless the victim was soothed by music.

The Bite of Epeira diadema.—The bite of the common garden spider has been recently proved by Kobert and Sachs to be poisonous.

The Bite of a Bengal Spider.—Fink has recently described a herpetic eruption on the face of Bengalee children due to a spider bite; for this he recommends fumigating the face with the smoke evolved when lumps of mustard-oil cake, burned in a charcoal fire, are dropped into a basin of cold water.

Diagnosis.—Bee-stings, scorpion-bites, and ordinary skin bacterial infections must, of course, be distinguished from spider-bites, with which, without doubt, they have been often confounded. The local symptoms and the history ought to be some guide.

Prognosis.—This is generally good.

Treatment.—Prevent absorption by the proximal ligature, open the wound by an incision, and apply alkaline solutions—*e.g.*, weak solutions of ammonia or carbonate of potash, or equal parts of spirit of ammonia and water as a wet dressing. It appears to us that a strong permanganate of potash solution ought to be given a trial.

3. Acarina.

The Ixodoidea, or ticks, are well known to cause severe symptoms by their bites, apart from the introduction of any parasite such as a *Piroplasma* or *Spirochæta*.

The anatomy of these arthropods is given in detail in Chapter XXVIII., p. 689, to which reference should be made, but a few remarks are necessary concerning the act of biting, which has been studied by Nuttall.

The tick pierces the skin by means of the teeth on the digits of its chelicerae. The digit is capable of being extended by an internal muscle, and turned outward by an external muscle. These movements, occurring alternately, cause the teeth to cut the skin, and as the chelicerae work deeper and deeper, the hypostome is dragged into the wound, and by its recurved teeth keeps the tick in position. The palps but rarely enter the wound. During this act of biting it is believed that the salivary glands pour a considerable amount of secretion into the victim, but the nature of this fluid and its action requires further investigation. Nuttall, drawing attention to the immunity following bites, says that it is probable that this secretion is toxic in its action.

The Effects of the Venom.—With regard to the Argasidæ, *Argas persicus* Oken has an evil reputation in Persia, where its bite is said to cause severe pain, fever, lassitude, delirium, convulsions, and even at times death in new-comers, while natives are immune.

Bordier considers that these symptoms are due to the injection of a poison, but this would hardly appear to be likely, as Lounsbury found in his own case in South Africa that the bite caused only slight itching. If the symptoms are properly described in Persia, it would indicate that the tick introduced some parasite into the new-comer which caused a definite disease to which the native had acquired an immunity.

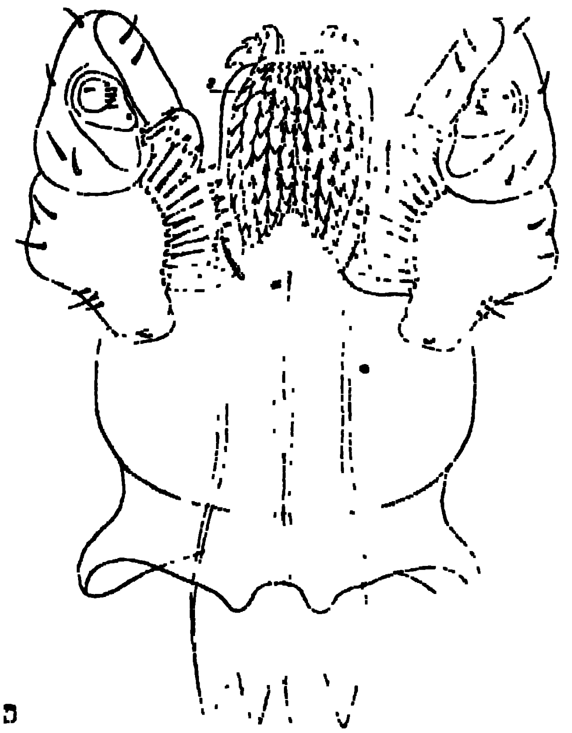

FIG. 18.—VENTRAL ASPECT OF THE MOUTH-PARTS OF A TICK (*Hæmaphysalis punctata* CANESTRINI AND FANZAGO).

(After Nuttall, Cooper, and Robinson, *Journal of Parasitology*.)

1, Chelceræ, showing teeth; 2, hypostome, showing rows of recurved teeth; 3, palp.

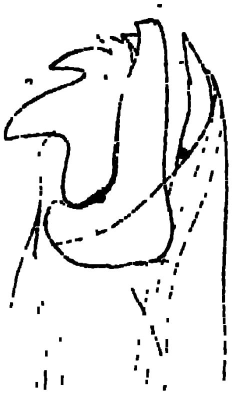

FIG. 19.—CHELICERA FROM THE SAME TICK.

(After Nuttall, Cooper, and Robinson, *Journal of Parasitology*.)

1, Internal digit; 2, external digit.

Argas reflexus Fabricius may cause local pain and swelling, with sometimes an erythematous eruption, while the site of the bite is marked for years by a cicatrix. The bite of *A. brumpti* Neumann is also severe.

Ornithodoros moubata Murray inflicts a very painful bite, with much swelling and the formation of raised hard wheals, in Europeans, which may last several days.

Ornithodoros turicata Dugès may cause swelling and numbness all over the body, with vomiting and diarrhœa, accompanied by an urticarial eruption and profuse perspiration, with rigors, fever, headache, and backache if the poisons enter a vein. Locally, an ulcer may form at the site of the bite. *O. talaje* Guérin Méneville causes severe itching and pain.

With regard to the Ixodidæ, *Ixodes ricinus* causes severe dermatitis, which may be followed by pustules and abscesses, with œdema, lymphangitis, and lymphadenitis, associated with fever.

Treatment.—The treatment of tick-bites is first to detach the tick, which is by no means easy, as the recurved teeth of the hypostome hold on to the wound very firmly. The best plan is to rub any oil into the ventral surface of the tick, thus interfering with its respiration, and compelling it to detach itself from the host. With regard to *O. turicata*, it is advised to apply the actual cautery, as the effects of the bite are so severe. According to Wellman, *Ornithodoros* bites should be treated by bathing in very hot water, after which bicarbonate of soda should be applied in strong solution. Itching may be allayed by a menthol ointment (1 to 2 per cent.).

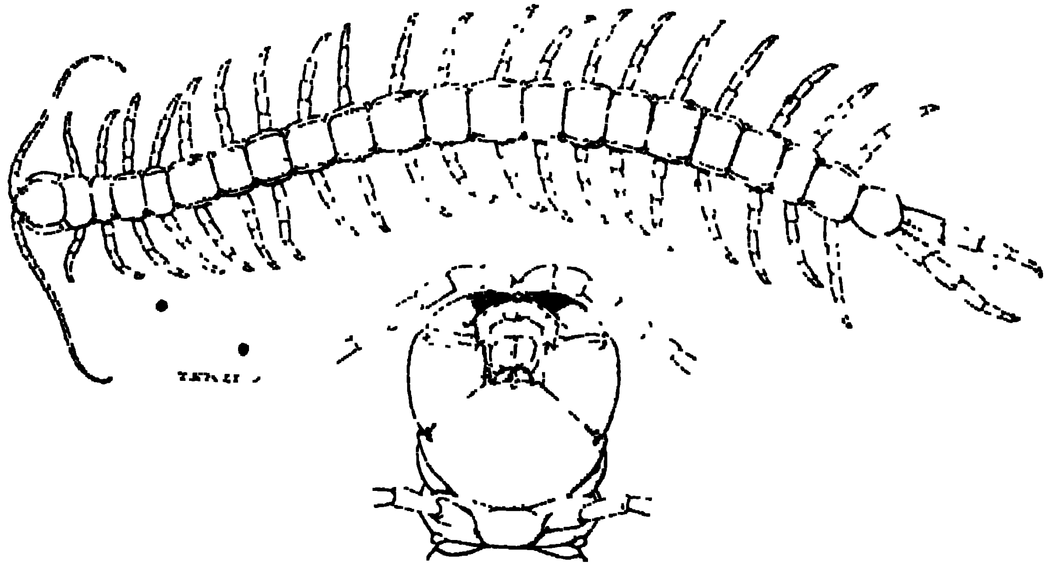

FIG. 20.—*Scolopendra morsitans* Linnæus.

As regards prophylaxis, badly infected native huts should be burnt, while ordinary houses may be fumigated with sulphur or carbon bisulphide, or sprayed with kerosene or boiling water. Beds must always be raised from the ground, and the feet of the bedstead placed in water containing kerosene, while pyrethrum powder may be dusted between the coverings of the bed. Wellman insists that natives should not be allowed to sleep in or near the quarters of Europeans.

2. CHILOPODA.

The class Chilopoda includes the Scolopendridæ, or centipedes, which are animals with a head and a uniformly segmented trunk, possessing numerous legs. They are very common all over the world, but the tropical species are much larger than those which inhabit the Temperate Zone. They live under stones in shady places, especially in woods. The poison apparatus of the centipedes is formed by the appendages of the first trunk segment being modified so as to form a large pair of jaws, at the base of which the poison gland lies. The duct of this gland opens on the apex of the claw, and therefore, as there are two jaws, a centipede-bite will show two minute punctures or drops of blood.

The venom is primarily intended to kill their prey, which consists of small insects and larva

Geographical. The most noted species are *Scolopendra cingulata*, France, Spain, Italy; *S. gigantea* Koch, *S morsitans* L., *S. heros*, Africa, India, Indo-China, Equatorial America; *Geophilus longicornis* Leach, Mid-Europe.

The Venom. The venom is an acid opalescent liquid, but little miscible with water For experimental purposes it can be obtained by treating the lower lip and the hooks with normal saline solution.

When injected into the veins of rabbits, it causes an immediate paralysis, with coagulation of the blood, while under the skin it forms a large abscess.

Effects of the Venom. The poison causes local and general symptoms. At first there is itching, but this is quickly followed by intense pain, which extends all over the limb A red spot appears at the site of the bite, which enlarges and becomes black in the centre, and sometimes there are lymphangitis and lymphadenitis The general symptoms are great mental anxiety, vomiting, irregular pulse, dizziness, and headache.

Diagnosis. The diagnosis is obtained by the history and the presence of the two minute punctures.

Prognosis. The prognosis is good, though small children have been known to die from the effects of a sting. Adults, as a rule, recover in about twenty-four hours at the most

Treatment. Bathe the part well with a solution of ammonia (1 in 5 or 1 in 10). After bathing, apply a dressing of the same alkali, or if there is much swelling and redness, an ice-bag.

If necessary, give hypodermic injections of morphia to relieve the pain. At a later period, fomentations may be required to reduce the local inflammation.

3. HEXAPODA.

The Hexapoda, or insects, contain many species injurious to man.

The orders to which the principal venomous species belong are: (1) Anopleura; (2) Hemiptera; (3) Hymenoptera; (4) Lepidoptera; (5) Diptera; and (6) Coleoptera.

1. Anopleura.

This order includes the lice, which cause much irritation by their bites. The nature of the venom, however, is not known, and the lice are of more importance as carriers of disease, and will therefore be dealt with more fully in Chapters XXX. (p. 749) and XXXV. (p. 872).

2. Hemiptera.

The Hemiptera (Chapter XXXI., p. 761) include the families of the Clinocoridæ, or bugs, and the Reduvidæ, or cone noses. In the latter family is classified *Phonergates bicoloripes* Stål, which, according to Wellman, produces a very painful bite in man in Angola. Another member of this family, as yet not named, has been described by King in the Sudan, where it bites human beings on the hands and wrists, producing small red lumps, which, however, soon disappear. It is said to be closely related to *Phonergates bicoloripes*.

BUGS.—These hemipterons secrete a strongly alkaline poisonous secretion in their salivary glands. This poison flows down the ducts of the stylets, and passing into the wound made by the bite, dilates the capillaries, causing an increase of blood in the area bitten. This, of course, is advantageous to the insect, allowing it to obtain a quantity of blood in a short space of time. Clinically the poison causes red blotches and local swellings.

It is, however, more convenient to discuss these venomous insects along with other parasites in Chapter XXXI., p. 761, as it enables a more systematic description to be given, especially as the nature of the venom is quite unknown.

3. Hymenoptera.

In this order come the bees, wasps, and ants.

APIDÆ.

The members of this family which sting are well known, and it is by no means infrequent to hear of animals and even at times human beings in the tropics suffering severely from bee-stings, and more rarely dying from the effects.

The species generally credited with evil effects are: *Apis mellifica* L., the hive-bee; *Vespa vulgaris* L., the wasp; *V. germania* Fabr.; *V. crabo* L., the hornet; *V. orientalis*, the hornet; *Bombus hortorum* L., the bumble-bee; *B. lapidarius* L., and *Xylocopa violacea*, the wood-bee.

Historical.—The venom of the bee was first studied by Brandt and Ratzeburg in 1833, then by Paul Bert in 1865 and Carlet in 1884, but the chemical nature was first investigated carefully by Josef Langer in 1897, and in 1904 Phisalix made experiments on sparrows.

Anatomical.—The body of the bee is divided into head, thorax, and abdomen, from the posterior end of the last of which projects the sting in the form of a chitinous sheath, narrow posteriorly and wider anteriorly. This sheath contains two barbed darts, and into its wider portion (which possesses a cleft by which air can penetrate into it) two or three ducts from glands open. The principal opening belongs to the duct of the 'acid gland,' and opens anteriorly into a sac—the poison reservoir—which leads into a long, slender, coiled tubular gland, either bifid anteriorly or subdivided into two glands. This long gland ramifies amongst the contents of the abdomen. The second opening, which lies alongside the first, belongs to a small, irregular, tubular gland called the alkaline gland, or gland of Dufour. The third opening, when present, leads into a lanceolate or ovoid accessory poisonous gland.

The Venom.- The venom freshly extruded from the bee's body weighs from 0·2 to 0·3 milligramme, and is a transparent acid fluid with a bitter taste, a peculiar aromatic smell, and a specific gravity of 1·1313. It contains about 30 per cent. of solid matter when dried at the room temperature.

The acid reaction is believed to be due to formic acid, and the smell to volatile substances, but neither of these have any connection with the poisonous properties of the venom.

The preparation of venom in quantity was carried out by Langer as follows: Several thousand fresh stings with their venom-sacs were placed in 96 per cent. alcohol, which was in due course filtered off, when the stings were dried at 40° C., then pulverized and extracted with water. The resulting extract, which, when filtered, was a clear yellowish-brown fluid, was then precipitated by 96 per cent. alcohol. The precipitate, after washing with alcohol and ether, was dissolved either in ordinary water or in the same acidulated slightly with acetic acid. From this solution Langer obtained an albumin-free active body after repeatedly precipitating with a few drops of concentrated ammonia and again dissolving as above. The active principle is, therefore, not albuminous, and is thought to be an organic base, the nature of which, however, is not known. This poison is destroyed or its activity lessened by oxidizing agents, such as potassium permanganate, and also by ferments, such as pepsin and rennin.

Subcutaneously injected, the venom produces great local irritation, but heating to 100° C. for fifteen minutes destroys this effect.

Intravenous injections into dogs produce convulsions, trismus, nystagmus, emprosthotonos, and death from respiratory failure. This action is believed by some authors to be due to a neurotoxin, but the blood after death is very fluid, and the red corpuscles are destroyed, indicating a marked hæmolysis, while all the organs except the spleen show hæmorrhages and hyperæmia; so that the effects may not be due so much to the action on the nervous system as to that on the blood. The convulsive effects can be destroyed by heating to 100° C. for thirty minutes, when the poison becomes merely narcotic. All effects are annulled by heating to 150° C. for fifteen minutes.

The venom, therefore, contains:

1. Inflammatory poisons, which are thought to come from the acid gland.
2. Neurotoxins:—
   (1) Convulsive, thought to be derived from the alkaline gland.
   (2) Narcotic, secreted by the acid gland.
3. Hæmolysins.

With regard to the last, Morgenroth and Carpi have shown that a lecithide is formed which is 200 to 500 times more hæmolytic than the venom alone. There is, therefore, a similarity between this poison and cobra-venom.

The only marked features recorded in human post-mortems are hyperæmia of the meninges and bloody exudation into the ventricles of the brain.

Immunity.—There appears to be no doubt that bee-keepers often attain a considerable amount of immunity against the venom.

Thus, Langer says: Out of 164 bee-keepers, 11 were immune from the first; while of the 153 at first sensitive, 126 became more or less immune, and 27 did not. Of the 126 more or less immune persons, 14 said that they were not affected even when several stings were inflicted quickly one after the other.

Bee immunity, however, is only passing, and does not last, and the keepers say that the first sting in the early part of the year may produce a strong effect.

Calmette has immunized a mouse, so that it could resist doses of the venom which would surely have been mortal otherwise.

The Effects of the Venom.—Usually the symptoms are merely local, and limited to pain in the part, redness, and swelling of the skin, and disappear in a few hours. Suppuration is rare, and blood-poisoning very rare, only taking place occasionally if the sting is on the eyes, ears, lips, or in feeble old people.

Slight fever may result in sensitive people, and sometimes general constitutional symptoms, such as nausea, faintness, great weakness, vomiting, precordial distress, difficulty in breathing, coldness of the extremities, with an eruption on the skin like measles, or with wheals. These symptoms may pass on to delirium, unconsciousness, and more rarely death.

Vespa orientalis causes semi-unconsciousness, the face becoming pale and cyanosed, the skin of the extremities cold with a clammy sweat; respiration becomes shallow and sighing; the pulse quick (130 to 140), irregular, and barely perceptible. On recovery from this state of shock, the patient complains of a sensation of tightness in the throat, and œdema may develop in the neck and face, as well as slight fever (100° to 102° F.), all symptoms disappearing in twenty-four hours.

The ordinary bee may at times cause severe symptoms, of which the following is an example: a lady was stung in the forehead, and in four minutes swelling of the eyelids and lips began, which rapidly spread to the arms, and was associated with acute abdominal pain. The hands became rigid in the position of *main en griffe*, and pain and stiffness was felt in the throat, together with difficulty in speaking. There was also vomiting and a sense of chilliness, followed by exhaustion. Recovery was rapid.

Diagnosis.—There is usually no difficulty in this, the history being clear.

Prognosis.—Usually the prognosis is very good; the only dangers are in children and old feeble persons, and in multiple stings.

Treatment.—The usual treatment is by applications of weak solutions of ammonia, which answers well. Carbolic acid (1 in 20 or 1 in 10) is satisfactory if applied immediately after the sting. Potassium permanganate may be tried.

Calmette advises a solution of calcium hypochlorate (1 in 60) or eau de Javel (1 in 100). When there is much swelling, apply iced compresses or an ice bag. When general symptoms develop, strychnine injections may be used.

FORMICIDÆ.

Ants may appear rather insignificant in the Temperate Zone, but in the tropics they are most active, and their bites are very painful.

Many ants—*e.g.*, *Myrmica* and *Ponera*—have a poison apparatus analogous to that of the bees, which has just been described.

The Venom.—The venom is well known to contain formic acid, but there must be more than this in the venoms of the tropical species, though nothing is known on the subject.

The Effects of the Venom.—The symptoms are usually only local—that is to say, pain, inflammation, and swelling at the site of the bite—but in the case of the large tropical ants general symptoms of faintness, shivering, and temporary paralysis may be produced. Indeed, dried red ants made into a paste have already been noted as an arrow-poison (Chapter XI., p. 180).

In Ceylon there is a species of very small ants which infest the beds and bite people while asleep, producing urticarial pomphi.

Treatment.—Apply weak solutions of ammonia, carbolic solution (1 in 20), or camphorated alcohol, to the part. As a preventive measure against the ants infecting beds, spread some powdered camphor in the beds and sheets.

4. Lepidoptera.

Caterpillars of many butterflies are well known to be venomous in the tropics, causing marked skin eruptions, and even a feeling of illness associated with a slight rise of temperature.

Wellman reports that in Angola the most common stinging caterpillar is that of the tiger-moth (Arctiidæ), called locally 'ochipia'—that which burns—which produces an angry eruption associated with much pain. Another belonging to the Limacodidæ, called 'Epuvi,' he describes as causing urticaria. A third, belonging to the Liparidæ, also causes severe local, and at times reflex nervous symptoms. We are acquainted with stinging caterpillars in Ceylon and the Gold Coast, but we have not determined the species. In the former, a bombyx larva living on the *Hibiscus* plant is apt to cause skin irritation. In India, the 'komlah' of the Terai is liable to cause intense irritation if it touches the skin. According to Brooke, the larvæ of *Neæra lepida* and *Adolia* are known to be venomous. Recently Bleyer has described caterpillars belonging to the Bombycidæ of Brazil which possess peculiar stinging organs, the venom from which produces locally urticaria and dermatitis, as well as general symptoms which are best treated by the local application of a 2 per cent. solution of menthol in æther, chloroform, and rectified spirits, and by the administration of a mixture containing liquor ammoniæ acetatis.

Porthesia Chrysorrhœa.—The caterpillar of this brown-tailed moth is reported from America (Massachusetts and New Hampshire) as causing a peculiar skin eruption, which Tyzzer says is caused by the penetration into the epidermis of peculiarly modified microscopic hairs called the nettling hairs, which are sharply pointed and barbed. These hairs are specially arranged for penetration, and possess an irritating substance which can be destroyed at 115° C. The other hairs are innocuous. The poison causes necrosis of the cells of the epidermis, together with the formation of small vesicles and inflammation of the corium

The **Symptoms,** which are generally those of an urticarial dermatitis, but occasionally erysipelatous-like, may be divided into two groups: (1) *severe,* due to contact with the caterpillar; (2) *mild,* due to hairs blown into the air and lodging in skin or under-garments. But it must be remembered that some people are very sensitive and others almost immune.

Treatment.—The best treatment is to clear away the hairs with a little alkaline lotion (bicarbonate of soda 2 per cent.), and then to apply an ointment of ichthyol (10 per cent.).

5. Diptera.

The classification of the Diptera is given in Chapter XXXII., p. 775, to which reference should be made.

Culicidæ. The irritation of mosquito bites is most noticed by the new-comer to the tropics, for as years go by a kind of partial immunity is acquired, and the bites are much less noticed. Some people appear to have a partial natural immunity to the bites, but this is uncommon.

Only the female mosquito bites and sucks blood, which is supposed to be required for the nutrition of the eggs. When the female mosquito alights upon the skin, it does not always bite at once, but may move from one part to another, apparently testing the different parts of the skin by its labellæ *

Having selected a given area of skin, it moves the palpi away from the proboscis dorsally, and at the same time rotates the labellæ on their hinge-joints outwards.

The labium is now pressed against the skin, and is bent into the form of a bow, convex posteriorly. An opening in the skin is then made, in which the mandibles and maxillæ work like saws, while the head of the mosquito can be seen rocking from side to side.

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* For the anatomy of the proboscis see Chapter XXXII., p. 776.

During this process respiration is going on quietly, but at times, according to Schaudinn, a violent contraction of the abdomen is noticed, which is said to be due to the carbonic acid in the superficial layers of the skin, for he found that when carbon dioxide gas acted upon mosquitoes a like contraction was produced.

As this process is proceeding, an irritating substance, the chemical nature of which is not known, is injected under the skin, and it is evident that this happens before the mosquito begins to suck blood for the irritation is present when the insect ceases to bite before drawing up the blood.

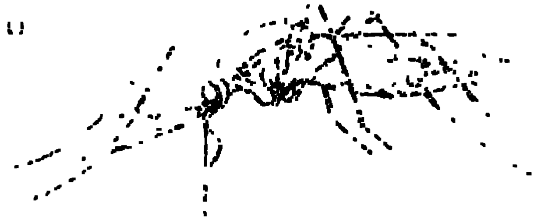

FIG. 21 AN ANOPHELINE MOSQUITO (*A. maculipennis* MEIGEN) IN THE ACT OF BITING.

(After Nuttall and Shipley, *Journal of Hygiene*.)

Note that the proboscis does not enter the wound and that it is bent convex posteriorly. Note the distension of the abdomen as seen by the space between the terga and the sterna. In the natural condition this space would be bright red from the blood in the abdomen.

There has been much dispute as to where this substance comes from, but this appears to have been settled by Schaudinn, who triturated the isolated salivary glands in salt solution, which he applied to a wound with negative result. On the other hand, when

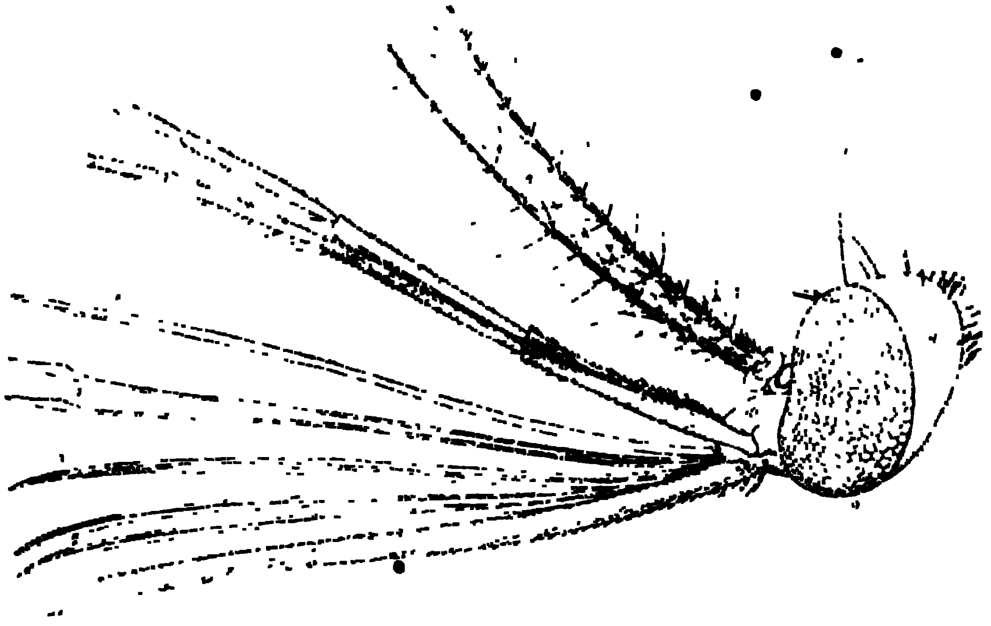

FIG. 22.—HEAD OF *Anopheles maculipennis* MEIGEN.

(After Nuttall and Shipley, *Journal of Hygiene*.)

1, Labium; 2, maxillæ; 3, hypopharynx; 4, mandibles; 5, labrum; 6, palpi; 7, antennæ; 8, occiput; 9, eye; 10, clypeus.

he applied the isolated œsophageal diverticula to a scratch, he obtained the characteristic irritation and redness. These œsophageal diverticula contain gas-bubbles and bacteria or moulds. The bubbles were shown by Schaudinn to contain carbon dioxide by applying baryta-water to the diverticula, when a precipitate was obtained. The fungi need further investigation, but they or their products appear to be the real cause of the irritation, for when Schaudinn pressed the carbon dioxide out of the sac the signs characteristic of the bite were still produced. It appears probable, therefore, that the powerful abdominal contraction mentioned above expels the gas, bacteria, and fungi from the œsophageal diverticula and the saliva from the salivary glands

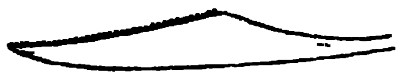

FIG. 23.—ANTERIOR END A MANDIBLE.

(After Nuttall and Shipley, *Journal of Hygiene.*)

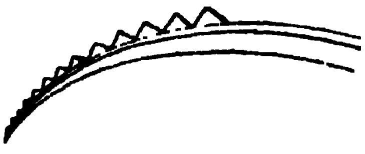

FIG. 24.—ANTERIOR END OF A MAXILLA.

(After Nuttall and Shipley, *Journal of Hygiene.*)

It is possible that the chemical products of the fungi, by causing local irritation, bring more blood into the particular area of skin affected, and thus enable the mosquito to get her supply quickly, for feeding only takes two to three minutes, during which time some mosquitoes will so overfill themselves with blood that it may be ejected *per anum*. The use of the carbonic acid is probably to prevent the coagulation of the blood, which is drawn up the large blood-tube formed by the labrum epipharynx and hypopharynx by the suctorial action of the pump-like pharynx.

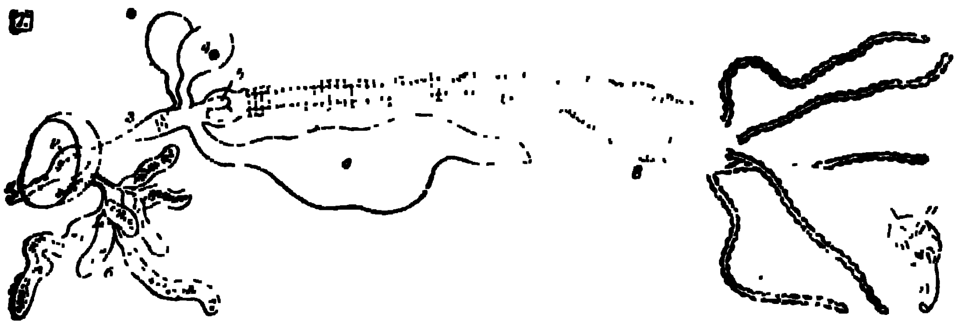

FIG. 25. THE ALIMENTARY CANAL OF *Anopheles maculipennis* MEIGEN.

(After Nuttall and Shipley, *Journal of Hygiene.*)

1, Mouth and buccal cavity; 2, pharynx; 3, œsophagus; 4, dorsal and ventral œsophageal diverticula; 5, proventriculus; 6, salivary glands; 7, narrow portion of ventriculus; 8, so-called stomach; 9, malpighian tubules; 10, intestine; 11, rectum; 12, anus.

Symptoms.—Shortly after a mosquito has bitten a person, a sensation of itching is experienced in the affected part, which on examination is seen to be inflamed and reddish, while a wheal not unusually develops, especially in persons new to the tropics. Sometimes a papule or even a nodule may form on the site of the bite, while more rarely scratching leads to secondary infection and the formation of boils, lymphangitis, or lymphadenitis.

Treatment.—The itching may be relieved by dilute solutions of ammonia (Scrubb's Ammonia is a favourite remedy), or by a 5 per cent. solution of carbolic acid, or 1 per cent. alcoholic lotion of menthol. Inflamed bites may be cleaned with 1 in 40 carbolic lotion, and afterwards dressed with boracic ointment. Local septic poisoning should be treated by boracic or carbolic fomentations, while boils and abscesses must be opened.

Prophylaxis.—The prevention of mosquito bites will be discussed in the chapter on Malaria (Chapter XI.).

Other Diptera.—Numerous flies other than the Culicidæ cause irritation by their bites, such as fleas, but the nature of the venom not being well known, they will be considered together in Chapters XXXII., p. 771, XXXIII., p. 814, and XXXIV., p. 857.

In Cape Colony there is a superstition that the 'bee moth'—*i.e.*, death's-head moth, *Acherontia atropos* Linnaeus—is poisonous. This is not so.

6. Coleoptera.

Beetles and their larvæ are capable of inflicting severe bites or wounds by means of stiff hairs. *Silvanus surinamensis* L., the saw toothed grain beetle, is said to bite people. Wellman describes the larva of a beetle, which the natives of Angola call 'ochisia,' which means 'to be left alone,' whose bristles will even penetrate the skin of the sole of the foot, causing pain, inflammation, and even sloughing, when trodden upon

BLISTER BEETLES.—Chalmers and King in 1917 have drawn attention to the beetles *Epicauta sapphirina* Macklin, 1845, and *Epicauta tomentosa* Macklin, 1845, as the cause of 'seasonal vesicular dermatitis' in Khartoum, while P. H. Ross had studied in 1916 the same complaint in Nairobi, where it was caused by *Pæderus cribipunctata* Epp (*sic*), and P. da Silva had traced in 1912 similar outbreaks in Brazil to *Pæderus columbinus* de Laporte, 1832; Eysell to *Pæderus peregrinus* Fabricius, 1801, in Malaysia, and Rodhain and Houssian to a species of the genus *Pæderus* Fabricius, 1775. Finally, Roubaud has stated that *Epicauta flavicornis* Dujardin, 1838, is the cause of the same complaint in Senegal.

The whole subject, however, belongs to Chapter XCVI., the Dermatozoiases, and is only mentioned here for the purposes of reference.

It will be noted that the various authors only mention two genera—viz., *Epicauta* Dejean, 1803, which belongs to the family *Cantharidæ* Leach, 1817, and *Pæderus* Fabricius, 1775, belonging to the family *Staphylinidæ*, which latter lack the appendage on the ventral aspect of the claws which is so characteristic of the former.

The life-history of these beetles is very complicated, and much of it is spent under the ground, hence the seasonal factor in the eruption caused by cantharidin, which is present in the fluid exuding from the insect, and especially from what may be termed the knee-joint, when irritated.

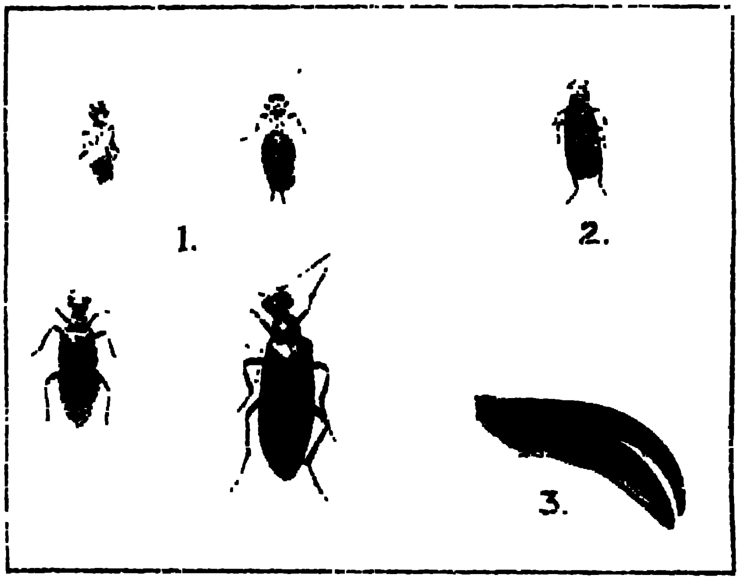

Fig. 26. Blister Beetles.

1, Upper and smaller *Epicauta tomentosa* Macklin, 1845, and the lower and larger *Epicauta sapphirina* Macklin, 1845; 2, *Mylabris nubica* de Marseul, 1857; 3 a claw of *E. sapphirina*, to show the long appendage which is usually closely applied to it.

MOLLUSCA.

A venomous snail of unknown genus and species is described in the Solomon Islands. These snails possess radulæ provided with pointed tubular teeth, armed anteriorly with a barb. These teeth are connected with a poison gland, and are capable of injuring men and producing severe wounds. Bites of the cones and augers (Terebridæ) are said to be poisonous.

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CHAPTER XV

VENOMOUS ANIMALS (*continued*) PISCES AND AMPHIBIA

Pisces – Zoological classification – Geographical distribution – Poison by bite – Poison by stings – Amphibia – References.

PISCES.

ALL over the world, but especially in tropical seas, there are fish which for purposes of defence secrete poisonous fluids from special glands. These fish have been but little studied, and still less is known about the nature of their venom and its physiological action. A great deal, however, is known by residents in the tropics about wounds inflicted by these fish, and the doctor practising therein is bound sooner or later to come across not merely persons who know a good deal in a general way about the subject, but those who either are suffering or have suffered from the poisoning. It is therefore necessary that the tropical practitioner should have some knowledge of venomous fish.

The subject might be studied by classifying the fish zoologically, and then taking them seriatim and describing their poison and its effects; but though a zoological list will be given, this does not seem so satisfactory as to follow Bottard in his special classification based on the manner in which the fish inflicts the poison.

Venomous fish may be classified into:–

Class I. Fish which poison by their bite.
Class II. Fish which poison by barbs (spines) connected with special glands.
Class III. Fish which poison by a secretion prepared by the skin glands. This class is illustrated by the lamprey, which is only known to produce poisoning when eaten.

It will be understood from the above classification that venomous fish are to be distinguished from poisonous fish—*i.e.*, from fish which cause symptoms of poisoning when their flesh is eaten—for the flesh of venomous fish can be eaten with impunity. The poisonous fish and their effects have been briefly described in Chapter XIII., p. 193, under the heading Poisonous Food.

During the spawning season the quantity and the virulence of the poison of venomous fish generally increase, and, indeed, some genera—*e.g.*, Cottus—are only venomous at that time. Poisonous glands, being protective, occur more commonly in weak and small rather than in large fish, hence they are more frequent in bony than in cartilaginous fish, which latter are usually of large size. Venomous fish are often conspicuous by form or colour.

Historical.—The history of our knowledge of venomous fish has been well written by Faust, who points out that it was Aristotle, the Father of Ichthyology, who first established the fact that fish could produce poisoned wounds, and that after his day information on this subject appears to have been very uncertain, and doubts were cast upon the facts ascertained by him. Modern knowledge began in 1841 by Allman writing a paper on the stinging properties of the lesser weaver (*Trachinus vipera*), which, he said with all reservation, was probably due to a poison-gland at the base of the opercular valve. Further researches were made by Byerley in 1849, Günther from 1864 to 1881, Corre 1865-81, Gressin 1884, and Savtschenko, who produced his excellent atlas in 1886. It is, however, Bottard, in his thesis on 'Les Poissons Vénimeux' in 1889, who first gave a clear account of these fish, and he has been followed by Courtière in 1899, Briot in 1902-04, and Evans in 1907. The nature of the poison or poisons, and its or their physiological effects, still require considerable research.

Effects of the Poison.—As far as investigations have gone, it appears as though the venoms of the different fish only varied quantitatively, and not qualitatively. The effects are local and general. The local effects consist in painful sensations, swelling of the part, which may spread over the whole limb, suppuration, and even gangrene. The general symptoms appear to be due in the first instance to the action of the venom on the central nervous system, which shows itself in excitation, and later insensibility and paralysis. An action on cardiac muscle has also been recorded. In man death has been known to occur from wounds of *Synanceia brachio*.

Persons Chiefly Affected.—The persons chiefly affected by the venom are cooks and fishermen, but the latter are well aware of the danger.

Diagnosis.—Diagnosis is to be obtained by the history of the injury.

Prognosis.—This is usually good, but prompt treatment is needed.

Treatment.—The treatment of a poisonous wound due to a fish must be based upon the following principles:—

1. Prevent as far as possible the poison entering the general circulation.
2. Neutralize the poison as far as possible locally.
3. Treat the general symptoms.

1. *Prevent the Poison entering the General Circulation.*—The wound will usually be on an arm or a leg, and therefore it will be quite

easy to apply proximally a tight bandage with the same precautions as mentioned under Snake-Bite (see p. 274).

2. *Neutralize the Poison Locally.*—This should be done by opening the wound and letting it bleed while washing it with 1 per cent. solution of permanganate of potash, or by rubbing in crystals of the same substance, and then applying fomentations and aseptic dressings.

3. *General Treatment.*—The pain must be relieved by hypodermics of morphia, and nervous symptoms by bromides; syncopal attacks by stimulants and hypodermics of strychnine; failure of respiration by artificial respiration.

Zoological Classification.

The venomous fish may be classified as follows:—

- Subclass I. Elasmobranchii.
  - Order 3. Selachii.
    - Suborder 3. Raii.
      - Family Myliobatidæ.
        - Myliobatis aquila Linnæus.
          - Aetobatis narinari Euphrasen.
      - Family Trygonidæ.
        - Trygon pastinaca Cuvier and other species.

- Subclass V. Teleostei.
  - Grade A. Physostomi.
    - Suborder 2. Cyprini siluriformes (Ostariophysi).
      - Family Siluridæ.
        - Plotosus anguillaris Bloch, 1793.
        - Saccobranchus fossilis Bloch.
    - Suborder 4. Anguilliformes (Apodes).
      - Family Murænidæ.
        - Muræna helena Linnæus.
  - Grade B. Physoclisti.
    - Suborder 10. Acanthopterygii.

- Division 1. Perciformes.
  - Family Acanthuridæ.
    - Acanthurus luridus.

- Division 7. Trigliformes (Scleroparei).
  - Family Triglidæ.
    - Trigla hirundo Linnæus.
  - Family Scorpænidæ.
    - Synanceia brachio Cuvier and Valenciennes, 1826.
    - ,, verrucosa Schneider.
    - Scorpæna grandicornis Cuvier and Valenciennes, 1826.
    - ,, diabolus Cuvier and Valenciennes, 1826.
    - ,, porcus Linnæus.
    - Pterois antennata Bloch.
    - Pelor filamentosum Cuvier and Valenciennes, 1826.
  - Family Cottidæ.
    - Cottus scorpius Linnæus.

Division 8. Blenniformes.

Family Trachinidæ.
Trachinus draco Linnæus.
,, vipera Cuvier and Valenciennes, 1826.
,, radiatus Cuvier and Valenciennes, 1826.
,, araneus Riss.

Family Uranoscopidæ.
Uranoscopus scaber Linnæus.

Family Callionymidæ.
Callionymus lyra Linnæus.

Family Batrachidæ.
Batrachus tau.
,, grunniens Bloch.
Thalassophryne reticulata Gunther.
,, maculosa Günther.

Addendum.--Serranus outabili (Cuv. and Val.) and Holocanthus imperator (Bl.) are looked upon as possibly poisonous, but there is no definite evidence. The Siluridæ are believed to be poisonous, because some of them possess sac-like organs opening into the axillæ of the pectoral fins, on which there are powerful spines.

Geographical Distribution.

The geographical distribution of venomous fish is in temperate and tropical —

Teleostomi.

Plotosus anguillaris ..	Indian Ocean
Muræna helena	Mediterranean.
Acanthurus luridus ..	Tropical Atlantic
Trigla hirundo	English Channel.
Synancēia bracho .. .	Tropical Pacific
,, verrucosa ..	Indian Ocean.
Scorpæna grandicornis .	Waters of the Antilles.
,, diabolus	Indian Ocean and Tropical Pacific
,, porcus	Mediterranean.
Pterois antennata	Seas of the Indies and Equatorial Pacific.
Pelor filamentosum .	Waters of l'Isle-de France.
Cottus scorpius	Seas of Europe, Asia, and North America.
Trachinidæ.. .. .	Waters of Europe.
Uranoscopus scaber .	Mediterranean.
Callionymus lyra . .	Waters of France.
Batrachidæ..	Waters of Tropical America and India.

Leaving, however, the zoological classification, we will consider the venomous fish according to Bottard's classification, excluding Class III.

CLASS I.

FISH WHICH POISON BY THEIR BITE.

The type of this class is the genus *Muræna*, all of which possess powerful teeth capable of inflicting severe bites. According to Calmette, there are more than one hundred species in tropical and subtropical seas. *Muræna helena* L. is found in the Mediterranean, and *Muræna moringa* Cuv. in the tropical Atlantic.

The poison apparatus consists of a pouch lying above the covering of the palate lined with epithelial cells, secreting the venom. This pouch is capable in larger species of holding about ½ c.c. of poison, and possesses three or four strong conical teeth curved with an anterior convexity. These teeth are not grooved or channelled, but are easily moved and erected, and are enclosed in a sheath formed by the mucosa of the palate. The poison collects between the teeth, and simply flows down them into the wound.

The venom has not been studied, except so far as to show that it has some digestive action. The effect on man is not certainly known, but is supposed to lead to syncope.

Another fish, the bite of which is much dreaded, is *Tetrodon fluviatilis*, which is found in the waters of Indo-China, and frequently attacks the natives, especially children.

CLASS II.

Fish which Poison by Means of Stings associated with Poison Glands.

Bottard classifies the poison apparatus of this class into three groups:—

1. Apparatus entirely closed, and therefore before the poison can escape a membrane must be ruptured:

Synanceia brachio.
,, verrucosa.
Plotosus anguillaris.

Apparatus partially closed:

Thalassophryne reticulata.
,, maculosa.

3. Apparatus in more or less direct communication with the exterior:—

Trachinus vipera.
,, draco.
,, radiatus.
,, araneus.
Cottus scorpius.
,, bubalis.
,, gobio.
Callionymus lyra.
Scorpaena porcus.
,, scrofa.
Pterois antennata.
Pelor filamentosum.
Acanthurus luridus.
Uranoscopus scaber.
Trigla hirundo.

The poison glands are generally placed at the base of the dorsal or anal fins, or under spines on the operculum. The gland communicates with one or more rays of the fins. The barbs may be:—

1. Grooved, but having the groove converted into a canal by a membrane, which must be ruptured for the poison to escape.

2. Canalized by channels which lead to apertures near its tip.

This arrangement of the rays agrees with the types of poison apparatus mentioned above.

Section 1. Poison Apparatus Entirely Closed.

The apparatus is connected with the dorsal fin, and is passively defensive—that is to say, the fish cannot eject the poison unless the barb is broken.

EXAMPLES.—*Synanceia* (*brachio* and many other species); *Plotosus arab.*

Synanceia (*brachio and many other species*).—This fish, called 'rapau de mer' in Réunion, 'laffé' in Mauritius, 'ikan Satan' in Java, and 'nohu' in Tahiti, is distributed through the waters of the Indies, Cochin China, New Caledonia, and the Pacific Ocean.

Its poison apparatus is connected with the dorsal fin, which has thirteen barbs, each of which is supplied with two poison reservoirs, to which belong ten or twelve tubular glands. It cannot eject the poison itself, but if trodden upon by the naked foot, the barbs enter the skin, and the poison is pressed mechanically into the wound. The venom is limpid, bluish, and slightly acid. The symptoms are severe pain, spreading up the limb. The sufferer becomes violent, throwing himself from side to side, and even asking to have his foot cut off. Sometimes syncope and death may take place. In other cases abscesses and symptoms of blood-poisoning may be noted. The skin surrounding the wound becomes bluish, and may slough, in which case repair takes a very long time to be completed.

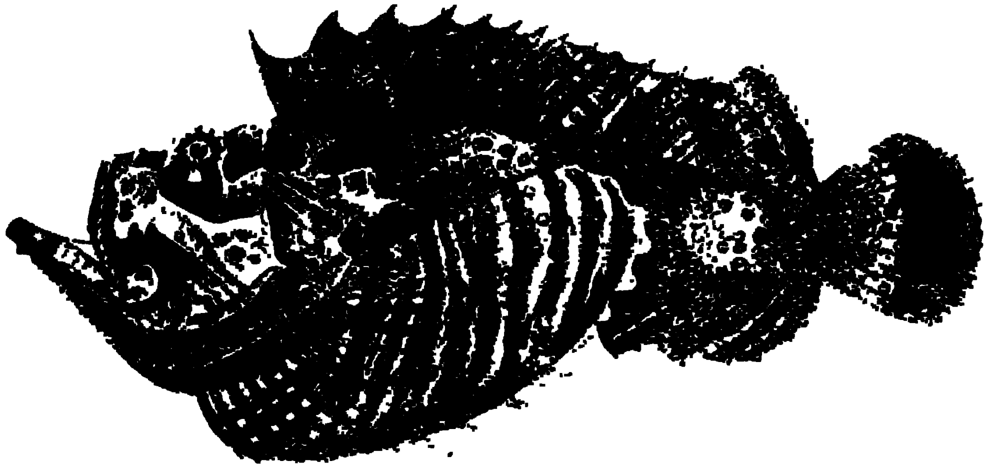

FIG. 27.—*Synanceia verrucosa* SCHNEIDER.
(From Savtschenko's 'Atlas of Poisonous Fish.')

Plotosus anguillaris.—This fish, called 'machoira' in Réunion and Mauritius, 'sanbilang' in Malay, 'koormat' in Abyssinia, is found in the waters of India, of the Seychelles, and other places mentioned above. The poison apparatus is connected with the dorsal fin, and the conditions which bring about the wound, together with the symptoms, resemble those of *Synanceia*.

Saccobranchus fossilis.—This fish is found in the waters of India and Ceylon, and wounds caused by its pectoral fins are much dreaded by the natives, as they produce severe inflammation and even tetanic symptoms.

Section 2.—Poison Apparatus Partially Closed.

The types of this section are *Thalassophryne reticulata* Günther, which is found near Panama, and *T. maculosa* Günther, which is chiefly found in the Gulf of Bahia (Brazil).

In these fish the poison apparatus is double, there being hollow barbs on the gill covers and on the back close behind the head. The barb on the gill cover, which is bent somewhat upwards, is conical in shape and pierced by a central canal, which is connected with a poison reservoir situated at the base of the barb. The cells lining this sac are probably those which secrete the poison. The venom, therefore, is capable of flowing along this canal without being forced by muscular exertion. The barbs on the dorsum of the fish consist of two spines pierced, as in the case of the opercular spine, by canals which communicate with poison reservoirs. When the barbs are erected, the poison flows out of the peripheral openings of the central canals, and thus can enter any wound caused by them. The nature of the venom and its physiological action are not known, but it is supposed that it will be like *Synanceia* and *Trachinus*, though there is no ground for this supposition.

The poison apparatus of *Batrachus tau* of the waters of North America and *B. grunniens* of those of the Antilles are said to be identical (Calmette) with that just described for *Thalassophryne*.

Section 3.- -Poison Apparatus in more or less Direct Communication with the Exterior.

This section contain [illegible] number of fish, [illegible]e best studied of which is *Trachinus draco*.

Trachinus draco.- This fish pos[illegible] two sets of poison apparatus, the one a barb on the oper[illegible], and the other connected with the dorsal fin. The barb on the operculum possesses a groove which is converted into a canal by a fine membrane, which leaves an opening near the point of the spine. This barb, which is slightly erectile, pierces the operculum. At its base lies the poison gland, partly covered by an adductor muscle, which helps to press the poison into the canal and to erect the spine. When the barb enters the flesh of another animal, the above mentioned membrane is stripped off and the poison enters the wound.

The dorsal apparatus consists of from five to seven spines joined together by a membrane, which is adherent almost to their tips. Each barb has a deep double channel, the two grooves of which join towards the base of the spine, and form a conical space, of which the walls are covered with cells which secrete the poison.

The first symptoms are very severe pain of a burning or lancinating character. The part then tingles and becomes painfully numb, and this may spread along the limb, and appears to travel along the nerves, though the joints are particularly tender. This is followed by palpitation, fever, delirium, vomiting, and syncope. The area affected becomes swollen and inflamed, and if neglected may suppurate or even turn to gangrene. The symptoms may last from two to three hours to several days.

The venom has been studied by Günther, Gressin, Bottard, Briot, and Phisalix. It has also been studied by Evans, who, after washing the fish, collected it by means of an aseptic hypodermic syringe, then dried it *in vacuo*, reduced it to a fine powder, and finally dissolved it in normal saline or in water. He collected the poison from about 2,000 fish. The venom is clear, transparent, and very slightly acid. Hypodermically injected, it causes mortification and local paresis, necrosis, and hæmorrhage. Intravenously injected, it causes failure of the heart and respiratory paralysis, associated with first a rise in the blood-pressure, which is followed later by a marked fall. It also appears to have a hæmolytic effect, which is supposed to be due to its amboceptors uniting with endocomplements (lecithin) in the red cell. It will thus be seen that the poison in some respects resembles snake-venom. The venom is lethal to fish, frogs, and mammals. Thus, 0·015 gramme of dried venom killed a frog, and 0·02 gramme a mouse.

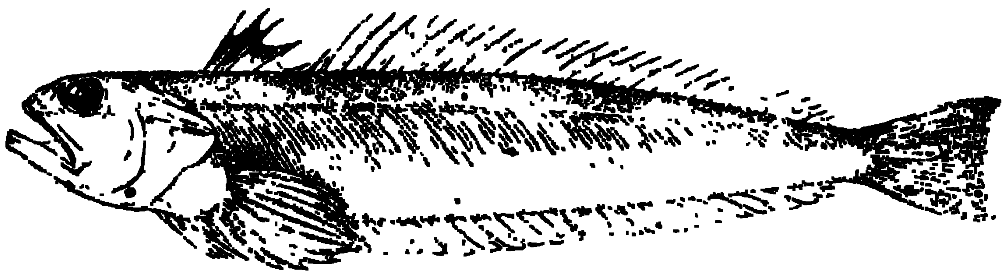

FIG. 28.—*Trachinus draco* LINNÆUS.

According to Briot, who has succeeded in immunizing rabbits, the venom contains a ferment capable of digesting proteid.

Trachinus radiatus.—Pohl has studied the poison of this fish, and finds that it stops the heart in diastole. The effect of applying the poison to the heart of the frog is to first produce strong contractions, which gradually become weaker and weaker, until they cease and the heart stands still in diastole. The poison has, however, no effect on skeletal muscle.

Cottus.—The genus *Cottus*, widespread in the Northern Hemisphere, possesses a poison apparatus which resembles that of the genus *Trachinus*, but is less developed, and consists of poison glands lying in culs-de-sac in the opercular spines. The cells of the gland only secrete the venom during the spawning season, from November to the end of January.

Callionymus.—In *Callionymus* the operculum terminates in three conical spines like a trident, and in addition possesses another spine directed upwards, and these are supplied in the spawning season with a small quantity of venom from the gill membrane, which, according to Bottard, has little effect on man.

Scorpæna scropha. In this fish the poison apparatus is said to exist not merely in the dorsal fin, but also in the operculum.

In the dorsal fin, the first three rays, which project about one-third of their length beyond the membrane of the fin, are grooved posteriorly by three channels, which are converted into canals by a fine membrane, and communicate with the poison gland.

On the operculum there are three small spines, of which the longest alone is connected with a poison gland.

When handled incautiously, a poisoned wound may result from one of these poison spines entering the skin. The action of the poison has been studied by Pohl, Brunton and Briot. Brunton describes the effects of the poison as being exactly the same as that of *Trachinus draco*, and Pohl thinks that the poison acts on the heart in the same manner as he describes for *Trachinus*.

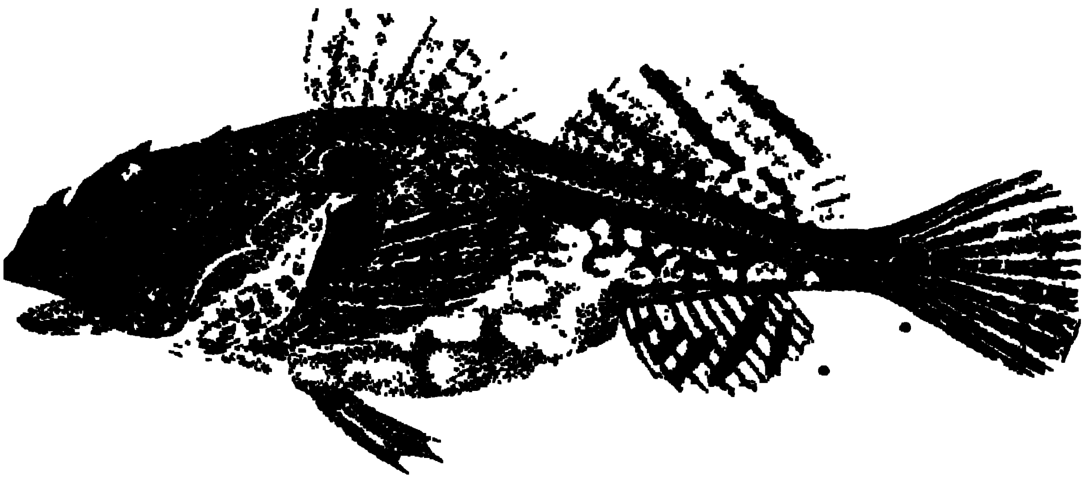

Fig. 29.—*Cottus scorpius* Linnæus.

(From Savtschenko's 'Atlas of Poisonous Fish.')

On the other hand, Briot thinks that it is quite different from *Trachinus*, and that the effects produced are by secondary infection of the mechanical wound caused by the spines. Brunton's description of the symptoms in man might possibly be due to *Trachinus* only, as he does not mention specifically whether it was *Trachinus* or *Scorpæna* which affected the person. His experiments on animals with both fish appear, however, to have caused the same symptoms. He pressed the spines of the poison organs against the hind-limb of a guinea-pig or a rat. In a few minutes the animal began to suffer pain and twitching in the injured limb, followed by tremors and convulsions (if disturbed), and later by death from collapse.

The description which he gives of the symptoms in human beings for either *Scorpæna* or *Trachinus* is given below, but reference to his original paper will, we think, convince the reader that he is really dealing with a *Trachinus* sting.

The symptoms of an attack may be described thus:—

A sharp prick is felt as the spine enters the skin, and this is followed in a few minutes by burning and itching, which shortly become stabbing pains, increasing in violence and passing up the limb. The sufferer now lies down and writhes and cries in agony, while sweat breaks out on his brow, and flashes of light pass in front of his eyes. He begins to feel a sensation of suffocation, and puts his hand to his throat and heart, while the pulse is felt to be intermittent. Presently he loses sight of the bystanders, and in a little becomes delirious, crying out and suffering from convulsions. This condition may lead to collapse and death, or, after lasting several hours, may gradually subside, but the convalescence is slow, and the patient may take several months to recover.

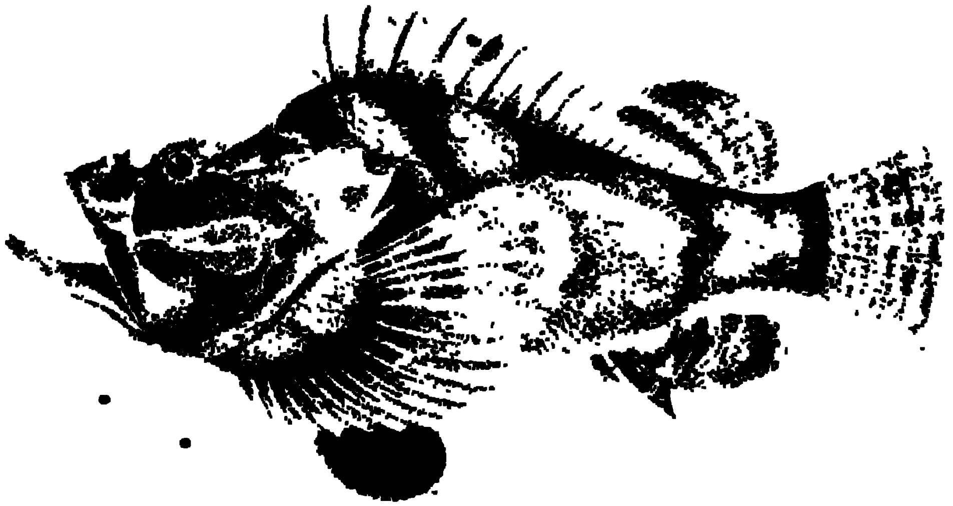

FIG. 30. *Scorpæna diabolus* CUVIER AND VALENCIENNES.
(From Savtschenko's 'Atlas of Poisonous Fish.')

The local conditions show at first merely the prick of the spine, but the aperture may be pigmented by the covering membrane already alluded to. The puncture does not bleed, but the skin around for about ½ inch is whiter than usual, and outside this redness appears, but soon all the surrounding skin is red, turning as time passes darker and darker, till it becomes black and œdematous. The prick now discharges fluid. In a day or so the affected area sloughs and separates, leaving a deep wound. Sometimes a spreading gangrene ensues, which necessitates amputation. In milder cases the part remains painful and swollen for about three days before recovery.

Pterois antennata.—The poison apparatus is connected with the dorsal fin, and is said to resemble that of the Scorpænidæ.

Pelor filamentosum.—In this fish the poison apparatus is connected with the dorsal fin, and resembles that of *Pterois* and *Scorpæna*. With regard to *Pelor japonicum* Cu. and Val., Scheube says that he knew of a case in which a sting on the thumb resulted in phlegmonous and gangrenous symptoms so severe that the arm had to be amputated.

Acanthurus luridus.—*Acanthurus luridus* possesses a poison apparatus connected with the dorsal and anal fins like that of *Scorpæna.*

Elasmobranchii.—Associated with the poisonous fish of the *Teleostei* must be placed those of the *Elasmobranchii*, of which the sting rays (Trygonidæ) and eagle rays (Myliobatidæ) alone produce toxic symptoms by blows with the tail, which carries a spine. These Rays are found all over the world, and we have received information as to their effects from persons who have been in British Guiana, in Australia, and in Ceylon, in which island stings are well known on the west coast, particularly about Dutch Bay.

Dr. Crevaux has studied Rays from the Orinoco, and has shown that their barbs are canalized and the canals connected with poison reservoirs. This poison is said to be so severe as to be able to kill a man in forty-eight hours. The symptoms of *Aëtobatis narinari*, called the Bishop ray, and of *Trygon pastinaca* (from Japan), are violent pain, a tendency to syncope, with locally a rapidly forming swelling, which soon becomes the seat of a violent inflammation and even at times gangrene. The symptoms of the sting, as observed by us in Ceylon, are local pain and swelling. The general symptoms are not severe. *Trygon sephen* and *T. walga* Müll. and Hen. are known in Indian waters.

A large number of these *Elasmobranchii* have not got special poison glands, and the venom must come from the ordinary skin glands.

Amphibia.

Toads and salamanders have been celebrated for ages as venomous animals, the poison being found in their parotid glands and skin. In toads Faust has shown that there are two poisons—(1) an acid, bufotalin, and (2) a neutral body, bufonin, the former being the more active. It is, as a rule, scarcely toxic to man, only irritating the mucous membranes, especially the conjunctiva; but to small animals it is toxic.

In salamanders Zalesky and Faust have found two bodies, one an inorganic base—salamandarin—and another an alkaloid—salamandaridin; but this poison and the digitalis-like poison of Bert and Dulartre in frogs are not of sufficient practical interest to concern us here.

According to Vulpian and Caparelli, *Triton cristatus* (Laur) gives a creamy secretion from the glands of the skin at times which is poisonous to many animals, but the chemical nature of which is not known.

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CHAPTER XVI

VENOMOUS ANIMALS (*concluded*)—REPTILIA AND MAMMALIA

Reptilia: Ophidia—Historical—Classification—Geographical distribution—The act of striking—The venom—Entry of the venom into the body—Minimum lethal dose—Effects of the venom—Excretion of the poison—Immunity—Diagnosis—Prognosis—Treatment—Prophylaxis—Lacertilia. *Mammalia*. References.

REPTILIA.

THE Reptilia include two groups which are of interest to medical men in the tropics—viz., the Ophidia and the Lacertilia; but the former is infinitely more important, as it includes the venomous snakes.

OPHIDIA.

Definition.—*Reptilia* with limbs absent or vestigial; without movable eyelids, or ear openings, with retractile elongated forked tongue, transverse anus, paired copulatory organs, and elastic ligament in place of symphysis menti.

Remarks.—The bite of certain snakes causes ophidismus, or snake poisoning.

Historical.

The history of the study of snake bite, and their effects may be divided into three periods:

1. Period of ancient theories.
2. Period of one venom.
3. Period of more than one venom.

1. **Period of Ancient Theories.** The ancients were acquainted with a number of snakes, which they described under the terms *Echis* and *Colubra*, but it is not known definitely to what species these referred. *Echidna* was a term used to denote the female viper.

They were acquainted with the main symptoms of a snake-bite, and had many remedies, including the tying of a ligature around the part followed by cupping after scarification, and the administration of wine and theriac, the last mentioned being a celebrated remedy which, among other substances contained the burnt body of the viper. Celsus recommends the sucking of the wound, but only if there are no ulcers on the gums, palate, and other parts of the mouth.

2. **Period of One Venom.** In 1664 Redi studied the effects of viper-bites by experiments on animals, and Moise Charas, in 1669, noted the important fact that the blood of animals bitten by vipers was coagulated, and came to the conclusion that the symptoms and death were due to this coagulation.

In 1767 Abbé Felix Fontana made a number of observations on animals bitten by vipers, and in 1796 Russell published an account of his experiments on Indian snakes. In 1821 Davy gave an account of the effects on animals of the bites of three Ceylon snakes.

In 1843 Prince Lucien Bonaparte published his important discovery that the venom of the adder contained an active substance, which he called viperine, or echidnine, capable of being precipitated by alcohol

In 1845 Brainard showed that if an animal dies at once after the bite of a rattlesnake, the blood will be found to be clotted, but if it lives for some time it will be fluid.

In 1860 Weir Mitchell laid the foundations of modern investigations into snake-venom in his classical paper on the poison of *Crotalus durissus*.

In 1867 Sir Joseph Fayrer began his work on Indian snakes, which resulted in the publication of his magnificent atlas on the Thanatophidia of India in 1872, and several papers by himself and Sir Lauder Brunton in 1873-75.

About the same time Vincent Richards published some valuable remarks on snake poisons and their antidotes

In 1883 Wall wrote a most excellent little book on the colubrine and viperine snakes of India.

In 1886 appeared a most masterly paper by Weir Mitchell and Reichert, in which they state that the active principles are globulins and peptones (proteoses). These researches indicating a proteid nature for the venom were confirmed by Wolfenden and Kanthack, and did away with Gautier and Blyth's ideas as to their alkaloidal nature.

In 1892 Martin alone and with Smith studied the venom of Australian snakes (*Hoplocephalus* and *Pseudechis*), and concluded that the venom contained three proteids an albumin and two proteoses (proto and hetero), the latter, however, being alone virulent.

In the meanwhile observers had not been backward in making attempts to find the physiological antidote suggested by Weir Mitchell and Reichert, for in 1887 Sewall showed that by repeated injections of the venom of *Crotalus*, pigeons could be gradually rendered resistant against strong doses of that poison; and a little later Reichert obtained the same result with regard to the venom of the French viper. In 1892 Calmette published the first of his celebrated series of investigations, showing that successive inoculations of heated venom produced in animals a certain degree of resistance to quantities of the poison otherwise surely fatal. Calmette worked largely with the cobra, and produced in rabbits and guinea pigs a true immunity. He further concluded that animals vaccinated against the cobra also withstood with impunity mortal doses of the venom of the viper and other snakes (*Bungarus*, *Cerastes*, *Naja haje*, and *Pseudechis*).

Phisalix and Bertrand also studied the question of obtaining an immunity against the bite of the viper. Fraser of Edinburgh, in 1895, confirmed these results of Calmette. Since then there has not been the slightest doubt that Calmette' serum is of the greatest value in certain cases, especially against cobra-venom.

In 1881 permanganate of potash was recommended as an antidote by Professor de Lacerda, of Rio de Janeiro, and by Badaloni in Italy in 1882-84, and lately this remedy has again been strongly recommended by Rogers, of Calcutta, and there appears to be no doubt as to its efficiency; but the question of remedies will be dealt with in their proper place.

It will thus be seen that at the close of this period there is a general belief that the venom of all snakes has virtually the same active principles, which are thought to be proteids, and that, though they may differ in amount, and hence their effects be different, still, it is only a quantitative, and not a qualitative, difference; and, further, that one antivenene is effectual against all kinds of venom.

3. **Period of more than One Venom.**—The third period, extending up to the present, is that in which there is the conception that there are at least two definitely separate types of venom, one of which may be called the colubrine type, having as its example *Naja tripudians*, and the other the viperine type,

which may be exemplified by the *Vipera russellii*. In addition, however, there are venoms which show characters belonging to both types.

Weir Mitchell alone and with Reichert indicated that there was a difference between viperine and colubrine poisons; and C. J. Martin, working on *Pseudechis*, a colubrine snake, discovered the intravascular clotting, and suggested that the sudden death caused by *Vipera russellii* might be due to this cause, which hypothesis Lamb and Hanna confirmed.

The difference in the working of these two classes of venoms is still further accentuated by the researches of Rogers, and later by those of Lamb, which clearly prove that Calmette's antivenene will neutralize the colubrine, but not the viperine, venom.

In 1902 a most valuable paper appeared, by Flexner and Noguchi, showing that, in addition to the neurotropic principles, the venom contained agglutinins for the erythrocytes and for the leucocytes which were probably identical, and lysins for erythrocytes and leucocytes which were separate.

They also pointed out that venom contained hæmorrhagins, and lessened the bactericidal powers of the blood. They showed that antivenene neutralizes venom by removing the hæmolytic and antibacteriolytic actions. These results have been confirmed and extended by Kyes, Sachs, Lamb, and others.

The position at the present time is that, though snake-venom is extremely complex, still, three kinds of venom may be recognized:—the colubrine type, the viperine type, and the mixed type. In this last both colubrine and viperine types are represented, but one is predominant. It is probable that the main action of both types is on the nervous system, but that other principles in the venom may mask this important action.

With regard to treatment, there is no doubt as to the value of Calmette's rum in cobra-poisoning, and Lam [illegible] cobra and *Vipera russellii* poisoning, thoug [illegible] method of ligatu [illegible] incision, together with the application of permangana [illegible] potash, is sti [illegible] the most practically useful method of treatment.

Classification.

The order Ophidia includes a large number of families, of which only two are of importance to the tropical practitioner—viz., Colubridæ and Viperidæ.

FAMILY COLUBRIDÆ BOULENGER, 1890.

Definition.—*Ophidia* with ectopterygoids (transpalatines) and supratemporals present with teeth in both jaws, but without coronoids, while the prefrontals are not in contact with the nasal bones.

The Colubridæ are divided, in works on snake poisons, into the non-venomous and the venomous, and the latter are joined with the vipers to form a subclass of the order Ophidia called Thanatophidia, or poisonous snakes; but this classification is by no means satisfactory, as will presently be shown. There is no external character, easily ascertainable, by means of which every poisonous snake can be recognized and distinguished from a harmless snake. All rules given to the contrary break down sooner or later, but the mouth can be opened and the poison-fangs can usually be easily seen.

The usual classification of the Colubridæ is into three series:—

1. **Aglypha Poisonous Colubridæ possessing solid ungrooved teeth.**—The Aglypha are usually stated to be non-poisonous, but the observations of Phisalix and Bertrand on *Tropidonotus* (sp. ?), and Alcock and Rogers on *Zamenis mucosus* and *Tropidonotus piscator*, prove that the saliva of these species is poisonous to rats,

mice, and guinea-pigs. Thus hypodermic injections of the saliva of the two last-named snakes will cause convulsions and death from failure of respiration in rats and mice.

Therefore the saliva, though it may not be known to have affected even a child, must be looked upon as poisonous, and the Aglypha must be grouped with the other Colubridæ and the Viperidæ under the head Thanatophidia.

The Aglypha are divided into three subfamilies: Acrochordinæ, Colubrinæ (rat-snakes), and Dasypeltinæ (African egg-eating snakes).

Some of the important species are *Tropidonotus natrix*, the common British snake, and *Coronella austriaca*, a rare snake found in South England. *Tropidonotus fasciatus* is the North American water moccasin, *Zamenis mucosus* the Indian rat-snake, and *Dasypeltis scabra* is the African egg-eating snake:

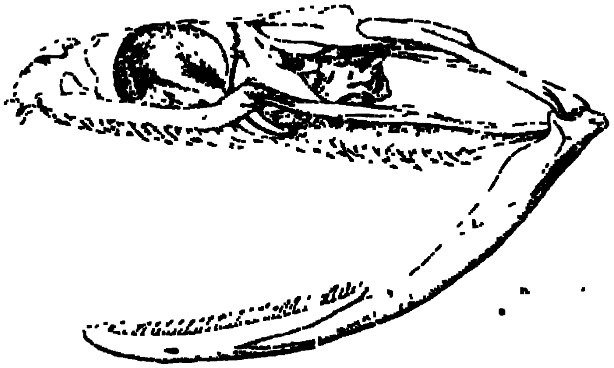

FIG. 31. SKULL OF *Tropidonotus natrix* LINNÆUS.

All the teeth are solid, there are no grooved or perforated fangs hence the name *Aglypha*, but the saliva may be poisonous. Note the length of the maxilla

2. **Opisthoglypha -Poisonous Colubridæ with one or more of the hinder teeth of the upper jaw grooved.** -Early last century there was a great controversy as to whether these snakes were poisonous or not, and it is generally stated nowadays that, though poisonous, their venom is weak, and that the position of the poison-fangs at the back of the mouth prevents the bite from hurting man. Quelch has, however, recorded cases in which bites on the fingers from *Erythrolamprus æsculapii* L. and *Xenodon severus* have caused severe inflammation.

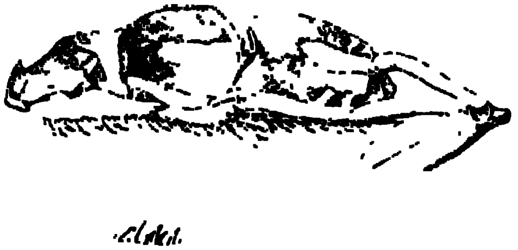

FIG -SKULL OF *Cœlopeltis monspessulans*

Note the fangs in the rear ot the upper jaw; hence the name *Opisthoglypha*. These fangs are grooved.

The following list is given by Faust of those known to be poisonous to animals: *Cœlopeltis monspessulans* Herm., *Trimorphodon biscutatus* D. and B., *Tarbophis savignyi* Descr., *Dryophis prasinus* Russl., and *Leptodira annulata* L.

The Opisthoglypha are divided into three subfamilies:-

(1) *Dipsadomorphinæ—Opisthoglyphida with well-developed mouth, and nostrils situated at the side of the head.*—They include the Indian tree-snakes.

(2) *Elachistodontinæ—Opisthoglyphida with rudimentary teeth on the palatine and pterygoid bones.*—Their venom is said to be so weak and their poison-fangs so unfavourably situated that they are not to be considered as dangerous to man. They include the Indian egg-eating snakes.

(3) *Hemalopsinæ—Opisthoglyphida with nostrils valvular and situated on the upper part of the snout.* They are all water-snakes.

3. **Proteroglypha.—Poisonous Colubridæ with the front teeth in the upper jaw well developed to form fangs, and grooved anteriorly. The bases of these fangs are connected with ducts which lead from well-developed poison glands.** These snakes are well known to be highly dangerous to man and animals. They are divided into three subfamilies—Elapinæ and Hydrophinæ.

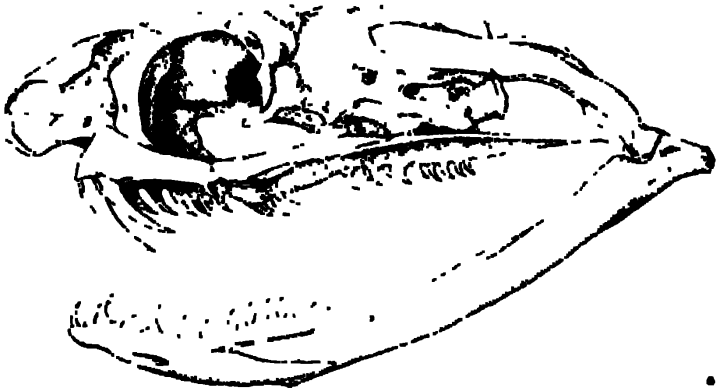

FIG. 33.—SKULL OF *Naja tripudians* MERREM.

Note the pair of short rigidly attached fangs situate in the front of the upper jaw, hence the name *Proteroglypha*. These fangs are grooved. Note the shortening of the maxilla.

Elapinæ—Proteroglypha living on land, and possessing a cylindrical tail.—Among these are classed the cobras, whose proper name is cobra-di-capello—*i.e.*, the snake with the hood, so called because, when excited, it expands the skin behind the head by throwing outwards the cervical ribs.

Buddhists regard these snakes with reverence, because one with seven heads is said to have placed its expanded hoods over Buddha's head, and thus to have protected him from the glare of the mid-day sun.

The genera of the Elapinæ (Boulenger) are: *Naja* Laurenti; *Bungarus* Daudin; *Hemibungarus* Peters; *Callophis* Gunther; *Doliophis* Girard; *Boulengerina* Dollo; *Elapechis* Boulenger; *Aspidelaps* Fitzinger; *Walterinnesia* Lataste; *Dendraspis* Schlegel; *Ogmodon* Peters; *Glyphodon* Günther; *Pseudelaps* Duméril and Bibron; *Diemenia* Gray; *Pseudechis* Wagler; *Denisonia* Krefft; *Tropidechis* Gunther; *Notechis* Boulenger; *Rhinoplocephalus* F. Muller; *Brachyaspis* Boulenger; *Acanthophis* Daudin; *Elapognathus* Boulenger; *Rhynchelaps* Jan; *Furina* Duméril and Bibron; *Elaps* Schneider; *Sepedon* Merrem; *Micropechis* Boulenger; *Hoplocephalus* Cuvier.

Naja tripudians Merrem, the cobra with one spot, or a pair of spectacles on its hood, is common in India and Ceylon. *N. bungarus*

Schlegel., the king cobra, or hamadryad, is not so common, but is feared because of its size, and because it is said to attack people. *N. haje* L. is Cleopatra's asp, and is well known as a resident of Egypt and North Africa. *N. regalis* Schl., is found on the Gold Coast. *N. nigricollis* Reinhart is found on the Gold Coast and in Sierra Leone.

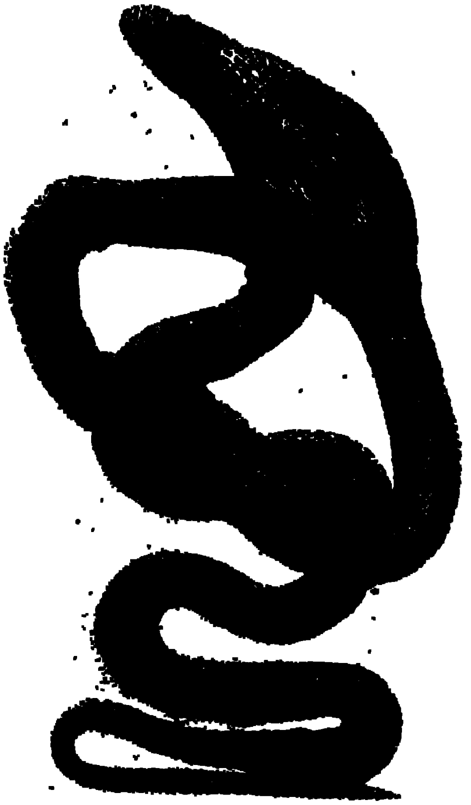

FIG. 34.—*Naja tripudians* MERREM, 1781. THE COBRA.
Note the pair of spectacles on the hood.

The kraits are also included in this family, and are: *Bungarus candidus* L., the true krait, and *B. fasciatus* Schn., the banded krait, with yellow and black bands, both of which are common in India, while *B. ceylonicus* Gthr. is the carawalla of Ceylon. The Elapinæ are the only poisonous snakes of Australia, and include *Notechis scutatus* Ptrs. and *N. pseudechis*, and *Acanthophis antarcticus* Shaw, the death adder, recognized by the spines on its tail.

FIG. 35.—SIDE VIEW OF THE HEAD OF THE COBRA.

Elaps corallinus Wied, the coral snake, with black and red bands separated by narrow rings of a yellow colour, is found in Columbia, British Guiana, Venezuela, and Brazil

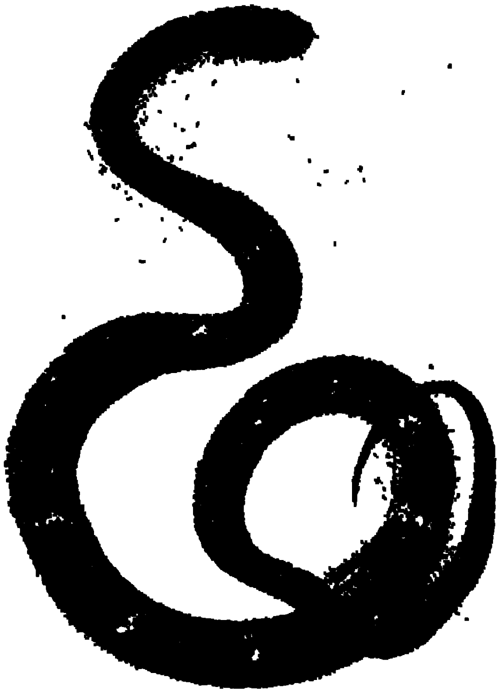

FIG 36.—*Bungarus ceylonicus* GÜNTHER.
This is the Carawalla of Ceylon.

The *Sepedons* are hooded snakes like cobras (*Sepedon hæmachates* Lacép. of South Africa), and are supposed to throw their venom so far that there is a danger of it getting into the eyes of animals and human beings, and causing severe conjunctivitis.

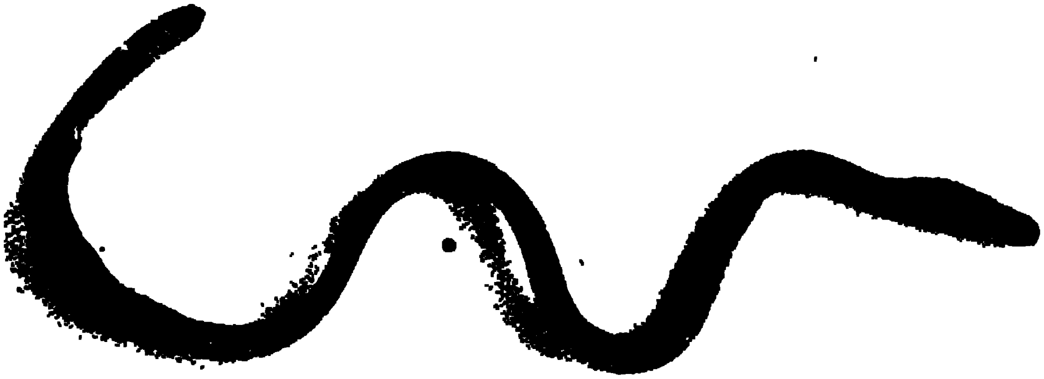

FIG. 37.—*Hydrus platurus* LINNÆUS.
This is a typical sea-snake. Note the flattened spotted tail.

None of these snakes are found in Europe or America.

Hydrophinæ—Proteroglyphæ living in the sea, and possessing a flat tail.—These snakes can be seen swimming in families far out in the Indian Ocean, but are also found in all Eastern tropical seas.

FIG. 28.—*Vipera russellii* SHAW.

This is the Tic Polonga of Ceylon

The genera of the Hydrophinæ (Boulenger) are:—*Distera* Lacépède, *Acalyptus* Duméril and Bibron, *Hydrophis* Daudin, *Enhydrina* Gray; *Hydrelaps* Boulenger; *Hydrus* Schneider; *Thalassophis* Schmidt; *Enhydris* Merrem; *Platurus* Latreille; *Aipysurus* Lacépède.

The best-studied species is *Enhydrina valakadien* Boie. Another species, *Distera semperi* Garm., lives in fresh water in the Philippine Islands. It is, of course, dangerous to fishermen.

FAMILY VIPERIDÆ BONAPARTE, 1840.

Definition.—The vipers are characterized by their triangular head and their tubular poison-fangs (hence the name Solenoglypha), with are situated anteriorly in the mouth, and are provided with a wide foramen, piercing the base anteriorly for connection with the duct of the poison gland. They possess a stout body and short tail, and are all viviparous.

The Viperidæ are divided into:—

- **Crotalinæ** Boulenger.—Vipers with a deep pit, probably sensory in function, situated between the nostril and the eye on each side of the head.
- **Viperinæ** Boulenger.—Vipers without such a pit.

Crotalinæ.—The Crotalinæ include the rattlesnakes, so called because they have a number of horny rings which fit into one another at the end of the tail.

The genera of the Crotalinæ (Boulenger) are:—*Crotalus* Linnæus; *Sistrurus* Garman; *Ancistrodon* Beauvois; *Lachesis* Daudin.

There are two divisions of rattlesnakes in America—*Crotalus* and *Sistrurus*—distinguished by the former having many small, and the latter only nine large, scales on the top of the head.

The best-known rattlesnakes are *Crotalus horridus* L., *C. scutulatus* Kenn. of Texas, *C. confluentus* Say, of the Pacific, *C. durissus* L., and *C. cerastes* Hallow.

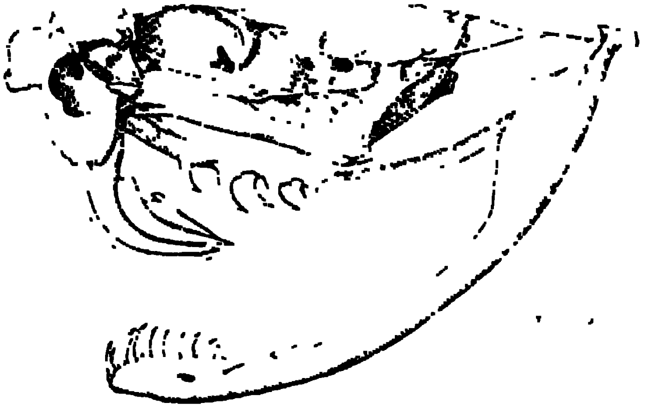

FIG. 39.—SKULL OF *Crotalus horridus* LINNÆUS.

Note that in place of the long horizontal maxilla of the other three skulls there is only a small vertical movable maxilla on each side of the anterior part of the skull. It can be recognized by carrying the enormously developed fang which is canalized and is virtually a hypodermic needle for the injection of the venom. Note the reserve fangs, which should lie flat against the skull.

FIG. 40.—SIDE VIEW OF THE HEAD OF A RATTLESNAKE (*C. horridus*).

FIG. 41.—END OF THE TAIL OF *C. horridus* TO SHOW THE RATTLE.

Other genera are *Ancistrodon*, with *Ancistrodon piscivorus* Lacép., the water moccasin, and *A. contortrix* L., the copper-head, *Lachesis*, with *Lachesis lanceolatus* Lacép., the celebrated fer de lance of Martinique; *L. anamallensis* Gthr. and *Sistrurus*, with *Sistrurus ravus* Cope and *S. miliarius* L.

Viperinæ. The true vipers include: *Vipera berus* L., the adder of England; *V. russellii* Shaw, the handsome viper of India and Ceylon; *Bitis arietans* Merr., the puff adder of the Gold Coast; *Cerastes cornutus* Forskål, the horned viper of North Africa; and *Echis carinatus* Schn., the viper of the Pyramids, called 'efa.'

The genera of the Viperinæ (Boulenger) are:—*Vipera* Laurent; *Causus* Wagler; *Bitis* Gray; *Pseudocerastes* Boulenger; *Cerastes* Wagler; *Echis* Merrem; *Atheris* Cope; *Atractaspis* Smith.

Geographical Distribution.

Asia.—ELAPINÆ: *Naja tripudians*, *N. samarensis*, *N. bungarus*; *Bungarus fasciatus*, *B. candidus*, *B. ceylonicus*; *Hemibungarus*, *Callophis*, *Doliophis*.

HYDROPHIINÆ: *Enhydrina valakadien*, *Hydrus platurus*, *Enhydris curtus*, *Hydrophis obscurus*, and many others.

VIPERINÆ: *Vipera berus*, *V. renardi*, *V. raddii*, *V. lebetina*, *V. russellii*, *Pseudocerastes persicus*; *Cerastes cornutus*; *Echis carinatus*.

CROTALINÆ: *Ancistrodon halys*, *A. himalayanus*, *A. hypnale*, and others, *Lachesis flavoviridis*, *L. sumatranus*, *L. borneensis*, etc.

Africa. ELAPINÆ: *Naja haje*, *N. flava*, *N. melanoleuca*, *N. nigricollis*, *N. anchietæ*, *N. goldii*; *Sepedon hæmachates*; *Boulengerina stormsi*; *Elapechis guentheri*, etc., *Aspidelaps scutatus*, *Walterinnesia ægyptia*, *Dendraspis viridis*, etc.

VIPERINÆ: *Causus rhombeatus*, etc., *Vipera ammodytes*, etc., *Bitis arietans*, *B. cornuta*, *B. gabonica*, *B. caudalis*, *B. atropos*, *B. nasicornis*, *B. peringueyi*, *B. inornata*, *Cerastes cornutus*, *Echis carinata*, *Atheris chlorechis*, *Atractaspis congica*, etc.

Australia and Oceania. ELAPINÆ: *Ogmodon vitianus*, *Glyphodon tristis*; *Pseudelaps muelleri*, etc., *Diemenia psammophis*, etc., *Pseudechis porphyriacus*, etc.; *Denisonia superba*, etc., *Micropechis elapoides*, *Hoplocephalus variegatus*, etc., *Tropidechis carinata*; *Notechis scutatus*, *Brachyaspis curta*, *Elapognathus minor*; *Acanthophis antarcticus*, *Rhynchelaps australis*, *Furina calonota*, etc.

HYDROPHIINÆ: *Hydrus*, *Thalassophis*, *Hydrelaps*, *Hydrophis*, *Distira*, *Enhydris*, *Enhydrina*, *Aipysurus*, *Platurus*.

America. ELAPINÆ: *Elaps*, many species, *Micropechis elapoides*; *Ancistrodon piscivorus*, *A. bilineatus*, *A. contortrix*, *Lachesis mutus*, *L. lanceolatus*, and many others, *Sistrurus miliarius*, *S. catenatus*, *S. ravus*; *Crotalus adamanteus*, *C. horridus*, *C. confluentus*, *C. atrox*, *C. oregonus*, *C. cerastes*, *C. mitchelli*, *C. terrificus*, and others.

The Act of Striking.

The poison is secreted by glands, which are either modified upper labial glands or a pair of glands occupying the sides of the head behind the eyes, and which are the homologues of the parotid gland of other animals. (An account of the structure of the glands can be found in 'Spolia Zeylanica' 1913.) The duct usually begins as a receptacle which runs the whole length of the gland. This receptacle is of importance, as it enables the reptile to store the venom. Into this receptacle the smaller ducts of the gland open, and from it the main duct runs forward just above the line of the lip, to a point below the eye. It is now bent backwards, and ends on a small papilla on the anterior wall of the sheath of mucous membrane, which embraces the base of the fang.

Weir Mitchell describes a sphincter muscle of reddish appearance, and composed of non-striated muscle, on the course of the duct of *Crotalus*, but no such sphincter has been described in the other snakes.

The poison from the duct either runs along a groove on the anterior surface of a long tooth called the fang, or else along a canal formed by the sides of the groove meeting and coalescing by the bending of the developing dentine. It should be clearly understood that the venom duct does not directly communicate with the groove or canal in the tooth, but ends close to it, the venom being conducted into the groove by a fold of mucous membrane. The vipers have the longest fangs, measuring nearly 1 inch.

The poison-fang projects downwards and backwards in the closed mouth, being firmly attached to the alveolar process, and it is entirely due to the free mobility of the cranial bones one on the other that the fang can be placed in such a position as to be able to enter the skin of the victim.

The act of striking, as described by Weir Mitchell in *Crotalus*, is as follows: In preparing to strike, the snake first of all throws itself into its well-known characteristic attitude, with the lower part of the body coiled, the tail slightly projecting, and the head raised a few inches

The tongue now darts backwards and forwards, and the air of expiration, in passing through the narrow glottis, produces the characteristic hissing. The muscles on the convexity of the coils now contract and straighten the snake, so that the head is thrust suddenly upwards, forwards, or downwards, as required. The maximum thrust is half of the body-length, the usual one-third; but the reptile judges this for itself, and sometimes makes mistakes. The jaws are widely separated, and the head is bent back on the cervical vertebræ, and a muscle called the spheno-pterygoid, which, passing from the basal orbito-sphenoid region backwards, to be inserted into the inner dorsal surface of the pterygoid, contracts, and draws forward the pterygoid, thus pushing upwards the ecto-pterygoid (transversum), and causing the superior maxillary bone to rotate forward on its lachrymal articulation, and thus to erect the fang. This motion, when it reaches its limit, is checked by ligaments, and now the lachrymal yields a little to the force applied to the maxilla, with the result that the whole muzzle of the snake is elevated, and produces the curious appearance which it has when preparing to strike. The fang now enters the flesh of the victim, and the head of the snake is drawn violently backwards, too much action being prevented by the muscles of the spine. In the meanwhile the spheno-pterygoid, acting from the pterygoid, and together with the external pterygoid, rotates the maxilla and pulls the fang backwards, and so drives it deeply into the flesh.

The lower jaw now closes on the bitten part, and this act squeezes the fluids from all parts of the glands forward into the duct, and not merely deepens the wound, but injects the venom forcibly into it.

The snake then has to disentangle itself, and in so doing may lose its fang. But this is of no moment, for fangs are shed naturally, and there are a number of tooth-germs in different stages of development ready to take the place of the lost tooth.

Sometimes the fangs have not been properly erected, and therefore only their convex borders touch the skin of the victim, in which case the venom will flow on to the skin, but the fangs will not penetrate.

The Venom.

Collection.—The venom can be collected by making the snake strike a watchglass covered with a thin, tightly stretched piece of indiarubber sheeting, or by chloroforming the snake and squeezing the poison out of the glands into a vessel.

In order to preserve this venom, it must be quickly dried over calcium chloride or sulphuric acid in a desiccator, when it will keep for years—*e.g.*, Weir Mitchell kept his *Crotalus* venom for twenty-three years, and then found it active.

Physical Characters.—The quantity of the venom obtained depends upon many factors, such as the general condition and size of the snake, whether it has previously ejected venom, and whether it has been long in captivity—a condition in which the secretion diminishes.

An adult cobra in good condition is said by Martin to give from 0·6 c.c. to 1·1 c.c., and this should yield from 200 to 370 milligrammes of solids. Calmette gives 124 milligrammes of liquid venom, yielding 35 milligrammes of dry venom for *Naja haje* Linnæus.

The water-snake, *Enhydrina valakadien* Boie, gives only 9·4 to 2·3 milligrammes of dry venom, according to Rogers.

A *Vipera russellii* Shaw gives from 0·6 c.c. to 1·0 c.c. of liquid, which yields 150 to 250 milligrammes of solids.

According to C. J. Martin, *Notechis scutatus* Ptrs. gives 205 milligrammes of liquid, containing 73 milligrammes of solids, *Notechis pseudechis* 160 milligrammes of liquid and 91 milligrammes of solids.

According to Calmette, *Lachesis lanceolatus* Lacép. gives 320 milligrammes of liquid venom, containing 127 milligrammes of solids. *Cerastes cornutus* Forsk. from Egypt gave 123 milligrammes of liquid and 27 milligrammes of solids, and *Crotalus confluentus* Say gave 370 milligrammes of liquid and 105 milligrammes of solids; while *Crotalus durissus* L., according to Flexner and Noguchi, yields from 309 to 170 milligrammes of dry venom; and *Ancistrodon piscivorus* Lacép. from 180 to 125 milligrammes.

The different venoms vary in physical characters, as may be judged by a few descriptions.

Cobra-venom, when fresh, is a transparent, almost colourless fluid, with a syrupy consistence and a disagreeable bitter taste. When dried, it becomes yellowish-brown, and may be kept for months. It can decompose and become of a dark brown colour, possessing a disagreeable odour.

Crotalus-venom, according to Mitchell, may vary from a pale emerald-green to an orange or straw colour, and when dried resembles dried albumin. It has no taste or smell.

The poison varies, being clear and limpid or pale straw or yellow in colour, which is said to vary with the degree of pigmentation of the snake and the concentration of the venom. The specific gravity varies from 1030 to 1044 (Weir Mitchell) for *Crotalus*, 1110 for *Cobra*, and 1077 for *Vipera russellii*. Microscopically, there may be only a few epithelial cells and salivary corpuscles and bacteria, all due to contamination with fluids from the mouth.

Chemical Analysis.—The reaction of pure venom is acid.

The ultimate analysis was made by Armstrong for Sir Joseph Fayrer, and is as follows:—

Crude Dried Poison.

Carbon	43·5
Nitrogen	13·43

Alcoholic Extract.

Carbon	45·76
Nitrogen	14·30
Hydrogen	6·60
Sulphur	2·50
Ash	Traces.

These figures merely indicate the presence of proteid in some form, and, as a matter of fact, Armstrong found reactions indicating the presence of albumin; but it must be remembered that Prince Charles Lucien Bonaparte had already shown that a proteid existed in the venom of the viper, and that the toxicity was carried down with this when precipitated, and, further, that Weir Mitchell had corroborated his statements while examining Crotalus-venom.

Weir Mitchell and Reichert went further, and discovered toxalbumins of the nature of globulins (which must be considered to include the more modern proteoses) in venom. They considered these proteids, which they found to be poisonous, to be the true active principles of the venom. In this they have received support from Phisalix and Bertrand, who separated from viper-venom two toxalbumins—echidin, which acts locally; and echitoxin, which acts generally—and also from C. J. Martin and Smith, who showed that the proteoses consisted of proto- and heteroproteose, with perhaps a little deuteroproteose, and that true peptones were absent.

The reader will, therefore, not be surprised to hear that venom gives proteid reactions—*e.g.*, Millon's, the xanthoproteic and the biuret—and that precipitates appear on the addition of picric acid, copper sulphate, and alcohol, and on saturation with sodium chloride, magnesium chloride, or ammonium chloride, and, lastly, that it coagulates on heating.

With regard to heat, it is found that viperine venoms more readily lose their toxicity than colubrine—*e.g.*, 80 to 85° C. will destroy most of the former venoms, while it takes 120° C. to do the same to those of the latter with certainty.

If venom is only heated to the temperature of first coagulation, and then filtered, it will be found that the filtrate still gives a precipitate with alcohol, and is still active, though its virulence is diminished, and that this action is mostly on the nervous system.

The analysis of venom, however, does not stop with toxalbumins, for, as Ewing pointed out long ago, they contain true toxins allied to those produced by bacteria, and recently Faust has separated from the toxalbumins a very poisonous non-nitrogenous substance called *ophiotoxin*.

The knowledge of these toxins is principally due to the work of Flexner and Noguchi on the venoms of *Crotalus durissus*, *Ancistrodon piscivorus*, *A. contortrix*, and *Naja tripudians*.

The work of these investigators, coupled with that of C. J. Martin, Calmette, Lamb, Weir Mitchell, Reichert, Stewart, Rogers, and others, have shown that snake-venoms are very complex liquids containing some, but not in any one venom all, of the following active principles:—

1. *Neurotoxins.*
   (1) Acting principally on the respiratory centre.
   (2) Acting principally on the vasomotor centre.
   (3) Acting upon nerve end-plates in striated muscle, particularly on those of the phrenics.
2. *Agglutinins.*
3 *Cytolysins.*
   (*a*) Hæmolysins.
   (*b*) Leucolysins.
   (*c*) Hæmorrhagins.
   (*d*) Other cytolysins.
4. *Antihæmolysins.*
5 *Antibactericidal substances.*
6. *A fibrin ferment.*
7. *An antifibrin ferment.*
8. *A proteolytic ferment.*
   A cardiac and vascular tonic.

Of these principles, the most important are the neurotoxins, the cytolysins, and the fibrin ferment.

The analysis of the venom, according to Martin, may be effected by:

(1) Dialyzing and filtering the venom through a gelatin filter supported in the pores of a Pasteur Chamberland filter. *Fibrin ferments and hæmorrhagins do not dialyse.*

(2) Heating from 70° to 100° C., when some *neurotoxins* and some *hæmolysins* will not be affected.

(3) Hæmolysins can be separated from neurotoxins by digestion with red blood cells mixed with serum which has previously been heated to 56° C.

Neurotoxins and other cytolysins can be separated by the method of Flexner and Noguchi, which will be described later. It must be clearly understood that the venom of any one snake does not contain all these principles.

1. NEUROTOXINS. The neurotoxins are the most important active principles of the venom of many snakes, especially the colubrine snakes. They have been studied in *Ancistrodon contortrix* by Flexner and Noguchi, who tested the anchoring power of the various tissues of the body for the principles in venom in the following manner: They took a definite weight of tissue washed in tepid, sterile, normal saline solution, and after triturating it in a sterile mortar, mixed it in test-tubes with a given number of minimal lethal doses (M.L.D.) of the venom. The mixture, after being placed in a thermostat for one hour, was centrifugalized, and the supernatant fluid injected into guinea-pigs. They first took 2 grammes of the organs, and mixed them with three times M.L.D., calculating that after centrifugalizing there should be left at least two M.L.D.

The results were as follows:—

Control guinea-pig died in 45 minutes.
Brain-injection guinea-pig died in 19 hours.
Blood-injection guinea-pig died in 3 hours 50 minutes.
Adrenals-injection guinea-pig died in 2 hours 35 minutes.
Spleen-injection guinea-pig died in 2 hours 10 minutes.
Liver-injection guinea-pig died in 1 hour 30 minutes.
Kidney-injection guinea-pig died in 1 hour 55 minutes.
Muscles-injection guinea-pig died in 1 hour 30 minutes.

Next they tried two M.L.D., with the following results:—

Brain-injection guinea-pig survived.
Blood-injection guinea-pig died in 28 hours.
Liver-injection guinea-pig died in 19 hours.

From these experiments they conclude that snake-venom contains a neurotoxic principle, which is the chief poison, and which unites in multiple minimal doses with the nerve cells, but that, even if this chief toxic principle be removed, there is still left sufficient hæmolysin to cause death.

This neurotoxic substance has been shown by Rogers in the cobra and the Hydrophidæ to attack the respiratory centre in the medulla, the respirations becoming both fewer in number and less in amplitude minute by minute, until they cease if sufficiently large doses are administered, but when smaller doses are given there is at first a temporary stimulation.

Further, he shows that the neurotoxic substance can paralyze the end-plates of the phrenic nerves in the diaphragm shortly after the failure of the respiratory centre in the medulla.

The blood-pressure does not appear to be affected by the poison, and, in fact, the circulation can be kept going for a long time after cessation of breathing if artificial respiration is resorted to—a fact first shown by Brunton and Fayrer.

On the other hand, with regard to viperine snakes—*e.g.*, *Vipera russellii*, *Bitis arietans*, *Crotalus horridus*, and *Lachesis anamallensis*—Rogers concluded that the neurotoxin acted upon the vasomotor centre in the medulla—a point which was noted by Weir Mitchell and Reichert as a cause of the variation of the blood-pressure in Crotalus poisoning.

There are thus several neurotoxic elements in snake-venom, of which two great groups can at present be provisionally described:

(1) Colubrine neurotoxic element, acting upon the—(1) Respiratory centre in the medulla; (2) the end-plates of the phrenic nerve.

(2) Viperine neurotoxic element, acting upon the vasomotor centre in the medulla.

Kilvington has studied the effects of the venom of *Hoplocephalus curtus* Günther (*Brachyaspis curta* Schleg.) on nerve cells, and found that the nerve cells of the central part of the cervical enlargement showed a breaking-up of the Nissl granules into a fine dust-like deposit. The nucleus may become indistinct, but it remains in the centre of the cell. The cells are unequally attacked. Those around the central canal are most severely injured, while the motor cells are little affected. In sudden death no change is noted. He says that the character of the changes are of the same order as those described by Marinesco as toxic degeneration, and are very like those following the fatal dose of abrin. Inflammatory and vascular changes are absent.

As to the cause of this cytolysis, it would appear from the researches of Flexner and Noguchi that it is probably due to the union of an endocomplement (capable of being neutralized by calcium chloride, and therefore not lecithin) in the nerve cell with an amboceptor in the venom. This neurotoxin, according to Ehrlich's denomination, is neurotropic—*i.e.*, unites only with nerve cells—and monotropic—*i.e.*, has affinities for one tissue only.

These facts have been demonstrated by Flexner and Noguchi in cobra-venom by first treating it with erythrocytes to remove the hæmolysin, and then heating it to destroy the hæmorrhagin, thus leaving only the neurotoxic principle to act on the animal.

They found that after cerebral injection the appearance of the nervous symptoms was almost immediate, while with other methods of injection the development was more gradual.

The first effect of the neurotoxin was irritation (convulsions), and the final paralysis. By cobra-venom, death was caused by respiratory paralysis. Intracerebral injection of a viperine venom like that of *Crotalus*, however, caused but slight symptoms.

They further found that the venoms of *Ancistrodon piscivorus* Lacép. and *A. contortrix* L. occupied an intermediate position between the colubrine and viperine venoms, containing both neurotoxins and hæmolysins in considerable quantities. From these experiments it was possible to classify venoms into the three classes given above.

2. AGGLUTININS.—Agglutination of the red cells was first described by Weir Mitchell and Reichert, and that of the leucocytes by Halford and Ralf.

The reaction can be studied by adding a 0·01 per cent. to 10 per cent. solution of dried venom in normal saline to washed corpuscles suspended in normal saline.

The time required for agglutination depends upon the strength of the solution of venom, and the effect upon the corpuscles depends upon whether they come together quickly or slowly. In the former case they are not damaged, while in the latter their shape is considerably altered. Agglutinins are destroyed by heating the venom to 75°-80° C.

The agglutinins for the red cells appear to be the same substances as those for the white, and in both cases they appear to act prior to the cytolysis of the cells.

3. THE CYTOLYSINS.—(*a*) *Hæmolysins.*—Fontana many years ago noted that the blood of animals bitten by vipers was fluid, and Weir Mitchell and Reichert described the hæmoglobin dissolving out of

the agglutinated red corpuscles, which finally became invisible when treated with Crotalus-venom. Feoktistow showed that a 2 per cent. solution of the venom of *Vipera berus* destroyed red corpuscles in eighteen to twenty-four hours. Martin has demonstrated also that the venom of *Pseudechis* in 0·1 per cent. solution destroyed the red corpuscle.

Flexner and Noguchi showed that these hæmolysins must be looked upon as amboceptors, which require a complement, and this they obtain in the bactericidal principles found in the serum of the victim. Hence, when they join with the erythrocytes and the complement, they not merely produce hæmolysis, but they take away the bactericidal powers from the blood. If, as was found to be the case in *Necturus*, they are incapable of uniting with the complements, they are incapable of damaging the bactericidal properties of the serum; for it was found that hæmolysis was but slightly produced in the blood of *Necturus*, and then only after long periods, and at the same time the serum of *Necturus* did not lose its bactericidal effects to *Bacillus coli communis* and *B. typhosus*.

The hæmolysins have been further studied by Kyes, who showed that in some animals the venom alone could hæmolyze the washed red cells, whereas in others it could not do so until some fresh serum was added. In the first class came man, dog, rabbit, guinea-pig, and horse, and with reference to these he came to the conclusion that the complement was contained in the red blood cell itself—*i.e.*, was an endocomplement. In a further research with Sachs, he shows that this endocomplement is attached to the stroma of the red cells. Further, they conclude that it is the lecithin of the stroma which acts as the complement, and support this by experiments showing that lecithin prepared from the yolk of an egg can act as a complement for the venom, and dissolve cells which are not affected by the venom alone. They look upon the fatty acid radical of the lecithin as being probably the active agent.

In the second class—viz., those animals whose erythrocytes are not affected by venom alone without the presence of serum—come the ox, sheep, and the goat; but Kyes found it very easy to produce solution by the addition of foreign sera—*e.g.*, ox blood by venom and guinea-pig serum; sheep blood by venom and guinea-pig serum—which clearly showed that the venom was an amboceptor, and agreed with the results of Flexner and Noguchi.

Further, he showed that by heating the serum to 56° C. for half an hour this action was destroyed, but if heated to 65° C. for half an hour hæmolysis took place. In other words, serum contained two possible complements: (1) free in the serum, and destroyed by heat; (2) only in heated serum. Kyes and Sachs consider (1) to be complements in the restricted sense of the term, and that there are differences in their workings from that of the lecithin complement. More recently, however, they have doubted this, and begun to believe that the serum merely frees the lecithin, which acts as the true complement.

In (2) the lecithin, being free, is able to combine with the amboceptor and cause the hæmolysis. They further show that if a blood solution is heated to 62° C., it is inactivated, owing to the union at this temperature of the lecithin directly to the hæmoglobin.

They therefore came to the conclusion that the reason why there was a difference in the action of the venom on red cells was that in the first class—*e.g.*, man, etc.—the lecithin was so loosely bound to the cell that it was available as a complement for the venom amboceptor, whereas in the other cases it was more closely bound, and therefore was not available.

Kyes then went a step further, and mixed 40 c.c. of a 1 per cent. solution of cobra-venom in a 0·75 per cent. salt solution, with 20 c.c. of 20 per cent. solution of lecithin in chloroform, and then centrifugalized the mixture. The result was the separation of chloroform and water into two layers; from the former the cobra-venom lecithin could be precipitated by the addition of pure ether. This body possessed hæmolytic but no neurotoxic properties, which entirely remained in the water. Thus Kyes clearly supports the fact first pointed out by the late Dr. Myers that the neurotoxic and hæmolytic actions are quite separate.

This cobra-venom lecithin differs in many of its properties from cobra-venom and from lecithin—*e.g.*, it is soluble in water, which lecithin is not; it is soluble in alcohol, chloroform, and toluol, which the cobra-venom amboceptor is not.

Kyes found that the lecithin was active with the blood cells of all the species he examined, and that the absolute quantity necessary for hæmolysis was the same for the blood cells of different species. Thus lecithin corresponding to 0·003 milligramme of the dry cobra-venom was capable of hæmolyzing 1 c.c. of a 5 per cent. suspension of the erythrocytes of guinea-pig, rabbit, man, or ox.

The lecithide acts very quickly on the red cells (twenty-four times more quickly than the venom), which is due to the fact that no time is spent in developing the real toxic agent—*i.e.*, the lecithide.

The lecithide is not destroyed by heating to 100° C. for six hours, and is little affected by Calmette's serum.

Kyes went further, and studied the lecithides of—(1) *Lachesis anamallensis* Günther; (2) *L. lanceolatus* Lacép.; (3) *L. flavoviridis* Hallow; (4) *Crotalus durissus* L.; (5) *Vipera russellii* Shaw (6) *Naja bungarus* Schleg.; (7) *Bungarus candidus* L.; (8) *B. fasciatus* Schn.

All these poisons, on the addition of sufficient lecithin, destroy blood cells, and, except in the first and the third, the absolute quantity of the poison is the same as that mentioned just above.

That of *Lachesis anamallensis* Günther is, however, twenty-five times weaker, and *L. lanceolatus* Lacép. ten times weaker, this being due to the fact that the former forms only one-twenty-fifth and the latter one-tenth the usual quantity of lecithide.

Hence Kyes concludes that the hæmolytic element of all snakes is an amboceptor possessed of a haptophore group for the erythrocyte, and a toxophore group for lecithin, which contains the active element for the hæmolysis. The haptophore group, however, probably differs in different poisons, for Lamb has shown that, while cobra-venom will unite with Calmette's antitoxin, poison of *Vipera russellii* will not. *Bungarus* and *Naja bungarus* act like the cobra, and *Lachesis* and *Crotalus* do not.

Noguchi investigated lecithin, and found it to be by no means an inert substance, and, further, that certain oleic compounds and oleic acid itself would act as venom activators.

He found that the addition of oleic acid or its soluble soaps to a non-activating serum in the ratio which corresponds to the percentages of fatty acids and soaps contained in some of the easily activating sera makes it highly active to venom. In the normal serum of a dog, however, he found that there was a lecithin compound acting like free lecithin. He further found that these two classes of activators could be differentiated from one another by calcium chloride, which annulled the first group, but was powerless against the lecithide. Non activating sera do not contain this lecithin compound, and other lecithides—*e.g.*, lecith albumin—are powerless.

When serum is heated, the non-coagulated portions contain a lecithin activator, as described by Kyes, which is identical with Chabrié's albumon; but this does not exist preformed in unheated sera, and is due to the high temperature altering other proteid lecithides into albumon.

He further found ovovitellin to be one of the best lecithin proteid activators. He finally came to the conclusion that the reason why some red corpuscles (man, etc.) are acted upon by venom, while others (ox, etc.) are not, depends solely upon the amount of fatty acids, and perhaps also of soaps and fats, contained in the corpuscles, to the stroma of which they are attached. They exist plentifully in corpuscles easily affected, and in small amount in those not easily affected.

The position at the present moment is, therefore, that snake-venom produces hæmolysis by its amboceptors uniting with complements contained in the sera of the majority of mammals and birds investigated, and that these complements are fatty acids and soaps (belonging principally to the oleic series).

Further, there are endocomplements in the erythrocytes of certain species, and these are of the same nature as those in normal sera, and are attached to the stroma of the corpuscle.

Finally, the reason why heated sera become active at high temperatures after losing their activity at lower temperatures is because of the conversion of the proteid lecithides into another form of lecithide called albumon, which is an activator.

For the controversy between von Dungern, Coca, supported by Mainwaring on the one side and Kyes on the other, reference must be made to the original papers given in our list at the end of this chapter.

(*b*) *The Leucolysins.*—Weir Mitchell and Reichert had noticed in their researches that the mobility of leucocytes absolutely ceased in crotalus poisoning. Martin studied this carefully with Pseudechis venom, and says that for the first fifteen minutes he could see no change in the white cells, but they exhibited no amœboid movements. At the end of this time the nuclei in some of them were very distinct, as if fixed by acetic acid. They then became intensely granular, and soon began to swell, and their outlines to grow less distinct, until they disappeared, leaving only a small heap of granules.

Flexner and Noguchi studied this phenomenon, and found that leucocytes with large coarse granules were most quickly affected; next came the fine granular varieties; and last of all the lymphocytes. They found cobra poison much more vigorous than that of crotalus. As to the leucolysins, they proved that they were separate from the hæmolysins by treating washed red corpuscles with copperhead venom until the supernatant fluid, after centrifugalization, ceased to have any effect on red cells. This fluid was then brought into contact with leucocytes, when lysis without agglutination took place. If, however, washed leucocytes were treated first, the supernatant fluid was found to be actively hæmolytic. They therefore concluded that the hæmolysins were distinct from the leucolysins, but that the agglutinins were probably the same.

We are not aware of further researches as to the nature of the leucolysins, though obviously such researches are required.

(*c*) *Hæmorrhagin.*—Weir Mitchell and Reichert, by observing a mesentery moistened with crotalus-venom, came to the conclusion that the blood escaped from the vessel owing to damage to the wall.

Flexner and Noguchi found that by heating crotalus venom to 75° C. for thirty minutes, this hæmorrhagic power was lost, and along with it most of the toxicity, as ten or twenty M.L.D. were required to cause death with symptoms resembling cobra-venom. They conclude that this death must be due to the neurotoxic or hæmatoxic properties (hæmolysins and agglutinins) in the venom, and that, as the latter can be eliminated without any apparent loss of toxicity, it must be due to the neurotoxins.

The toxic principle lost by heating to 75° C., Flexner and Noguchi called hæmorrhagin. They studied its action in the mesentery by injecting the venom into the peritoneal cavity, or placing a minute particle of the dried poison on the exposed mesentery, and then removing specimens, which they fixed in Zenker's fluid, cut into sections, and stained with hæmatoxylin and eosin. They found that the extravasation of blood took place not by diapedesis, but through actual rents in the walls. These rents are not simple ruptures, but are apparently due to a cytolytic action upon the endothelial cells of the capillaries and the walls of the small veins.

(*d*) *Other Cytolysins*.—Flexner and Noguchi have found that the amboceptors in venom can act upon a number of the cells of the body—*e.g.*, liver, kidney, testicle, and ovary—causing lysis, the complement being probably either endocellular or in the lymph-stream. The nature of the complement is, however, quite unknown at present, but is probably different from the complement acting on the red cells, as its activity is destroyed by heating to 60° C. for some time. The histological effects of these toxins can be noted particularly in the microscopical appearances in the liver and kidney. The liver shows necrosis and fatty degeneration of its cells, and, as a reactionary process, leucocytic infiltration around the bile-passages. In the kidney, the glomeruli show intense congestion of their capillaries, often associated with ruptures of their walls and hæmorrhage into Bowman's capsule. The cells of the tubules are necrotic and detached, filling the lumen. The whole organ is congested, and there may be interstitial hæmorrhages. The spleen is but slightly affected.

4. ANTIHÆMOLYSINS.—Weir Mitchell and Stewart have shown that if crotalus-venom is added to red corpuscles in a certain degree of concentration, no hæmolysis takes place. This fact has been confirmed by Myers and Stephens for the cobra, and Lamb for *Vipera russellii*.

Noguchi believes that the action is due to venom having the power in certain cases of precipitating the outer layer of the hæmoglobin, while in other cases this does not take place.

5. ANTIBACTERICIDAL SUBSTANCES.—Weir Mitchell drew attention to the fact that bodies of animals dead from crotalus poisoning rapidly decomposed, while Ewing found that the normal germicidal power of the serum was destroyed—a fact confirmed by Martin.

Flexner and Noguchi also investigated this action, and came to the conclusion that:—

(1) All venoms, when used in suitable quantities, destroy the bactericidal properties of many normal sera.

(2) The manner of this destruction consists in the fixation of the serum complements by the venoms.

(3) Venoms have no action upon the intermediary bodies of the serum.

6. FIBRIN FERMENT.—A fibrin ferment has been shown by Martin to be present in the venoms of the viperidæ and also of some of the colubridæ. In the former it is the active agent which causes the vascular clotting in small animals, with convulsions and sudden death. This coagulative substance has been shown by Barratt to be a thrombin.

7. ANTIFIBRIN FERMENT.—An antifibrin ferment—that is to say, a substance which in minute quantities is able to prevent the coagulation of the blood—is found in cobra and allied venoms.

8. PROTEOLYTIC FERMENT.—Venom contains a body of some description, probably a ferment, which is capable of transforming proteid.

Thus, Mitchell and Reichert long ago showed that muscle-fibres at the site of the bite were quickly softened by crotalus-venom, and Flexner and Noguchi have shown that gelatin is liquefied by both crotalus- and cobra-venoms, but that coagulated proteids are not acted upon. Microscopically the muscular fibres at the site of the bite are seen to have undergone necrosis and degeneration, and later a polymorphonuclear leucocytic infiltration may be noted.

9. CARDIAC AND VASCULAR TONIC.—Sir Lauder Brunton and Sir Joseph Fayrer showed that the poisons of the cobra had a stimulant effect on the heart, and that the circulation could be kept going for a long time after complete failure of breatning if artificial respiration is kept up—a fact of considerable importance if any antidotal treatment is available.

It is not clear whether this is due to direct action on the muscles of the heart, but it appears from Rogers' experiments that the effect on the bloodvessels is due to local action on the arterioles. This effect is produced by the cobra and *Vipera russellii* venom.

Entry of the Venom into the Body.

The poison, the characters of which have been described, is introduced into the body of man or that of an animal usually by the snake biting the skin and injecting the poison either subcutaneously or into a vessel. In the former case it will soon reach the bloodstream, and be distributed to the different parts of the body.

The effect of entry into a bloodvessel is to produce immediately the signs of the poisoning, whereas in the subcutaneous tissue it may take some time, and even be modified, especially in the viperine type.

The quantity injected by a cobra, according to Acton and Knowles, during the first strike, is 0·172 gramme (*i.e.*, $\frac{10}{16}$ of total venom in gland); during the second 0·1215; after which it steadily diminishes until it is not fatal to man (probably) about the seventh or eighth strike. Echis injects $\frac{10}{11}$ of total venom during first strike.

If the venom falls on the conjunctiva it is readily absorbed, and symptoms of poisoning will ensue, or an acute inflammation be set up.

Taken by the mouth, the venom of the colubridæ is harmless, provided there are no cracks or abrasions, and is destroyed by the saliva and pancreatic juice. Viperine venom, on the other hand, causes gastritis, gastro-intestinal hæmorrhage, and even death, without the appearance of the usual symptoms, a fact known to the natives of Ceylon with regard to the venom of *Vipera russellii*.

Minimum Lethal Dose (M.L.D.).

The minimum lethal dose varies with the species of snake, the condition of the snake, and with the species of the victim.

Tables are given by Calmette, and Martin and Lamb, showing the amount for different snakes and animals. Thus, the quantity of cobra-venom required to kill a kilogramme of a dog is 0·0008 gramme, and of a rabbit 0·0005; and that of *Bungarus candidus* for a rabbit is 0·0008 gramme, and that of *Enhydrina valakadien* for a rabbit is 0·00006 gramme, while the same for a cat is 0·0002. Putting it in another way, 1 gramme of cobra-venom will kill 1,250 kilogrammes in weight of a dog, 2,000 of rabbit, 2,500 of guinea-pig, 1,500 of rat, and 8,333 of mouse, and 20,000 grammes of horse.

Calmette calculates that, taking a man of average size, the minimum lethal dose might be halfway between the dog and the horse—*i.e.*, would be 0·015 gramme of cobra-venom—and 1 gramme will kill 10,000 kilogrammes of man, or 165 persons of the weight of 60 kilogrammes; but, of course, this is only a very approximate guess. Lamb calculates the M.L.D. for man to be 0·015 gramme of cobra-venom, and Fraser puts the same at 0·031 gramme, while other authors give cobra M.L.D. for man 0·010 gramme and echis M.L.D. the same figure.

Lamb gives a number of minimum lethal doses for snakes calculated per kilogramme of rabbit and injected intravenously, which are:—

Bungarus candidus	0·00004 gramme.
Enhydrina valakadien .	0·00005 ,,
Vipera russellii	0·0001 ,,
Naja tripudians and N. bungarus	0·00035 ,,
Bungarus fasciatus	0·0007 ,,

Effects of the Venom.

The effects of the venom have been carefully studied on warm and cold blooded animals by many observers for a long series of years, but there is a distinct difference in the action of different kinds of venom, and therefore it is as well to discuss the effect of each separately.

In doing this it will be noted that it is difficult to obtain undoubted cases of bites by definitely known snakes in man, and even when these are obtained the urgent necessity for treatment causes the symptoms to be little noted. Therefore it is necessary to detail first the experiments on animals, and then the symptoms found in man.

Colubrine Venom—*Naja tripudians* Merrem.—The experiments of numerous observers show that the effects of this venom on animals are:—

1. Paralysis of voluntary movement.
2. Salivation.
3. Marked effect on the respiration, which ceases before the heart.

In smaller quantities the paralysis becomes more marked, and in cases of longer duration several features are added:—

1. Local inflammation where the bite was inflicted.
2. Lachrymation.

3. Mucous discharges from the nose, respiratory organs, and stomach.

4. Very occasionally the mucous discharges are stained with blood.

Beyond obvious pain, the local effects are engorgement of the vessels with blood, and effusion into the tissues. If the animal recovers, there may be suppuration and sloughing of the affected part. The effects on the nervous system seem to be due to the action of the poison on the brain and spinal cord, and *pari passu* on the motor nerve endings. The most evident paralysis is that of the tongue, larynx, and pharynx, as evinced by the inability to retain the saliva within the mouth, to move the tongue, or to swallow. This is due to the action of the poison on the medulla.

There is also, as indicated above, clear evidence of action upon the respiratory centre, which has been carefully studied by Wall and others, who show that in large doses there is a progressive slowing, and in smaller doses first acceleration and then slowing of the respirations. There appears to be but little effect upon the heart and circulation or temperature.

The effect on the blood in causing hæmolysis was first demonstrated by Cunningham, who considered it the main feature. Not merely are the corpuscles dissolved, but the coagulability is reduced, and hence the blood-staining of the tissues and the urine in experiments on animals, provided that artificial respiration is kept up.

The effects of the venom on man are local pain in the neighbourhood of the bite, which appears as two small punctures about ¾ inch apart, usually exuding a blood-stained fluid. The pain increases in severity, and spreads up the limb on to the body. In a short time the victim feels intoxicated, and presently loses control of his legs, which become paralyzed, as may other muscles, including those of the jaw. There is often profuse salivation, and inability to speak or swallow. The pulse and respirations increase for a time, and then the breathing becomes slower, and death occurs from failure of the respiration, while the heart continues to beat for a short time after the respirations have ceased.

If recovery takes place, the urgent symptoms abate, some slight fever and local swelling occurs, while a large amount of urine is passed.

When examined post mortem, it will be found that the rigor mortis is well marked, while the blood is fluid in man, but coagulated in animals. If the corpuscles are examined soon after death, no change will be noted, but later they alter, and blood-crystals, indicating hæmolysis, may form. The parotids may be swollen. The brain is normal, but the pia mater is gorged with blood. The muscles are often of a dirty red colour. The lungs in human beings are generally congested, and the bronchi and smaller tubes filled with thin frothy fluid and intensely congested. Particles of food or remedies are to be found in the air-tubes because of the paralysis of the larynx. The right heart is distended with blood. The liver is congested and dark. The kidneys may be normal or intensely congested. The intestines show nothing in particular. The bladder is contracted

Microscopically, fatty degeneration of the liver and kidney, and necrosis of hepatic and renal epithelium, are to be seen, as well as round-celled infiltration along bile-ducts, which is probably due to excretion of poison.

Turning now to the colubrine snakes, which resemble the cobra, there are observations upon *Naja haje*, *N. bungarus*, *Bungarus candidus*, *B. fasciatus*, and the *Hydrophidæ*.

Naja haje Linnæus.—Calmette records that Dr. Deschamps observed a case of this bite in Senegal in which the snake bit the patient in the forehead. Almost immediately great weakness, accompanied by nausea and pains in the head and neck, set in. Locally two raised areas were seen, around which the tissue was œdematous. Cold sweats occurred. The œdema spread to the face, dyspnœa appeared, and the pulse became small and intermittent, paralysis set in, and the patient became comatose, but recovered on treatment with antivenene.

Naja bungarus Schlegel.—*N. bungarus*, the hamadryad, is by far the biggest of the Indian poisonous snakes. Rogers finds its venom very like that of the cobra, producing paralysis and death from failure of respiration, while the heart continues to beat for a time.

There is no intravascular clotting, and the hæmolytic action is very slight, but the phrenic nerve-plates are paralyzed. If small doses are given, the respirations are increased.

We are not acquainted with the symptoms exhibited by an undoubted case of this bite in a human being.

Bungarus candidus Linnæus.—As to *B. candidus* L., the commonest of all Indian snakes, there is not much to say, except that all researches (Fayrer, Wall, and Rogers) indicate that its venom is almost exactly the same as that of the cobra, but is slightly more virulent.

Cases of this bite are common. In brief, the symptoms are:—a sense of tightness across the chest, with paralysis, particularly of the muscles of the face, deglutition, and phonation. The conjunctivæ are suffused, the pupils dilated, the pulse and respirations quickened; the temperature is normal, and the local signs are not marked.

Coma and convulsions precede death, which is due to failure of respiration. Congestion of the meninges and brain and liquid blood are the principal signs found post mortem.

Bungarus ceylonicus (Günther).—*B. ceylonicus*, the Ceylon krait or carawalla, has been reported by Green to have killed a man in twelve hours. The man was bitten on the left foot at 4 a.m., and felt quite well till 5.30 a.m., when he felt drowsiness, which increased till 10 a.m., when he could hardly swallow and was very sick. Paralysis affected his legs, and he became cold. Artificial respiration was now resorted to, but at 2 p.m. he became very feverish and insensible, and died at 4 p.m.

Bungarus fasciatus Schneider.—The effects of the poison of *B. fasciatus* have been carefully studied by Wall, Lamb, and Rogers.

In acute cases death takes place quickly from failure of respiration; the blood is coagulated, and there is paralysis, and sometimes convulsions.

Chronic cases, on the other hand, last for days, during which there is loss of weight and emaciation, and perhaps some paralysis.

Microscopical examination of the cortex of the brain, medulla, and spinal cord shows diffuse chromatolysis, affecting a very considerable portion of the ganglion cells, being most marked in the cortex, next in the cord, least in the medulla. The cells show a rather deeply stained plasma, in which are scattered dust-like granules, the remnants of the Nissl bodies; many cells show vacuolation of the plasma, and some are reduced to mere outlines (ghost cells).

Rogers' experiments tend to show that even in injecting large doses the blood may not clot, and that the animal may be killed, as in cobra-venom, by direct action of the poison on the respiratory centre, and also on the nerve-endings of the phrenics, so that the venom appears to be a mixture of a viperine with a colubrine poison.

The only authentic case of human poisoning by *B. fasciatus* is mentioned by Fayrer, in which there was tingling sensation and later pain at the seat of the punctures, with some swelling, all of which disappeared in less than twenty-four hours.

Australian Snakes.—The symptoms produced by the bite of the Elapinæ in Australia are local swelling and pain, followed in from fifteen minutes to two hours by constitutional symptoms. The patient becomes unable to stand, signs of prostration, accompanied by vomiting, appear. The circulation begins to fail, the heart's action becomes weak, the extremities cold, and the skin blanched, while the respiration, after a preliminary excitation, becomes slowed. Coma now intervenes, the sensations being diminished and the pupils dilated, and death results from failure of the respiration, preceded sometimes by convulsions. The heart continues to beat after the circulation has ceased.

Elaps fulvius, the harlequin snake, which is found in the eastern parts of the Southern United States, causes great local pain, followed in one hour by drowsiness, unconsciousness, and collapse, lasting until death, or for a day or so if the patient recovers. Death usually ensues in about twenty-four hours after a bite, and in persons tending to recovery the danger of death is not escaped until three to four days have passed away, as the symptoms tend to recur periodically.

Spitting Snakes.—The known spitting snakes—*i.e.*, snakes which can project their venom to a distance—are *Sepedon hæmochates*, *Naja flava*, and *N. nigricollis*, *N. tripudians*, *Echis carinata*, with perhaps the addition of *Naja melanoleuca* and *Vipera russellii*; and it is possible that further observations will show that all the Colubridæ and Viperidæ have this power to a greater or lesser extent. Of course the action is not spitting in the correct sense of the word, but merely projection of venom, which causes conjunctivitis if it enters the eyes, and a saltish taste if it enters the mouth.

The Hydrophidæ.—Rogers experimented with *Enhydrina valakadien* Boie, *Distera cyanocincta* Daud., and *Hydrophis cantoris* Gthr., and came to the conclusion that their venom only differed from that of the cobra in the following points:—

1. They were more toxic.
2. They were much less hæmolytic, and hence caused no blood-stained effusion at the site of the injection.
3. They did not affect the coagulability of the blood; therefore the poison is almost purely neurotoxic.

There is at first an excitation of the nervous system, leading to a feeling of activity and vivacity, which, however, soon passes off. The earliest signs of distress begin with difficulty of articulation and feeling of stiffness in the body and of suffocation. The stiffness in the muscles increases, and occasional spasms occur, while signs of gastric irritation, with vomiting, appear. Convulsions and death may ensue after a day or so. The local signs may be slight.

Viperine Venom.—*Vipera russellii* Shaw, the *tic polonga* of Ceylon, is a good example of this type of venom. Wall's experiments show that a dog bitten by one of these vipers will become convulsed, and die within five minutes. The cause of this sudden death has been shown by Rogers to be intravascular clotting, which is best marked in the portal vein, and then only in small animals. Post mortem, there are hæmorrhages into the area of the bite, and into kidney and intestine.

In addition to these acute cases, there are also chronic cases, in which the local symptoms are more or less extensive subcutaneous hæmorrhages, around which there is much œdema. This hæmorrhage may be absorbed, or the area may slough, or an abscess, or even a spreading gangrene, may ensue.

The general symptoms are rapid emaciation, profound anæmia and lethargy, and in some cases hæmaturia and a discharge of blood from the bowel.

Rogers has carefully investigated these symptoms, and has pointed out that there is a remarkable fall of blood-pressure due to vaso-dilatation of the portal system, caused by action of the poison on the central, and not the peripheral vasomotor apparatus, the heart muscle being unaffected. Lamb and Hanna showed that in chronic cases there is deficiency in the blood coagulability.

In man there are the two small punctured wounds caused by the fangs, around which the skin is swollen and livid and painful. The swelling and discoloration spreads, and in the course of twenty-four hours the patient becomes at first excited, with thready pulse and hurried respirations, and later stuporous. The skin is clammy and covered with a cold sweat, while the swelling and discoloration spreads considerably, reaching the trunk. In due course convulsions set in, and death ensues from failure of the circulation. The post-mortem reveals congestion of the meninges and lungs with fluid blood, and nothing else of importance.

Bitis arietans.—The puff-adder poison was found by Rogers to work in much the same manner as that of *Vipera russellii*, but not to be so poisonous.

Echis carinata.—This is a very poisonous snake, and the effects of its bite resemble that of the cobra.

Wall records a case in which there was much local swelling, passage of blood in the urine, fæces, and vomit, elevation of temperature, and death from exhaustion, due to loss of blood, on the ninth day. Martin and Lamb record another case in which there was much swelling of the bitten part, due to exudation of liquid blood. Pain and tenderness were felt along the nerves, together with anæsthesia, extreme restlessness, with cold and clammy extremities, but no hæmorrhages. Loss of consciousness, with delirium, set in only a short time before death, which took place at the twenty-fifth hour.

Fayrer gives a good account of a chronic case, in which there was depression and faintness, coldness of the extremities, with swelling of the affected part, and marked hæmorrhages from eyes, gums, throat, nose, vagina, and under the nails.

The Crotalidæ are typically represented by *Crotalus horridus* of America, which has been carefully studied by Weir Mitchell and Reichert, and by *Lachesis*, which latter has been studied by Rogers in India.

Crotalus horridus.—The local effects are: —œdema, swelling, darkening of the parts with infiltration of incoagulable blood, breaking down of the tissues, putrefaction, and sloughing. There is no clotting of the blood, which, on the other hand, is fluid and incoagulable. There is a marked fall of blood-pressure, and respiration gradually ceases, due to the failure of the circulation, but there is no direct effect on the respiratory centre, and the phrenics are not paralyzed. The heart goes on beating after respiration ceases, but is slightly weakened. Post-mortem examination shows hæmorrhages into the peri- and endo-cardium, and into the peritoneum and pleura, but not in the brain or the medulla, while the whole portal system is much congested.

Rogers placed a loop of small intestine in an oncometer, and found that fall of blood-pressure was associated with a vaso-dilatation of the portal system, in which the blood was not clotted. This vaso-dilatation he considers may possibly be due to the action of the venom on the vasomotor centre in the medulla, and thinks that he is supported in his theory by the appearance of Traube-Hering curves in his blood-pressure tracings. Pearce notes acute glomerular lesions due to the endothelialytic body.

Weir Mitchell and others have carefully collected the symptoms following this bite. In most instances the bite is painful, and the part becomes swollen and discoloured, while both the pain and the swelling increase steadily. The swelling is due to the effusion of blood. Very seldom is there any lymphangitis or enlargement of the lymphatic glands. Vesication, sloughing, and gangrene may result if life is prolonged and the dose considerable. If, on the other hand, the amount of poison injected is inconsiderable, the swelling declines, and the pain disappears very quickly. Constitutional symptoms are said by some people to begin directly after the bite, but this is hardly likely, as man is a relatively large animal. Under exceptional circumstances it is recorded that the symptoms did not begin till about thirty minutes after the bite, but usually the length of time is only a few minutes. The person feels extremely faint, or complains that his lower limbs are not able to support him. There is no primary stimulating effect like that mentioned in other venoms. The patient staggers or falls, cold sweats bathe the surface of the skin, and nausea and vomiting occur. The pulse is rapid and feeble, the expression anxious, and, according to Mitchell, in a few cases the mind may be slightly disturbed, but this may be largely due to fear. If the patient does not die at this stage, the local symptoms mentioned above become very pronounced, and signs of general blood-poisoning show themselves, and often lead to death.

The post-mortem reveals that the brain is normal, but congested and somewhat œdematous; the trachea and bronchi are congested, and full of red frothy mucus; while the lungs are healthy, but somewhat congested. The peritoneum may contain a little fluid, and the mucosa of the stomach and small intestines may be intensely congested and infiltrated with serum. In some cases the blood is coagulated, in some it is fluid. The local swelling is due to serous exudation. The chief features of the post-mortem are vaso-dilatation of the portal system and fluidity of the blood.

Lachesis.—This snake shows the same symptoms as *Crotalus*, but it has some effect upon the respiratory centre, causing quickening of respiration before the slowing begins. The phrenics are not paralyzed. Moreover, it is possible that the first quick fall of blood-pressure observed is due to action of the poison on the heart, but the subsequent steady fall is due to the action on the vasomotor centres, as in *Crotalus*.

Kitajima says that the region of the bite becomes dark purple in colour and swells; that the pain is severe and burning; and that the lymph glands become enlarged and tender. The face is pale, the pulse feeble and rapid. Respiration is normal; a slight fever is not infrequent. Coldness of the extremities, with dyspnœa and cold sweats, come on just before death. Blood has been observed in the urine and fæces.

Excretion of the Poison.

It is believed that the poison leaves the body principally by the kidney, and to a less extent by the mucosa of the stomach, the salivary and mammary glands.

With regard to the kidney, there is some direct proof of the excretion, because the urine of a dog poisoned by *Enhydrina valakadien*, when injected hypodermically into a pigeon, caused death in twenty-two hours.

It is also stated that 1 drachm of the saliva of a dog poisoned by a cobra was capable of causing death in two hours.

With regard to excretion by the mammary glands, an infant is said to have died after sucking the breast of a woman bitten by a poisonous snake.

Immunity.

Having considered the chemical composition and physiological action of the venom, the next point to be discussed is immunity to its action.

Ancient and modern peoples have equally held the belief that a person who has been bitten by a poisonous snake and survived obtains some sort of immunity; generally the belief has been that this immunity is capable of protecting the individual against all kinds of snakes.

Ancient fables credited the Psylli of Africa, the Marsi of Italy, and Gouni of India, with immunity, on the ground that they had snake's blood in their veins.

The pig was long thought to be naturally immune; but this is a mistake, for the relatively slight effect of snake-venom is due to the presence of the thick layer of but slightly vascular fat which surrounds the animal's body. The mongoose (*Herpestes ichneumon*) is believed to be naturally immune to cobra-bite.

Acquired immunity is said to occur among natives, especially snake-charmers, and Europeans who have been bitten several times by snakes. The Eisowy of Western Barbary are said to have acquired such an immunity, and to allow themselves to be bitten by snakes proved afterwards to be poisonous by killing a fowl. The natives of Bushmanland, Namaqualand, and Damaraland are said to drink the venom of snakes as a protection. In Ceylon a cobra is said to have bitten a snake-charmer, and shortly afterwards a bystander. The snake-charmer escaped without symptoms, the bystander died.

The first scientific attempt to produce an artificial immunity was made by Sewall in 1887, when by repeated small injections he raised the resistance of pigeons so high that they were able to resist ten times the minimum lethal dose of the venom of a *Crotalus*. Kanthack also produced a partial immunity to cobra-venom in 1891. Kaufmann, a little later, obtained a similar result with the French viper.

In 1892 Calmette showed that by repeated inoculation of venom heated to 80° C. a certain amount of resistance was produced in animals. In 1894 he made researches on the venom of the cobra, and about the same time Phisalix and Bertrand investigated that of the viper, and showed that animals vaccinated with venom developed a true immunity, and those inoculated against the cobra-venom were able to resist mortal doses of *Vipera, Bungarus, Cerastes, Naja haje,* and *Pseudechis* venoms. Later they showed that the serum of an animal vaccinated by snake-venom contained antitoxins capable of producing an immunity in new animals.

Calmette obtained his serum from horses, but with great difficulty, as many of the animals died in the course of treatment from endocarditis and acute nephritis, while in others abscesses formed.

He found that in a fresh horse 0·025 gramme of cobra-venom was sufficient to kill the animal in twelve to twenty-four hours, but on vaccinating the animals for sixteen months, it was found that a horse could stand without reaction the injection of 2 grammes of cobra-venom—*i.e.*, eighty times the M.L.D.

From such a horse it was found possible to withdraw as much as 20 litres of blood in three bleedings spread over ten days, the serum being considered to be ready for use when 1 c.c. mixed with 0·001 gramme of cobra-venom produced no sign of intoxication when injected subcutaneously into a rabbit, and when, after injecting 2 c.c. of the serum into a rabbit of 2 kilogrammes weight, two hours later 1 milligramme of venom could be injected without results. This serum was said to preserve intact its antitoxic value in all climates The venom used for these injections was principally that of the cobra, with a slight admixture of other venoms.

In 1895-96 Fraser of Edinburgh confirmed Calmette's results, and believed that if an animal was so successfully vaccinated that it could resist the minimum lethal dose of one venom, it would also be able to resist that of other venoms. He believed that venom introduced into the stomach conferred immunity.

In 1897 C. J. Martin showed that Calmette's serum did not preserve animals against the venom of *Notechis scutatus*.

From 1901 onwards Lamb in India studied carefully the effects of snake-venoms, and came to the conclusion that Calmette's serum is active against cobra-venom, but is not useful against that of *Vipera russellii*, *Bungarus fasciatus*, or of *Echis carinatus*.

In 1902 Tidswell showed that serum prepared from the venom of *Notechis scutatus* did not neutralize the venoms of the cobra, *Bungarus fasciatus*, or *Vipera russellii*, and, further, had no effect on the venoms of the brown and black snakes and death-adder of Australia.

In the same year Lamb pointed out that there was a precipitin in venom-immune sera, and this point being further investigated by Hunter, the deduction was made that these precipitins were specific, and due to the coagulable proteids.

The following pure sera have been prepared:—

1. *Lamb's Pure Naja tripudians* Merrem *Serum.*—This serum is strongly antitoxic for cobra-venom, and in large doses for *Enhydrina valakadien* Boie, but has no effect upon *Bungarus candidus* L., *Brachyaspis curta* Schleg., *Echis carinatus* Schn., *Lachesis gramineus* Shaw, *Vipera russellii* Shaw.

It delays death in *Bungarus fasciatus* Schn., *Naja bungarus* Schleg., *Crotalus durissus* L.

2. *Lamb's Pure Vipera russellii* Shaw *Serum.*—This serum

neutralizes the venom of *Vipera russellii* and *Crotalus durissus*, but has no action upon—Colubridæ: *Naja tripudians* Merrem, *N. bungarus* Schleg., *Bungarus candidus* L., *B. fasciatus* Schn., *Enhydrina valakadien* Boie; Viperidæ: *Echis carinatus* Schn., *Lachesis gramineus* Shaw.

3. *Tidswell's Pure Notechis scutatus* Ptrs. *Serum.*—This serum has a strong antitoxic effect upon the venom of *Notechis scutatus*, but has no effect upon that of—Colubridæ: *Naja tripudians* Merrem, *N. bungarus* Schleg., *Bungarus candidus* L., *B. fasciatus* Schn., *Enhydrina valakadien* Boie; Viperidæ: *Vipera russellii* Shaw, *Echis carinatus* Schn., *Lachesis gramineus* Shaw, *Crotalus durissus* L.

4. *Noguchi's Pure Crotalus Serum.*—It has a strong effect upon *Crotalus* venom, and a slight effect upon *Ancistrodon piscivorus* Lacép., and none on the cobra.

5. *Noguchi's Pure Ancistrodon piscivorus* Lacép. *Serum.*—This has a marked effect upon moccasin-venom, and medium effect upon *Crotalus*, and none on cobra-venom.

6. *Brazil's Pure Crotalus horridus* L. *Serum.*—This serum is equally efficient for the venoms of *Crotalus horridus* or *C. durissus*, but is useless for cobra-venom.

The Caracas Commission reports that this serum is more efficacious against the venom of *Crotalus* than that of Calmette, which fails to neutralize the hæmorrhagins.

7. *Kitajima's Pure Lachesis flavoviridis* Hallow *Serum.*—This serum is specific for *Lachesis* venom, against which Calmette's serum is useless.

It is clear that the antisera mentioned above are very nearly specific, for they neutralize principally the venom of the species employed, and sometimes, in larger doses, that of some allied species.

It is obvious that this is of great importance in considering the serum treatment of snake-bite.

8. *Polyvalent Sera.*—Polyvalent sera prepared for more than two venoms are not very efficacious.

Diagnosis.

It might be thought that the diagnosis of snake-bite would be obvious, and that nothing need be written on the subject, but this is not always so, because snake-bite often takes place in the dark, and the nature of the snake is unknown.

The diagnosis may be divided into two heads:—(1) Has a snake bitten the person? (2) Was the snake a poisonous one?

The first thing to do is to tie a proximal ligature on the limb, and then to examine the area of the supposed bite. If there are absolutely no fang-marks and no venom on the skin, then obviously there is no danger; but fang-marks on the skin, or venom on mucous membranes (which, of course, may have cracks), or on skin with scratches, may be dangerous.

If there are no fang-marks, and the snake is forthcoming, examine it to see whether it is poisonous or not, especially to see whether there are fangs, and if non-poisonous, the patient's mind can be relieved at once.

Prognosis.

It appears that only a relatively small percentage of persons bitten by snakes (supposed to be poisonous) die. C. J. Martin and Lamb place it about 30 per cent., but much depends upon the quantity of venom injected and the rapidity with which symptoms develop. The recoveries from full doses of echis-venom in untreated cases is about 40 per cent., and of cobra-venom only 3 to 4 per cent. Personally, we believe that in most cases if treatment has been prompt, and the symptoms appear slowly, the outlook is by no means hopeless.

Treatment.

Snake-poisoning consists in the hypodermic or intravascular injection of a series of poisonous principles which act chiefly upon the nervous system and the blood.

The virulence of the poisoning depends upon the ratio of the quantity of the poison injected to the size of the animal. The same quantity of poison will therefore have a more serious effect upon a child than upon an adult. The less the quantity of poison which gets into the general circulation, the less the symptoms; hence the first indication for treatment is to prevent the passage of the poison, as far as possible, into the circulation.

The second indication for treatment is to neutralize the poison which has got into the system, and the third indication is to treat special symptoms as they appear.

1. **Prevent the Poison getting into the General Circulation.**—In order to prevent the poison getting into the general circulation, three points must be attended to:

(1) Stoppage of the flow of blood and lymph from the affected area.
(2) Free opening of the poisoned area.
(3) The neutralization of the poison locally.

(1) *Stoppage of the Flow of Blood and Lymph from the Affected Area.*—A person is usually bitten in the arm or leg, and in such a case the old treatment advised by Celsus should be carried out by applying a tight ligature round the affected limb on the proximal side of the wound, so as to compress the blood and lymphatic vessels. In order to do this successfully, the ligature must be applied to the arm or the thigh—*i.e.*, where there is one bone—and not the forearm or leg.

Such a ligature cannot be left in position indefinitely, otherwise gangrene will result; and after some attempts at neutralization of the poison have been made, it must be loosened for a couple of seconds and reapplied, and this must be repeated. It must be kept on for at least twenty or thirty minutes.

The advantages of the ligature or tourniquet have been known since ancient times, but C. J. Martin has shown that its principal action with colubrine poison is not merely to delay the absorption of the poison, but also to give time for any already absorbed to be excreted. In the viperine poisons, which coagulate the blood by fibrin ferment, it is most beneficial; for the blood, in coagulating locally, retains the poison, which therefore but slowly passes into the general circulation, and may, as Martin and Lamb suggest, unite with the cells near the bite.

There is therefore no doubt that the correct immediate treatment in a bite due to any kind of poisonous snake on a limb is the application of a proximal tourniquet.

(2) *Free Opening into the Poisoned Area.* -It will be obvious that the two minute punctures caused by the fangs are not sufficiently large openings into the area of the bite for the application of antidotes.

Therefore the next step is to cut, not merely round the apertures of the fangs, but also to extend the incision along the course of the veins and lymphatics, and in some cases to remove the piece of skin marked out. In this way the area of inoculation is freely opened.

(3) *Neutralization of the Poison Locally.*—The next indication is to diminish the toxicity of the poison as much as possible, and to do this the best remedy we at present possess is *permanganate of potash*, though recent laboratory experiments have thrown some doubt upon its efficacy.

This should be used in strong solution, and not as a solid, as the liquid penetrates better into the interstices of the wound, which should be well washed with it. For carrying out this treatment a most useful little case has been devised containing a little lancet for making the wound, and permanganate crystals for making a solution. This little case only costs a few pence, and can be carried without any inconvenience in the waistcoat pocket, and therefore should be carried by everyone in countries where poisonous snakes abound, especially when on business or pleasure in jungles or grassy places. Should there be no water available to make a solution, then the crystals can be rubbed into the wound.

If the bite is on the head or trunk, the incision should be made as above, and the resulting wound thoroughly soaked with permanganate of potash solution (3 per cent.). The subcutaneous tissue must be freely opened, otherwise the permanganate may be prevented from doing its work properly.

The after-treatment should be boric fomentations, frequently repeated at first; but if there is no marked swelling of the part, these may be gradually, not quickly, diminished in number, and finally a mild antiseptic dressing should be applied until the wound heals.

2. Neutralization of the Poison in the System.—We have already endeavoured to impress on the reader the following facts:—

(1) The specificity of snake-venom.

(2) The inutility of an antiserum prepared for one venom against another venom.

It now remains to consider these subjects from a practical point of view.

The serum most readily obtained is Calmette's, in 20 c.c. and 50 c.c. phials standardized against cobra and *Vipera russellii* venoms, and prepared by the immunization of horses against these venoms, as well as those of *Bungarus* (krait) and *Enhydrina* (sea-snake). Reliable sera are also prepared by the Indian Pasteur Institute of Kasauli for the venoms of the cobra and Russell's viper.

All these sera, unfortunately, deteriorate quickly unless kept in a dark and cool place, and, further, must be used in large doses, for even when fresh, 1 c.c. will only neutralize 1 milligramme of cobra-venom. A healthy cobra when it bites may inject from 250 to 350 milligrammes of venom, of which the minimum lethal dose may be estimated at 15 to 17·5 milligrammes for a person weighing 60 to 70 kilogrammes; therefore at least 350 c.c. of the antivenene must be injected intravenously, or ten to twenty times that amount must be injected subcutaneously—*i.e.*, from 3,500 to 7,000 c.c.

The antivenene, of course, will succeed in much smaller doses if a small quantity of venom has been injected, and will fail if the quantity be large. Therefore the obvious indication is to begin with 100 c.c. of antivenene, injected hypodermically, or far better intravenously, and to repeat this several times if necessary. The technique for the intravenous injection is as follows:—

An all-glass syringe should be carefully sterilized by boiling, and the skin over the vein must be cleansed with 1 in 40 carbolic and with absolute alcohol; a band should be tied round the arm, so that the vein shows up clearly, and the needle should be inserted with the aperture pointing proximally—*i.e.*, towards the heart—and should be felt free in the vein. The ligature should then be removed and the serum slowly injected. On removal of the needle, an antiseptic pad and bandage should be applied.

If, on the other hand, the species of snake which inflicted the wound is known, and the particular serum for that animal's venom happens to be available in good condition, then it should be used intravenously.

3. **Treatment of Special Symptoms**—(1) *Failure of the Respiration.*—The experiments of Fayrer, Brunton, and Rogers seem to indicate that in cases of poisoning due to cobra and sea-snake venoms artificial respiration should be resorted to when natural respiration is failing and medical aid or remedies are being sent for.

(2) *Failure of Circulation.*—In poisoning due to viper-venoms, which produce, according to Rogers, a paralysis of the central vaso-motor centre, he recommends that:—

(*a*) A binder should be applied to the abdomen and bandages to the legs, so that as much blood as possible may be available for maintaining the circulation of the brain and medulla.

(*b*) That hypodermic injections of adrenalin be used to constrict the peripheral vessels and to stimulate the vasomotor centre.

In both colubrine and viperine poisons it is obvious that the circulation should also be maintained by the applications of warmth, by stimulants, either alcoholic or ammoniacal, or by strychnine hypodermically.

Summary.—1. Apply proximal ligature.

2. Freely open the cellular tissue in the vicinity of the bite.

3. Wash the wound well with a strong solution of permanganate of potash (3 per cent.), or apply crystals.

4. Inject 100 c.c. of fresh antivenene intravenously.

5. Artificial respiration, if necessary.

6. Keep up the circulation by binders to abdomen, bandages to legs, stimulants, and hypodermic injections of strychnine.

Other Methods of Treatment.

Other methods of treatment which may be briefly mentioned are:—

Snake-Stones.—The cure which is strongly believed in by the native is the snake-stone. These stones are smooth, highly polished, very light, black bodies, said to consist of calcined animal bone soaked several times with blood, and calcined after each soaking. It is easy to understand that these stones are very hygroscopic, and when applied to a wound, cling tightly, and suck up fluids, and perhaps some poison. There are supposed to be three kinds of stones:—(1) Those composed of burnt bone; (2) those composed of chalk; (3) those composed of burnt vegetal substance. Of these three only the first is considered of value.

The method of use is as follows:—Puncture the wounds of the snake-bite slightly, and apply the stone, which adheres for about two minutes, and should then drop off into a vessel of water, after which it should be dried by a cloth, and applied again to the wound, when it will adhere for about a minute. It should be applied a third time. During application the limb should be rubbed towards the stone. The stones are used principally in India and Ceylon, but they are also known in Mexico as 'piedra ponsona.' It is hardly necessary to say that from the days of Redi it has been shown how useless these stones are.

Exorcism of the poison by shouting charmed verses is used in India. Numerous plants, seeds, earth moistened with urine, etc., have been extolled as cures.

Ammonia.—Of all the old remedies ammonia has lived the longest, and it is almost incredible that Fontana settled the question as to its lack of utility by his experiments on vipers more than 130 years ago. Whether given by the mouth, injected subcutaneously, or into a vein, it is useless, except as a stimulant, when it is certainly of no more use than alcohol. Fayrer has shown that if liquor ammoniæ is mixed in more than equal parts with venom, it does not destroy the poison.

Oils.—It is extraordinary how the remedies of the Middle Ages are clung to, and oil is still used, though known to be useless since the days of Morgagni.

Strychnine.—Many years ago Duncan recommended strychnine as a remedy for East Indian snake-bites. Recently Müller of Victoria, Australia, has strongly recommended the hypodermic injection of this drug. He says that never less than $\frac{1}{10}$ grain is to be used, and this must be increased in urgent cases to $\frac{1}{8}$ or $\frac{1}{4}$, and repeated every fifteen or twenty minutes, until the symptoms of snake-poisoning are removed. If a fang has perforated a vein, he recommends intravenous injection instead of subcutaneous The patient must be watched for twenty-four hours after the disappearance of the last symptoms, in order to combat a sudden relapse. Colonel Duke, in 1895, highly recommends this remedy.

Arsenic.—Arsenic is principally famous as the Tanjore pill, which was said to contain white arsenic and many other substances, but is quite useless.

Iodine.—Brainard's remedy was the injection of a solution of 10 grains of iodine and 30 grains of iodide of potassium, dissolved in 1 ounce of water, and probably owed its reputation to its caustic action.

Bromine was at one time considered a specific.

Caustics.—Fontana strongly advised caustics, which he considered to be useful, but long experience has shown their inutility.

Stimulants.—Brandy and whisky have been repeatedly vaunted, and so have sinapisms, warmth to the precordial region, and electricity along the spine, but all these are useless.

Energetic Movements.—Energetic movements, such as walking the patient about, flogging him, pinching him, have been advised, but are contra-indicated, as tending to exhaustion and to hasten the end.

Prophylaxis.

In the tropics Europeans and better-class natives seldom suffer from snake-bite, because they do not sleep on the ground, in the open or in small huts, like the lower-class native. Among the latter, however, any prophylaxis is difficult in regions such as India, because they reverence the cobra, and encourage it to take up its abode in their huts.

Gardens should be kept free from jungle or long grass, and gratings should be placed on the drains from bath-rooms, as snakes have often been found in these rooms.

Good strong boots and the puttee pattern of legging should be worn when going shooting or into the jungle. A lantern should be used when walking after dark, and the small permanganate case already mentioned should be carried in the waistcoat pocket in case of accidents.

LACERTILIA.

FAMILY HELODERMIDÆ Gray, 1838.

Synonym.—*Helodermatida* Fitz, 1843.

In the Helodermidæ there are two celebrated lizards—*Heloderma horridum* Wiegmann and *H. suspectum* Cope—which were placed by Sumichrast in the family Varanidæ, and though this may be disputed, still, it is probable that they are allied closely to that family.

GENUS HELODERMA Wiegmann, 1831

Heloderma horridum Wiegmann, 1834.

Synonym.—*Trachyderma horridum* Wiegm., 1829.

This lizard lives exclusively in Mexico in the hot zone which extends from the western slope of the Cordilleras to the Pacific. It inhabits the hot, dry districts of Jamiltepec, Juchitan, and Tehuantepec, where it lives in holes dug at the roots of trees or under vegetable débris. It is called 'escorpion' by the Creoles, and 'tala-chini' by the Zapotec Indians; and in 1651 Fernandez says it was called 'acastetepon' by the Mexicans.

When irritated, there escapes from its mouth a white, glutinous fluid, which is secreted by the large salivary glands. Its bite is much dreaded by the natives, who say that ill-effects are produced thereby and by eating its flesh. It may reach to a length of nearly five feet when old. We are not aware of observations on the bite or venom of this reptile.

Heloderma suspectum Cope, 1869.

Cope gave the lizard the name *suspectum*, because he suspected that its bite would be found to be poisonous. This lizard is found in the United States—in Arizona, Texas, Utah, New Mexico, and Southern California—where it is called the 'gila monster.' The poison apparatus consists of glands under the lower jaw and teeth in that jaw.

The poison gland in this species lies on either side of the lower jaw, and from its mesial aspect four ducts pass upwards, each towards its opening on the outer surface of the mandible, through which it passes obliquely upwards and inwards, to end at the base of a tooth near the termination of a groove.

The upper teeth are also grooved, but Schufeldt failed to find any gland wherewith they could be supplied with poison.

There appears to be no doubt as to the poisonous nature of the secretion from the glands above mentioned, for Bonberger records that a bite in the leg of a guinea-pig caused convulsions and death in three minutes.

Venom.—The venom was obtained by Mitchell and Reichert by making the lizard bite a saucer. It was found to be alkaline, with a weak smell, and to kill frogs, pigeons, and rabbits.

The effects of gila poison have been most carefully investigated by Weir Mitchell and Reichert, and by Van Denburgh and Wight.

The latter consider that it differs in no important respect from snake-venoms, causing death by acting rapidly upon the respiratory centre in the medulla, and causing paralysis of respiration. Its other actions are to first stimulate and then paralyze the heart by poisoning its muscular fibres. On inoculation, there is an immediate great fall of blood-pressure, but whether this is due to action on the vasomotor centre or not is not clearly known. There is a secondary gradual fall due to cardiac failure. The motor nerves and cells are not affected, but the sensory apparatus is at first rendered more irritable and then paralyzed. Coagulation of the blood is at first accelerated and then retarded, so that it may become incoagulable. Hæmolysis may occur. Local signs are almost nil, as a rule a little œdema and slight extravasation being present.

Symptoms.—Very severe pains radiating from the part, rapid swelling, faintness, profuse perspiration, may be noted

Treatment.—A proximal ligature should be applied if on a limb, and permanganate of potash, 1 3 in 100, should be used to bathe the wound, which, finally, should be dressed aseptically.

FAMILY LANTHANOTIDÆ Steindachner, 1877.

This family was formed for Lanthanotus Steindachner, 1877, which is the type genus. It is closely related to Helodermidæ.

Lanthanotus borneensis Steindachner, 1877.

This lizard, which is closely allied to *Heloderma*, is suspected of being poisonous, but there are as yet no proofs of this, especially as the teeth are not grooved, and there is doubt as to the presence of poison glands. Its habitat is Borneo, but it requires reinvestigation, as but few specimens are known.

MAMMALIA Linnæus.

The mammal suspected of causing poisoning is *Ornithorhynchus paradoxus*, belonging to the Monotremata.

MONOTREMATA Bonaparte, 1837.

Ornithorhynchus paradoxus Blumenbach, 1800.

As is well known, the males of this animal, which is only found in Australia, have large spurs projecting backwards from their hind-limbs. These spurs are hollow, and into them open the ducts of poison glands. The venom is an albuminous fluid containing albumoses.

Injected subcutaneously, it only causes local swelling, and the animal recovers in a few days. Injected intravenously, it causes fall in the blood-pressure and death from respiratory failure. The heart appears to be unaffected, but the blood in the venous system is found coagulated after death, which takes place in twenty-five to thirty minutes. The venom has no hæmolytic or proteolytic action.

The difference between the slight effect of the subcutaneous and the serious effect of the intravenous injection is thought to be due to the fact that the poison is but slowly absorbed.

In a man who was stung on the hand the symptoms were very severe pain, swelling in the hand, which rapidly spread up the arm, difficulty in opening the mouth, cold sweats, with severe sickness. Recovery took place in a few days as far as the general symptoms were concerned, but it was several weeks before the hand quite recovered.

The treatment has generally been ammonia, but the symptoms and the experiments point to a venom closely related to viperine poison, and we should recommend the proximal ligature and permanganate of potash—in fact, the treatment advocated for snake-bite.

O. paradoxus is often called *O. anatinus* Shaw, 1799.

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SECTION C

PARASITES

ANIMAL PARASITES
VEGETAL PARASITES

DIVISION I.: ANIMAL PARASITES.

Protozoa.
  Plasmodromata:—
    Sarcodina.
    Mastigophora.
    Telosporidia.
    Neosporidia.
  Heterokaryota:—
    Ciliata.
Metazoa.
    Trematoda.
    Cestoidea.
    Nematoda.
    Hirudinea
    Arthropoda.
Animal Carriers.

DIVISION II.: VEGETAL PARASITES.

Schizomycetes.
Fungaceæ.

CHAPTER XVII

PLASMODROMATA AND SARCODINA

Preliminary—Animal parasites—Nomenclature—Classification—Protozoa—Classification—Plasmodromata—Sarcodina—Gymnamœbida—Loeschia—Vahlkamfia—Dientamœba—Craigia—Thecamœbida—Chlamydophrys—References.

PRELIMINARY.

In tropical medicine the parasitic causes of disease are extremely important, and it is well to be clear as to the meaning of the term 'parasite.' A parasite is defined to be a living organism, animal or vegetal, which takes up its abode temporarily or permanently on or within other living organisms (called the hosts) for the purpose of obtaining food. Parasites may be divided into animal parasites and vegetal parasites, and it is with the former that we are concerned in this chapter.

ANIMAL PARASITES.

Animal parasites (zooparasites), in the process of obtaining their food, may cause disease by their mechanical action and chemical products, or by introducing into the host pathogenic micro-organisms.

As examples of the latter may be mentioned the transmission of the animal organism which causes malaria by certain members of a family of the mosquitoes, or that of the vegetal organism which is the cause of plague by certain fleas. Intestinal worms probably cause many of the symptoms of the disease with which they are associated by the introduction into the body of poisons through their bites, or, according to Sambon and other observers, by their active migrations before attaining maturity and reaching their selective anatomical habitat.

A well-known example of the irritation caused by the introduction of chemical poisons is the ordinary mosquito-bite already described, while *Trichinella spiralis* Owen, 1835, produces severe disturbance during its wanderings through the body.

Mechanically the jigger (*Dermatophilus penetrans* Guérin, 1838) causes much irritation to the foot, and *Loa loa* (Guiyot, 1778) to the eye.

Animals may be only '*temporary parasites*'—*i.e.*, they may only temporarily affect the host, as, for example, mosquitoes—or they may be '*stationary parasites*,' such as the malarial organism which lives in the red cells of the blood. These latter may be subdivided into 'periodical parasites,' which only spend a portion of their life-history within a host, and 'permanent,' which are parasitic throughout the whole life-cycle. As an example of the former may be mentioned the larvæ of certain flies which are parasitic, while the fly itself is not, and of the latter *Oxyuris vermicularis* (Linnæus, 1767) is a good example.

Animal parasites may be classified into *ectoparasites* or *epizoa*, affecting the skin and exterior of the host; and *endoparasites* or *entozoa*, affecting the internal organs or cavities of the host.

Until recent years the greatest confusion existed as to the nature of parasites. With our present knowledge it appears that parasites, however altered in structure some of them may have become during their parasitic existence, have been originally derived from free-living forms. It will, however, be noted that there are great differences in the structure and appearance between some of the permanent parasites and their nearest free-living affinities. This difference has been brought about mainly by environment.

The permanent parasite, particularly if an entozoon, has food prepared for it by its host in an easily assimilated form; hence there is no necessity for a complicated digestive apparatus, which in certain cases has entirely disappeared.

Further, certain parasites, having reached an organ which supplies them with suitable food, do not require organs of locomotion, for they have only to remain where they are, and the tissues of the host will subserve their purpose. Some of them have no necessity, as a rule, for locomotion for sexual purposes, because hermaphroditism is common, and even in cases where this is not found parasites often live in couples (male and female). Being enclosed in the body of the host, there is no necessity for sense organs; therefore these are much reduced, or are absent.

On the other hand, the parasite requires something to enable it to fix itself firmly to the tissues of the host; hence suckers and hooks are often found, and also clasping and clinging organs.

The chance of a parasite, locked up inside a host, successfully reproducing its species is small; hence reproduction assumes important features associated with the production of large numbers of new forms, which are often protected by shells or other coverings.

Reproduction may be asexual, especially in the protozoa, or sexual. Sexual reproduction in parasites is generally complicated, ending in the production of large quantities of eggs or spores; and very often the spores of the protozoa or the corresponding larval forms of the metazoa may travel through one or more intermediary hosts before they infect another definitive host—that is, one in which the sexual life-history is gone through.

With regard to the sexual process, it may be noted that often the male is smaller than the female, and in fewer numbers, but there are exceptions.

Usually parasites keep strictly to certain hosts called 'normal hosts,' but at times they are found in unusual hosts—for example, *Echinorhynchus gigas* (Goeze, 1782), which is usually found in pigs, may infect man. Such a parasite is called a 'chance parasite,' while objects mistaken for parasites are known as 'pseudo-parasites.'

The above are examples of simple parasitism; but there are parasites which are parasitic upon other parasites—a condition called 'hyperparasitism.' These hyperparasites may be secondary, tertiary, or quaternary, and their importance in disease has been emphasized by Sambon, who has shown that it may be one of the causes of the disappearance of malaria from a district, for the black spores found by Ross in mosquitoes infected with malaria are now known to be hyperparasites of the genus *Nosema*.

For further remarks see the article on Metazoan Parasites.

Nomenclature.—Medical men in the tropics are at present almost daily discovering new, or what are thought to be new, parasites, and are generally desirous of giving them definite names, but before doing so it behoves the discoverer to know and obey the international code laid down by zoologists, for which purpose they should study Stiles's pamphlet in the bulletins of the United States Public Health and Marine Hospitals Service.

Four rules may be mentioned here:—

1. **Language Rule.**—The name given to the parasite must be in Latin, and not in any vernacular.

2. **Rule of Priority.** The valid name for a genus or species is the oldest available name. Therefore, in describing a species or genus, give not merely the name of the authority who invented the term, but the date also.

3. **Rule of Homonyms.**—When two distinct genera or species of animals receive the same name, that applied earliest alone must stand.

4. **Rule of Appropriateness.**—No name is allowed to be changed simply because it is inappropriate.

With regard to disease there is no fixed rule, but we feel sure that if medical men would attempt to evolve a fixed method of nomenclature, much confusion would be avoided.

When an animal parasite causes a series of symptoms in a man or an animal, it is usual to name the affection by that of the animal causing the disease, together with the suffix 'iasis.' Thus, *Loeschia histolytica* (Schaudinn, 1903) causes loeschial dysentery and liver abscess, etc., which may be classed together under the term 'Loeschiasis'; or *Paragonimus ringeri* (Cobbold, 1890) causes a varied number of symptoms, which can all be classed together as 'Paragonimiasis.'

The drawback to this nomenclature is that, parasites being very often changed from genus to genus, such terms are not permanent. For instance, the same pathological condition may be indicated by various authorities with the terms 'Amœbiasis,' 'Entamœbiasis,' 'Loeschiasis.' We therefore prefer, wherever possible, to use common names for diseases—*e.g.*, 'Kala-azar.'

Classification.—The animals which cause and convey the diseases of man may be classified into the following subkingdoms: Subkingdom I., Protozoa; Subkingdom II., Metazoa.

SUBDIVISION A. PROTOZOAN PARASITES.

SUBKINGDOM I. PROTOZOA Goldfuss, 1817.

Definition.—Protozoa are unicellular animals, solitary or united into colonies, free-living or parasitic, with asexual reproduction (schizogony) by binary fission, budding or fragmentation and sexual reproduction (sporogony), or merely rejuvenescence by conjugation.

Remarks.—The border-line between unicellular animals and unicellular plants is very vague, and hence at present it is uncertain whether some forms should be classed with the bacteria and considered to be plants, or with the protozoa and considered to be animals. Therefore it is not unusual to call both 'protists.'

Phylogenesis.—There can be little doubt that the primitive form of protozoon must have been an animal with some of the characteristics of the amœba, and would most likely be free-living, most probably in water. This simple form, taken into the alimentary canal of higher animals, possibly benefited by the ease with which food was obtained and by the protection afforded by the new position, and thus became modified to suit its environment. The most important modification would be some protection for the earliest stages of its life-history, which would enable it to live in the outside world until taken up by a suitable host, and associated with this would be the necessity to produce large numbers of such protected spores, as the chance of one finding a suitable host must be relatively small. Such a type would be represented by the *Loeschia coli* Loesch, which is a parasite of man. Such a parasite may cause no harm to its host, which is fairly indifferent to its existence. On the other hand, a parasite may not find sufficient nutriment in the alimentary canal, and be compelled to seek better food, and perhaps more protection, by entering the glands of Lieberkühn, or even the submucosa of the bowel. Such a parasite might cause disease in its host, and would be illustrated by the *Loeschia histolytica* Schaudinn of man.

Such a process, however, took place not merely in man, but in many other kinds of animals, among which may be mentioned insects, in the alimentary canal of many of which protozoan parasites are found. In these insects the sexual process occurs, and therefore they are the definitive hosts, and may also be considered the primary hosts.

If these primary hosts become predatory, biting and sucking the blood of other animals—*e.g.*, vertebrates—then, during this process, they might pass the spores of their parasites into the blood of the vertebrata, and if these are not killed off (for some animals are repellent) by chemical substances, or destroyed by leucocytes, they might develop in the blood of some vertebrate (called tolerant), which thus becomes the secondary host.

It is, of course, possible that some of these blood protozoa may have been derived from parasites originally intestinal in the vertebrate, which found their way not merely into the mucosa of the bowel, but later into the blood-stream, in which they would be fairly well protected, and from which they would at first escape by becoming encysted in the intestinal wall, and then, bursting into the bowel, make their way to the exterior with the fæcal matter and so infect a new host. When blood-sucking animals became evolved, a new cycle would be open for them—viz., from the vertebrate through the blood-sucker back to the vertebrate—and thus the old method by way of the alimentary canal would be lost.

The origin of the protozoan blood-parasites of man may therefore be twofold: (*a*) from man's intestine into the blood; (*b*) from an invertebrate's alimentary canal into the blood of man.

The result of one or other of these methods is well illustrated by the malarial parasite, which passes through its sexual cycle in an *Anopheline* mosquito, which is its definitive and according to the view adopted, its primary or secondary host. When the infected *Anopheline* bites a man, the parasite enters into the blood-stream, in the red cells of which it develops and undergoes its asexual cycle. Man is therefore the intermediary, and either the primary or secondary, host of the malarial parasite, as mentioned above.

The blood-stream of man contains two different elements—(1) liquor sanguinis; (2) cells (*a*) red, (*b*) white. Therefore the parasite has two possibilities before it—either to live in the liquor or in a cell, or partially in one and partially in the other; and this last is what generally happens—*i.e.*, the parasite lives so much of its cycle in a cell and so much in the blood-stream. It would, however, appear that there is a great phylogenetic tendency for protozoan parasites to leave the liquor sanguinis and to reside in red cells (the malarial parasite) or in white cells or in endothelial cells (the Leishman-Donovan parasite).

Infection of the Embryo. Protozoan blood parasites apparently can be arranged in two categories as regards the infection of the fœtus, for some, like the malarial parasite (which is generally considered to be incapable), do not traverse the placenta, while others, like the *Spirochætes* and *Treponemata*, can do so. With regard to the infection of invertebrate eggs the matter is quite different, for many of these parasites infect the eggs, thus carrying the germs of disease into a new generation of blood-suckers.

It would appear as though the intracellular stage enabled the parasite to grow (*e.g.*, consider Schaudinn's history of the development of *Hæmoproteus noctuæ* in the little owl) and to multiply (*e.g.*, note the development and multiplication of the malarial parasite).

In the evolution of such hæmatozoan types some authorities (Woodcock) hold that the flagellate forms living in the blood-stream are to be considered the most primitive, and that the more truly cellular the parasite becomes the more it has evolved. Hence the *Hæmoflagellata*, or parasites freely moving in the liquor sanguinis, are with difficulty separated from the *Hæmosporidia*, or parasites which mostly live in blood cells. For many reasons some of these two groups of parasites were united together into one order of the flagellates by Hartmann.

Morphology.—Protozoan parasites vary in size from the large *Sarcocystidæ* in muscle to most minute forms in the blood (*Hæmoprotozoa*). In fact, it is possible that some forms may exist which we have not yet recognized, because their minute size prevents their being visible to the human eye, even when aided by the highest powers of the microscope.

The parasites themselves consist of protoplasm, which in some instances shows a modification into ectoplasm and endoplasm, the former being clear and hyaline and the latter dark and granular. In the protoplasm are to be found—(1) one or more nuclei, (2) chromidiosomes and chromidia, (3) metachromatic granules, (4) volutine granules, (5) metaplastic granules, (6) centrosomes, (7) archoplasm, (8) rhizoplast, (9) vacuoli.

(1) The nucleus in its simplest form is merely a collection of smaller or larger particles of chromatin (chromidiosomes or chromidia). A very simple form is that termed *Protokaryon*, in which one large chromidial mass (the Karyosome) lies in a delicate achromatic network of linin inside a vacuole filled with nuclear sap, called *enchylema*. Some chromidia may or may not be situated peripherally as well as more centrally. There is no definite membrane. The next advance is the vesicular nucleus, which consists of a definite nuclear membrane separating it from the cytoplasm. Inside this membrane there is an achromatic framework made of linin; a nuclear fluid or enchylema, lumps of a substance called *plastin* giving rise to the *nucleolus*, so common in the Metozoa and so rare in the Protozoa, and in association with chromatin to the *karyosome*, which in this instance is called the *endosome*, or Binnenkörper. The granular nucleus is a further evolution, and is produced by a more scattered condition of the chromatin.

The nucleus is therefore a complex body composed of chromatic and achromatic substances. It may be single, or divided into two principal masses—trophonucleus or nutrition-nucleus and kinetonucleus or motion-nucleus, or into macronucleus and micronucleus. The latter are quite different from the tropho- and kinetonuclei, for the macronucleus is trophic and kinetic, while the micronucleus is purely reproductive. The former is typically seen in the trypanosomidæ and the latter in the heterokaryota.

(2) Chromidiosomes are the smallest particles of chromatin which, when massed together, give rise to the chromidia which may be intranuclear or extranuclear. (3) The metachromatic granules or chromatoid grains represent stages in the anabolism or katabolism of chromatin. (4) Volutine granules stain like chromatin. They are composed of nucleic acid in combination, and represent reserve food material for the nucleus. (5) Metaplastic granules are products of cytoplastic anabolism or katabolism. (6) Centrosome is a

minute grain or pair of granules (diplosome) lying typically outside the nucleus close to the membrane. (7) The archoplasm is the clear protoplasm which sometimes surrounds the centrosome. (8) The rhizoplast is the portion of the flagellum (when present) which penetrates into the cytoplasm. The flagellar apparatus is described under the heading 'Mastigophora' in the next chapter. (9) The vacuoli may be either contractile vacuoles which are considered to be respiratory and excretory in function, or the food vacuoles, which begin with a globule of water taken in with the food. Into this vacuole an acid is secreted from the cytoplasm and digests the food, which is then absorbed. Then the vacuole with the undigested food travels to the periphery, and the waste product is extruded.

Protozoa generally have some power of movement by pseudopodia, cilia, or flagella, but under unfavourable circumstances they may lose this power, and, becoming quiescent, surround themselves with an envelope and become encysted. Unfavourable circumstances are lack of food, desiccation, irritating chemical substances, and unusual surroundings.

Life-History.—Reproduction in the protozoa takes place asexually or sexually. As long as conditions are favourable—*i.e.*, there is abundance of food—protozoa reproduce asexually by one of the following methods: (1) binary fission; (2) gemmation; and (3) sporeformation.

1. *Binary Fission.*—In binary fission there is first division of the nucleus, which sometimes takes place by amitosis, followed by that of the cytoplasm. Then the parasite divides into two more or less equal halves (Fig. 42). The other methods of nuclear division are by chromidial fragmentation or by mitosis, of which there are three types—(*a*) Promitosis, (*b*) Mesomitosis, (*c*) Metamitosis. In chromidial fragmentation the nucleus breaks up into minute chromidia, which eventually collect into two new nuclei. In Promitosis a prokaryon type of nucleus divides by the centrosome splitting into two, and giving rise to the central thread (centrodesmose) of the spindle. Then the karyosome divides by constriction, and the achromatic spindle is formed from the framework of the nucleus, and lies between the two separating karyosomes, with the centrodesmose in the middle. Then the chromosomes appear formed from the peripheral chromatin as well as from that of the karyosome.

There are two types of Promitosis—the simpler, in which no equatorial plate is formed, and the chromosomes are merely scattered along the spindle, and finally gather at opposite poles to form the daughter nuclei; and the more advanced, with an equatorial plate of chromosomes which may divide by either an equating or a reducing division. In Promitosis the nuclear membrane is negligible, while the whole process is confined to the nuclear area. In mesomitosis, which takes place in a nucleus in which the karyosome is reduced and in which there are more chromatic particles in the body of the nucleus, perfect karyomitotic figures are formed, but the whole process takes place inside the nuclear membrane. In metamitosis the polar caps of archoplasm situate in the cytoplasm assist in the mitosis.

2. *Gemmation.*—In gemmation the nucleus divides usually by mitosis into two or more nuclei, which either travel to the periphery, and become surrounded by small masses of protoplasm, which separate from the parent parasite—ectogenous gemmation—or remain in the cytoplasm, a portion of which becomes differentiated around each nucleus—endogenous gemmation.

The explanation of the two methods is that in ectogenous gemmation the buds are separated from the mother cell externally, while in endogenous gemmation the localized budding area sinks into the body substance of the mother cell, with the result that the buds are contained in a brood sac. This localized endogenous area is called a pansporoblast, though in some the entire organism forms a pansporoblast, which is considered to be phylogenetically derived from the localized condition—*i.e.*, the whole cell represents only the pansporoblast.

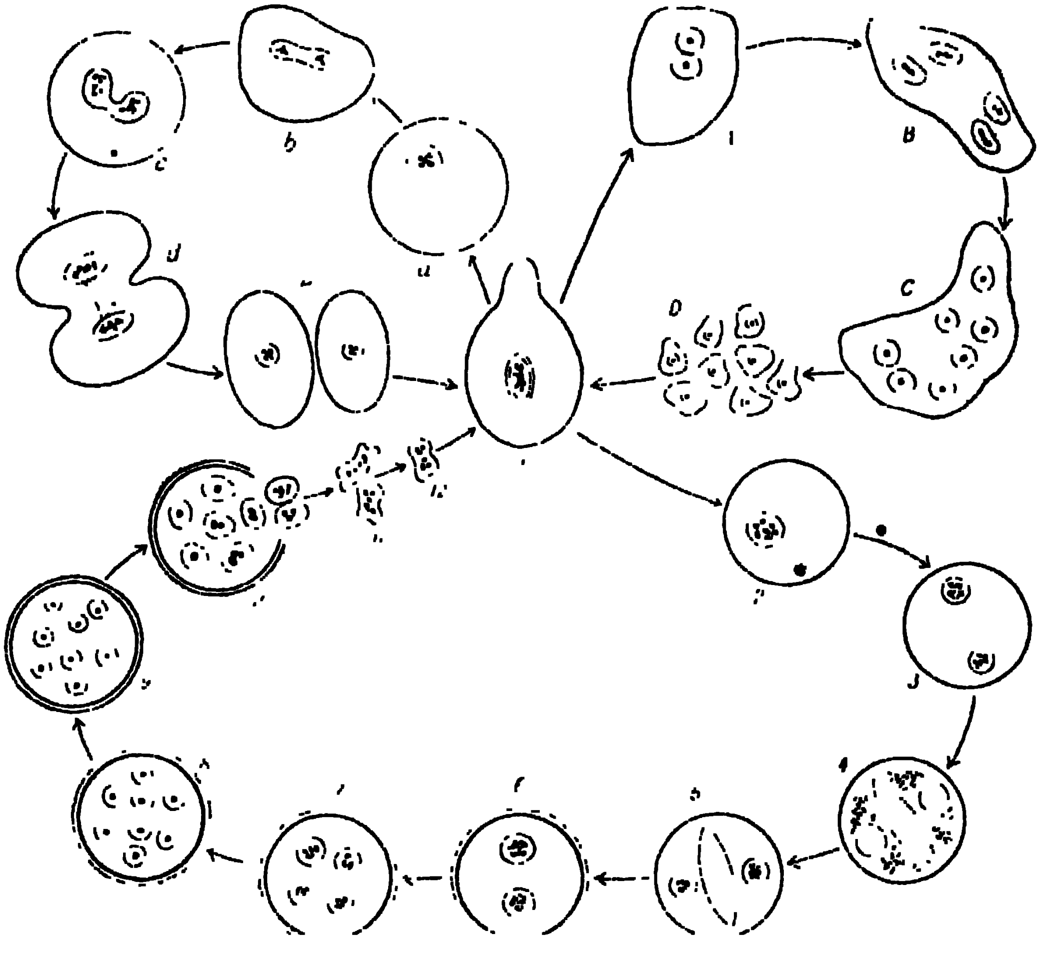

FIG. 42.—DIAGRAM OF THE LIFE-CYCLES OF *Loeschia coli* LOESCH, *emendavit* SCHAUDINN, 1903, SHOWING HARTMANN AND WHITMORE'S VIEWS AS TO ZYGOSIS.

1, *Loeschia coli*; *a-c*, stages in the process of binary fission by promitosis; A-D, schizogony by repeated division; 2-12, sexual reproduction or sporogony; 11 are the gametes, 12 the zygote, but these stages are not definitely known.

Plasmotomy.—Plasmotomy is the term applied to the intermediate division of the cytoplasm of multinuclear parasites into two or more masses, which afterwards may or may not reproduce by spore-formation.

3. *Spore-Formation.*—Instead of being considered a process of internal gemmation, the formation of pansporoblasts may be looked upon as a process of spore-formation proceeding while the organism grows, as is typically seen in the Neosporidia.

The typical asexual spore-formation or schizogony is, however, met with in the Telosporidia, in which the early stages absorb nutriment and increase in size, being therefore called trophozoites. When fully grown they form a quiescent body, the schizont, whose nucleus and cytoplasm divide into a number of small forms called asexual spores or merozoites, generally, however, leaving a little undivided cytoplasm laden with effete matter,

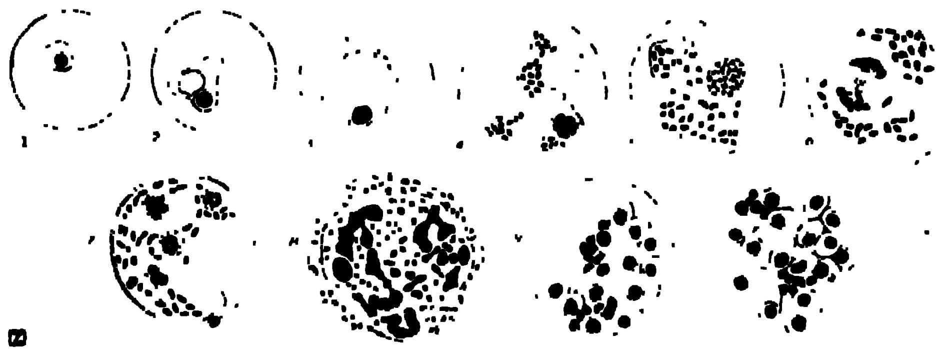

FIG. 43.—SCHIZOGONY OF *Plasmodium vivax* GRASSI AND FELETTI.
(After Schaudinn.)

1, Young trophozoite; 2, ring form; 3, ring form showing hæmozoin; 4, parasite with pseudopodia, 5, old trophozoite, 6, schizont showing commencement of first division; 7, schizont with four nuclei; 8, schizont with several nuclei (the corpuscle shows Schüffner's dots); 9, schizont divided into merozoites, 10, merozoites and hæmozoin free.

These merozoites are the forms by which the parasite multiplies in the given host, and are not the means by which new hosts are infected. They therefore enter new cells in the host in which they are formed, and, growing into a trophozoite, complete an asexual life-cycle, which is called the cycle of schizogony, or simply schizogony (Fig. 43).

A time arrives in the infection of every host when the food material for the given parasite is diminished by the numbers of forms produced by asexual reproduction, or when the tissues of the host react against the parasite by chemical substances, or phagocytosis, or by both methods combined.

When these adverse circumstances become sufficiently severe, changes take place in the parasite which produce forms capable of leaving the given host and existing outside it, either in a different species of animal or simply in the exterior, until an entry is made into a new host of the same species as before, when schizogony begins again.

The changes which the parasite has to undergo in spreading from one host to another are generally associated with sexual reproduction, and the whole cycle from a given host of a certain species to another host of the same species is called the cycle of sporogony, or, more simply, sporogony (Figs. 44, 45, and 46).

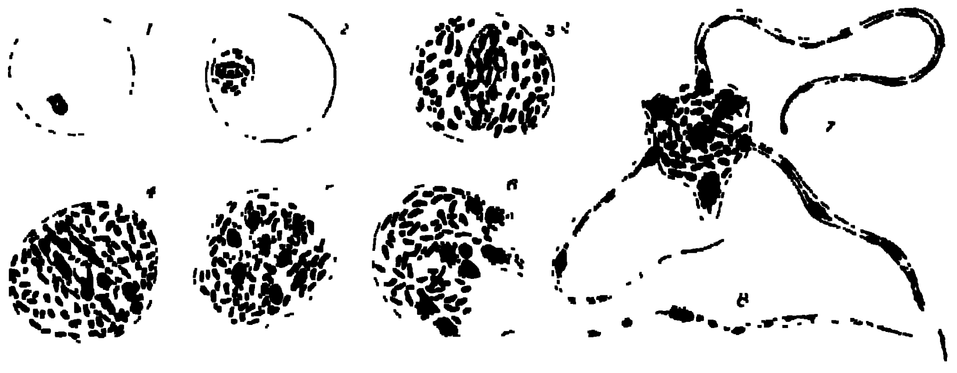

FIG. 44.—SPOROGONY OF *Plasmodium vivax* GRASSI AND FELETTI. DEVELOPMENT OF THE MICROGAMETE. (After Schaudinn.)

1, Young microgametocyte; 2, 3, older forms; 4, fully grown microgametocyte, as seen in the blood of man; 5, division of the nucleus (reduction) in the stomach of an anopheline; 6, nuclei have travelled to the periphery, which has grown out to form the commencement of a microgamete; 7, microgametocyte with three microgametes; 8, a free microgamete.

In adverse or changed circumstances, therefore, the merozoites develop into more resisting forms, which are called gametocytes, in which, by reduction of the nuclear material, the male and female elements in the nucleus are separated; the two elements may exist in the same cell or in separate cells, but usually the male element of one cell fuses (zygosis) with the female element of another cell, and forms a new individual with a new nucleus or synkaryon.

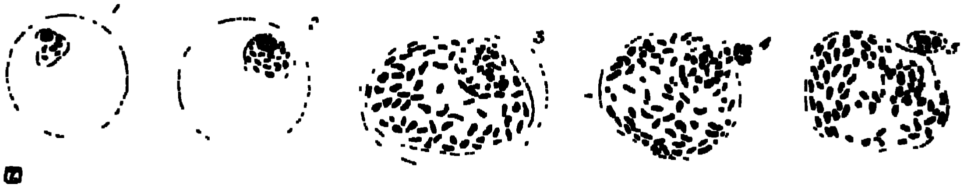

FIG. 45.—SPOROGONY OF *Plasmodium vivax* GRASSI AND FELETTI. DEVELOPMENT OF THE MACROGAMETE. (After Schaudinn.)

1-2, Young macrogametocytes; 3, fully developed macrogametocyte in the blood of man; 4, reduction and formation of a polar body in the stomach of an anopheline mosquito; 5, macrogamete and one polar body.

This new individual proceeds to reproduce itself rapidly by either binary fission or spore-formation. In the latter case, in order to prevent confusion, the terms employed are different from those used in asexual reproduction. The parasite is called a sporont, the spores sporozoites. The sexual reproduction takes place in the definitive host, which may be different from the intermediary host in which the asexual reproduction is found.

Parthenogenesis and Etheogenesis.—Reproduction is said to take place from a female type of parasite (parthenogenesis) or more rarely from a male type of parasite (etheogenesis), without any completion of the sexual process (Fig. 47).

An example of parthenogenesis is found in the malarial parasite, in which the female gametocyte is capable of resisting both the action of the chemicals of the body and drugs, and is therefore capable of lying dormant for some time. When given an opportunity for development, its nucleus and protoplasm divide into two portions, one of which degenerates and disappears, while the other forms merozoites and starts the cycle of schizogony anew. Another is described by Prowazek in *Herpetomonas muscæ-domesticæ*, but neither example has been definitely proved; and, indeed, of late grave doubts have arisen as to its truth. Nevertheless, we feel that it is necessary to keep some remarks upon the subject, as we feel that the last word has not yet been said, as we have seen once bodies very like those described by Schaudinn.

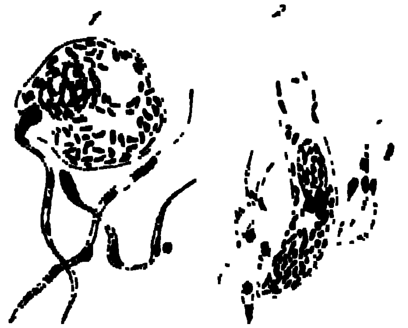

FIG. 46.—SPOROGONY OF *Plasmodium vivax* GRASSI AND FELETTI: ZYGOSIS. (After Schaudinn.)

1, Zygosis of one microgamete with the macrogamete; 2, oökinete and degenerate microgametes

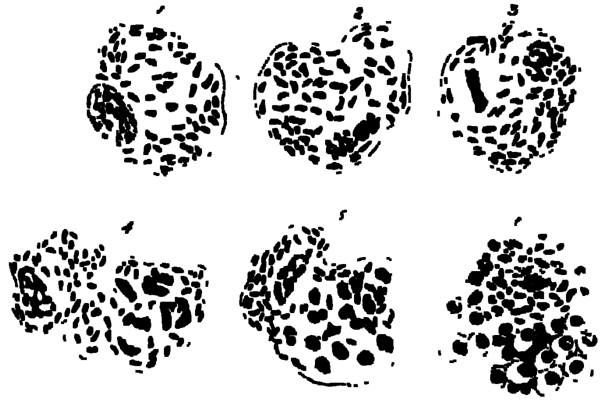

FIG. 47.—PARTHENOGENESIS OF *Plasmodium vivax* GRASSI AND FELETTI. (After Schaudinn.)

1, Macrogametocyte, 2, division of the nucleus; 3-6, formation of merozoites from one portion of the nucleus, and separation of the other portion with the hæmozoin.

Etheogenesis, a term introduced by Prowazek, is the much rarer change in the male parasite whereby asexual reproduction begins again. He described it in *Herpetomonas muscæ-domesticæ*, but Flu says that an error was made, and that the objects believed to be male elements were really stages in the life-cycle of a Microsporidian —*Octosporea muscæ-domesticæ*.

Pathogenicity.—The pathogenicity of the Protozoa is of the highest importance, as they are the causes of a large number of endemic and epidemic diseases in man and animals, as will be described in the following pages. They produce toxins; but these have not been well studied, with the exception of the Sarcosporidiotoxin, which is only toxic for rabbits and not for other animals. The toxins produced by the malarial parasites have been referred to on p. 203.

Classification.—The classification of the subkingdom Protozoa is by no means satisfactory at present, but for remarks upon this subject we refer the reader to Poche's article thereon written in the *Archiv für Protistenkunde*, vol. 30, in 1913.

The old classification was into four classes: (1) sarcodina; (2) mastigophora; (3) sporozoa; (4) infusoria.

The sarcodina move and capture food by pseudopodia; the mastigophora by flagella; the sporozoa are parasites without motile organs; and the infusoria move by means of cilia. When this classification was brought into use, practically nothing was known about the life-history of the protozoa, a more complete knowledge of which is still required.

Schaudinn's work with regard to the life-history of flagellates having failed to be confirmed, and Hartmann's binucleate theory having fallen into disuse, we have returned to Doflein's classification as set forth below.

Among the blood parasites of man and other animals there are found some wavy, thread like organisms (*Spirochætes* and *Treponemata*), with which must be classed some free-living forms whose position, even in the animal kingdom, has been disputed.

Most authorities believe that these forms are protozoa with a low type of nucleus, but so different are they from the ordinary phyla of protozoa that, following Doflein's and Fantham's suggestions, we shall place them in a separate section making them an Appendix to the Mastigophora, though Calkins thinks it better to leave them in their old position at present.

Further, the old group of the Sporozoa Leuckart, 1879, contains two such different groups of animals in its subdivisions into Telosporidia and Neosporidia that it is justifiable to do away with this combination, and to raise the two divisions to the rank of separate phyla.

Finally, the two nuclei of the infusoria are so totally different in function from the nucleus or nuclei of the rest of the protozoa that the Subkingdom is capable of being divided into two divisions:— the Heterokaryota or infusoria; and the Plasmodromata, under which heading come the other phyla.

In the present work the following classification is adopted:—

DIVISION A. PLASMODROMATA Doflein, 1901.

Phylum I.—*Sarcodina* Hertwig and Lesser, 1874.
Phylum II.—*Mastigophora* Diesing, 1866.
Phylum III.—*Telosporidia* Schaudinn, 1900.
Phylum IV.—*Neosporidia* Schaudinn, 1900.

DIVISION B. HETEROKARYOTA Hickson, 1903.

Phylum V.—*Ciliata* Perty, 1852.
Phylum VI.—*Acinetaria* Lankester, 1885.

Species.—Before commencing the systematic description of the Protozoa it may perhaps be as well to remind the reader that in the higher animals the distinctness of a species depends upon the fertility of its members *inter se*, but not usually with members of other species.

In protozoology and bacteriology many mere varieties have been called species, but such variants *lack any morphologically specific character*, and are merely separated from one another by *physiological characters*, which, as we have seen in the section on evolution of disease, can be made to alter by change of environment.

It is convenient and useful for purposes of identification and reference to give them names as though they were true species, and this does no harm so long as the reader does not expect to find morphologically specific differences in these forms, which can only be separated biologically and physiologically.

DIVISION A: PLASMODROMATA DOFLEIN, 1901.

Synonym.—*Cytomorpha* Hatschek, 1888.

Definition.—Protozoa in which the nucleus is not separated into reproductive (micronucleus) and non reproductive (macronucleus) portions.

Classification. The Plasmodromata may be divided into phyla according to the following scheme:—

(*a*) *With motile organs in adult stage*:—
  I. Move and capture food by pseudopodia—*Sarcodina*.
  II. Move and capture food by flagella—*Mastigophora*.
(*b*) *Without motile organs in adult stage*
  I. Spore formation distinct from and takes place after the trophic phase—*Telosporidia*.
  II. Spore formation and trophic stage proceed simultaneously—*Neosporidia*.

PHYLUM: SARCODINA Hertwig and Lesser, 1874.

Definition.—Plasmodromata which move and capture their food by means of pseudopodia.

Classification.—The Sarcodina may be classified as follows:—

(*a*) Without axial filaments in the lobose, filose, or reticulose pseudopodia—*Rhizopoda*.
(*b*) With central axial filaments in fine ray-like pseudopodia—*Heliozoa* Haeckel, 1866; *Radiolaria* Haeckel, 1861.

Remarks.—Only the Rhizopoda concern us at present.

CLASS: RHIZOPODA VON SIEBOLD, 1845.

Definition.—Sarcodina, parasitic or free-living, without axial filaments in their lobose, filose, or reticulose pseudopodia.

Classification.—This class may be divided into subclasses as follows:—

(*a*) With blunt loose pseudopodia which do not anastomose—*Amœbæ*.
(*b*) With fine branching and anastomosing pseudopodia—*Foraminifera*.

Remarks.—Only the Amœbæ concern us.

SUBCLASS: AMŒBÆ Ehrenberg, 1830.

Synonyms.—*Amœbina* Auctores (a misprint); *Chaidea* Poche, 1913; *Amœbidæ* Brown, 1859.

Definition.—Rhizopoda, parasitic or free-living, with blunt, loose pseudopodia which do not anastomose.

Classification.—The subclass Amœbæ may be divided into two orders as follows:—

(*a*) Without a shell—*Gymnamœbida*.
(*b*) With a shell—*Thecamœbida*.

ORDER I. GYMNAMŒBIDA Delage Hérouard, 1896.

Synonym. *Lobosa* Carpenter, 1861; *Amœbidæ* Broun, 1859; *Chaidæ* Poche, 1913.

Definition.—Amœbæ without a shell, but with a tendency of the peripheral plasm to harden into a membrane-like zone.

Type Genus.—*Amœba* Bory de St. Vincent, 1822.

Remarks.—The genera of this order are in a wild state of confusion. Calkins in 1912 gave a large number of genera—Amœba, Vahlkamfia, Naegleria, Craigia, Trimastigamœba, Entamœba, Paramœba, Trichospherium, Hyalodiscus, Chromaletta, Pelomyxa, Dactylosphera, Nucleophaga. In the same year Alexeieff created the genera Naegleria and Hartmannia for Amœbæ of the limax type, and also Proctamœba for Amœbæ parasitic in vertebrates, but the two last names have not come into general use. Doubtless many more exist.

Classification.—Those found in man up to the present may be classified into:—

1. *Loeschia* Chatton and Lalung-Bonnaire, 1912.
2. *Vahlkamfia* Chatton and Lalung-Bonnaire, 1912.
3. *Craigia* Calkins, 1912.
4. *Dientamœba* Jepps and Dobell, 1918.

They may be differentiated as follows:—

A. *Without uniflagellate stage*:—
  I. Typically uninucleate:—
    Ecto- and endoplasm distinct when moving. Nucleus with or without visible karyosome and centriole. Contractile vacuoles generally absent. Division by mesomitosis—*Loeschia*.

Ectoplasm only seen in outbursts. Nucleus with finely divided chromatin forming a membrane-like contour and with definite karyosome. Division by promitosis—*Vahlkamfia*.

II. **Typically binucleate, the two nuclei having the same size and structure.**

Ecto- and endoplasm distinct—*Dientamæba*.

B. ***With uniflagellate stage*** :—

Ectoplasm visible on movement. Endoplasm with or without a body like a *Nebenkörper*—***Craigia*.**

THE GENUS AMŒBA.

The old original genus Amœba seems to have been first described by Rösel von Rosenhof in 1775, under the heading the ***Small Proteus***, and to this organism Linnæus gave the name ***Volvox chaos***, which Pallas in 1766 turned into *Volvox proteus*. In 1822 Baron Bory de Saint Vincent, in the 'Dictionnaire Classique d'Histoire Naturelle,' vol. i., pp. 260-262, established the genus Amiba, calling *Volvox proteus* by the name *Amiba divergens*, which Ehrenberg in 1831 altered to *Amœba princeps* and Leidy in 1878 to *Amœba proteus*.

This original genus is now divided into the following genera:—

A. *Usually free living* :—

I. Without a flagellate stage in the life-cycle:—

(*a*) Usually uninucleate.

1. Large forms reaching to 1 millimetre in diameter, free living, with well differentiated ecto- and endoplasm and well developed pseudopodia. One or many large nuclei with doubly refracting membrane and chromatin concentrated into a single large karyosome or as granules diffused through nucleus. One or more contractile vacuoles—Genus 1, *Amœba* Bory de St. Vincent, 1822.

2. **Minute forms, free living or commensal, ectoplasm not well differentiated from endoplasm, moving as a finger-formed single pseudopodium or with irregular ectoplasmic bursts to form a general or local ectoplasm.** Nucleus single or double, with finely divided chromatin, forming a membrane-like structure and a definite karyosome. One contractile vacuole present as a rule—Genus 2, *Vahlkamfia* Chatton and Lalung-Bonnaire, 1911; ***emendavit*** **Calkins, 1912.**

(*b*) **Usually binucleate. Genus 3, *Dientamæba* Jeffs and Dobell, 1918.**

II. With a flagellate stage in the life-cycle:—
(*a*) Flagellate forms divide—Genus 4, *Paramœba* Schaudinn, 1896.
(*b*) Flagellate forms do not divide:—
1. Uniflagellate—Genus 5, *Craigia* Calkins, 1912.
2. Biflagellate—Genus 6, *Naegleria* Alexeieff, 1912; *emendavit* Calkins, 1912.
3. Triflagellate—Genus 7, *Trimastigamœba* Whitmore, 1911.

B. *Parasitic, commensal, or pathogenic* :—
I. Contractile vacuoles numerous; cysts give rise to gametes—Genus 8, *Entamœba* Leidy, 1879.
II. Contractile vacuoles absent; cysts not known to give rise to gametes—Genus 9, *Loeschia* Chatton and Lalung-Bonnaire, 1912.

The principal species of the genus Amœba are the type *A. proteus* (Pallas, 1766), *A. vespertilio* Penard, 1902, *A. verrucosa* Ehrenberg, 1838, and *A. terricola* Greeff, 1892, but the last two may be the same species.

The type species of Naegleria is *N. punctata* Dangeard, 1910, found in pond water and infusions.

Trimastigamœba has only one species, *T. philippinensis* Whitmore, found in tap water in Manila.

Entamœba has as its type species *E. blattæ* Bütschli, 1878, described in detail by Mercier in 1909 and 1910, who says that the gamete-forming cysts give rise to minute uninucleate gametes, which conjugate outside the cyst, while the copula develops directly into the trophozoite. This is very different from what is known concerning the life-history of Loeschia.

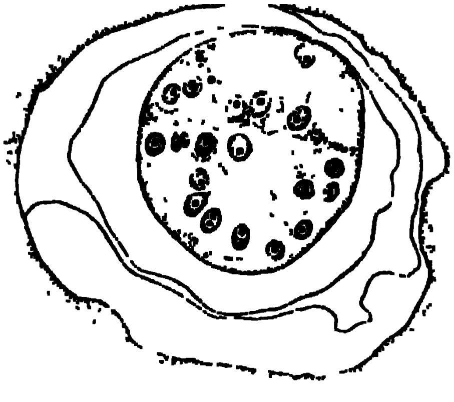

FIG. 48.—Cyst of *Amœba proteus* (Pallas, 1766). (After Carter.)

As the type genus is Amœba, and its type species *Amœba proteus* (Pallas, 1766), it is interesting to know its life-cycle, which is but little understood at present.

Miss Carter has, however, studied encystment, while simple division is fully established and schizogony is doubtful.

The precystic stage is characterized by the Amœba becoming sluggish, clearing its body of debris, and exuding a slimy mucus, which causes surrounding detritus to adhere to it, and so to form an outer protecting covering, inside which two membranous cyst walls, separated by fluid, are formed. The cysts measure 70 to 140 microns in diameter, and are found in England from late December to the middle of March. They are spherical and without means of attachment.

Inside the cyst the nucleus breaks down and the chromatin and plastin are distributed throughout the cytoplasm, in which they form secondary nuclei of the protokaryon type, and finally some 75 to 100 young nucleated amœbæ, which apparently do not become flagellate, and so far as is known do not form gametes, but this and the further development require investigation.

Metcalf has, however, observed zygosis in minute gametes of *Amœba proteus*.

Genus Loeschia Chatton and Lalung-Bonnaire, 1912.

Synonyms.—*Amœba* Ehrenberg, 1830, *pro parte*; *Entamœba* Casagrandi and Barbagallo, 1897; *nec Endamœba* Leidy, 1879.

Definition.—Gymnamœbida, with a vesicular nucleus containing a small karyosome (as a rule) and abundant peripheral chromatin, and dividing by mesomitosis, and with cysts containing four to eight nuclei, which form young amœbæ which are not known to be gametes.

Nomenclature.—The name Amœba was applied by St. Vincent in 1822 and by Ehrenberg in 1830 to free living forms, of which the type is *Amœba proteus*, which Poche thinks is the *Volvox chaos* of Linnæus; and the term *Endamœba* was given by Leidy in 1879 to the parasitic *E. blattæ* Bütschli, but this name cannot be applied to the human parasites, because Mercier's researches have shown that it may be different, and therefore it is necessary to use Chatton and Lalung-Bonnaire's term.

Remarks.—The genus is composed of amœba-like forms varying in size from 5 to 80 microns, and possessing distinct ectoplasm and endoplasm, which, however, may be only visible during motion. The ectoplasm is clear and hyaline, while the endoplasm may be either clear or finely granular. The nucleus usually has a karyosome and centriole. Reproduction is by simple division, schizogony, and cyst formation.

The species live in the alimentary canal of man and animals, but may enter other tissues and organs, and may be pathogenic or non-pathogenic.

It is still doubtful whether artificial cultivation has been performed successfully.

Type Species.—The type species is *Loeschia coli* Loesch, 1875, found in man, but used in the sense of the term as defined by Schaudinn in 1903, and not as defined by Loesch in 1875.

Classification.—Chatton and Lalung-Bonnaire suggested the formation of two subgenera—viz., Loeschia, characterized by cysts with eight nuclei, and Viereckia, distinguished by cysts with four nuclei, but this has not been adopted so far.

As there are a very large number of species described, we will give a list classified according to the part of the body in which they were discovered, but Schaudinn's statement made in 1903 should be remembered, '*The knowledge of the development is the first postulate of protozoon research*;' and because this knowledge is lacking so much confusion exists.

I. *Intestinal*:—

1. *L. coli* Loesch, 1875.
2. *L. histolytica* Schaudinn, 1903.
3. *L. tetragena* Viereck, 1907.
4. *L. tropicalis* Lesage, 1908.
5. *L. minuta* Elmassian, 1909.
6. *L. nipponica* Koidzumi, 1909.
7. *L. undulans* Castellani, 1905.
8. *L. williamsi* Prowazek, 1911.
9. *L. hartmanni* Prowazek, 1912.
10. *L. butschli* Prowazek, 1912.
11. *L. brasiliensis* Baurepaire-Aragao, 1912.
12. *L. dysenteriæ europaeæ* Popper, 1917.
13. *L. nana* Wenyon and O'Connor, 1917. (This is considered under Vahlkamfia (see p. 323.)
14. *L. minutissima* Brug, 1917.

The researches of Hartmann, Whitmore, Wenyon, Craig, Calkins, and James, have demonstrated that only two of these are good species, viz.:—

Loeschia coli Loesch, 1875.
Loeschia histolytica Schaudinn, 1903.

II. *Hepatic and renal*:—

L. mortinatalium Smith and Weidman, 1910.

This species was found originally in the liver and kidneys of a fœtus born dead.

III. *Buccal*:—

1. *L. gingivalis* Gros, 1849.
2. *L. buccalis* Sternberg, 1862.
3. *L. dentalis* Grassi, 1879.
4. *L. dentalis* Braun, 1883.
5. *L. buccalis* Prowazek, 1904.
6. *L. maxillaris* Kartulis, 1901.

There is only one good species, viz.:—

Loeschia gingivalis Gros, 1849.

IV. *Genito-urinary*:—

L. urogenitalis Baelz, 1883, which may be the same as *Amœba urinæ granulata* Ward, Coles and Friel, which the latter suggests comes from an organism like a protococcus taken into the alimentary canal. Chalmers and O'Farrell consider it to be *L. histolytica* in all probability.

V. *Pulmonary*:—

L. pulmonalis Artault, 1898.

This may be the same organism as *L. mortinatalium* Smith and Weidman, 1910, and both may be *L. histolytica*, as Chalmers and Atkey have reasons for believing that *L. pulmonalis* is very like *L. histolytica*.

VI. *In Abscesses :—*
  L. kartulisi Doflein, 1901.
VII. *In serous exudations :—*
  L. miurai Ijima, 1898.

All the above, except the last, are probably either *L. coli* or *L. histolytica*, while the last may be the Leydenia stage of *Chlamydophrys enchelys* Ehrenberg, which is often classified in the Foraminifera.

If this is accepted, we have only three species to consider—viz.:—

L. coli Loesch, 1875, *emendavit* Schaudinn, 1903.
L. histolytica Schaudinn, 1903.
L. gingivalis Gros, 1849.

And these may, with difficulty, be distinguished as follows:—

(*a*) *Size small—average* 12-20 *microns :—*
  Endoplasm often contains red blood-corpuscles, cysts with one nucleus—1. *Gingivalis*.
(*b*) *Size larger—average* 25-35 *microns :—*
  1. Endoplasm does not normally contain red blood-corpuscles. Cysts usually contain eight nuclei, but may have sixteen—2. *Coli*.
  2. Endoplasm normally contains red blood-corpuscles. Cysts contain one to four nuclei and characteristic chromidial bodies—3. *Histolytica*.

AMŒBÆ IN ANIMALS.—A full list of Amœbæ according to hosts was given by Hassall in 1913 (see references), and therefore we omit the full list given in previous editions, only a short list being given on p. 321 but we may say that in vertebrates and invertebrates a very large number of species have been described, but many of these will probably be found to be the same.

Type Species.—The type species in *Loeschia coli* (Loesch, 1875) Schaudinn, 1903, which we will now describe.

Loeschia coli Loesch 1875, *emendavit* Schaudinn, 1903.

Synonyms.—*Amœba coli* Loesch, 1875; *Entamœba coli* Loesch, 1875.

Probable Synonyms.—*Entamœba tropicalis* Lesage, 1908; *E. nipponica* Koidzumi, 1909; *E. williamsi* Prowazek, 1911; *E. muris* Grassi; and perhaps others (*vide supra*).

Definition.—*Loeschia* with cysts containing eight nuclei, cytoplasm almost always without red blood-corpuscles, ectoplasm invisible except when a pseudopodium is being protruded. Nucleus subcentral, vesicular, with cyclic changes not well marked. Karyosome often with two granules.

Nomenclature.—The correct name is *Loeschia hominis* Casagrandi and Barbagallo, 1897. The name *L. coli* was originally applied by Loesch to the pathogenic amœba which caused dysentery, but the nomenclature was reversed by Schaudinn (as Dobell has pointed out) in 1903, and it is most difficult to alter it at the present time.

History.—In 1859 Lambl published a note referring to the presence of an amœba, associated with other protozoa, in the motions of a case of dysentery, and this was followed by an account by Loesch in 1875 in which he states that he considers these amœbæ to be the cause of dysentery. Grassi, in 1879, was the first observer to demonstrate the presence of amœbæ in the motions of healthy people, and alone or with Calandruccio described encystment, while Calandruccio infected himself *per os* with the cysts. They both noted its non-pathogenicity. Lewis and Cunningham in 1881 saw them in the motions of persons suffering from cholera. In 1894 Celli and Fiocca described and named six species of amœba occurring in man, but it is doubtful what these really are; probably some of them belong to *L. coli*. Grassi's findings were confirmed by Koch and Kartulis, but Kruse and Pasquale in a classical investigation demonstrated that there were two kinds of amœbæ, one harmless and the other the cause of dysentery. It was not, however, until Casagrandi and Barbagallo investigated and defined *L. coli*, which is harmless, that it was possible for Jürgens to make his researches, which, extended by Schaudinn, ended in defining a second amœba named *L. histolytica*, which was considered to be the cause of amœbic dysentery. It has been studied in detail in 1912 by Hartmann and Whitmore with important results, and in an important memoir by James in 1914.

It seems to us that Wenyon's researches into *L. muris* are so important with regard to the opposing opinions of Schaudinn and Werner on the one hand, and Hartmann and Whitmore on the other, that we give this in detail.

Loeschia muris Grassi, 1881.

The life-history of this amœba has been carefully studied by Wenyon in 1907. *L. muris* lives in the cæcum of mice and rats, either freely amongst the contents, or upon the epithelial surface, or in the glands to their ends. It measures up to 30 to 40 microns in diameter.

The food appears to be anything at hand—bacteria, flagellates and their cysts, yeast cells, and cast-off epithelial cells.

The Trophozoite.—The narrow ectoplasm is only distinctly visible in the formation of the pseudopodia, while the granular endoplasm contains the food vacuoles and the nucleus, which latter is distinctly visible as a clear vesicle with a distinct nucleolus.

When stained, the nucleus is seen to have a definite fairly thick membrane, with chromatinic lumps at one or two points. The nucleolus or karyosome is chromatinic, and between it and the nuclear membrane is the linin network with scanty granules of chromatin scattered over it. This is the type of nucleus found in *L. coli*.

Multiplication takes place by binary division and by encystment. In the former a nuclear spindle is formed without chromosomes or an equatorial plate, as the chromatin gathers at the poles, and the nucleus after elongation becomes indented and then divided in the middle, and after some length of time the cytoplasm divides.

The precystic stage is distinguished by having its endoplasm cleared of all large inclusions, and is surrounded by a soft gelatinous wall, through which the remains of food materials can be cast out.

Cystic Stage.—A cyst is spherical or slightly oval, 12 to 14 microns in diameter, and contains a cytoplasm free from food particles, and may or may not contain a refractile body, while the nucleus is large and contains much chromatin. This nucleus divides, by simple division, forming two daughter nuclei, and this binucleate stage, which is of long duration, is characterized by the throwing out of chromatin from the nuclei.

Autogamy.—Each nucleus now gives off reduction bodies which are dissolved in the cytoplasm. These two nuclei are slightly different: in one it is evenly distributed, while in the other it is concentrated at one end; the former migrates towards the latter, and both become alike and throw out chromatin. The nuclei were not seen to fuse, but they elongate greatly, spindles are formed, and they divide, giving rise to four nuclei—*i.e.*, two pairs at opposite poles of the cysts, composed of one nucleus from each of the original forms extending to the opposite pole of the cysts.

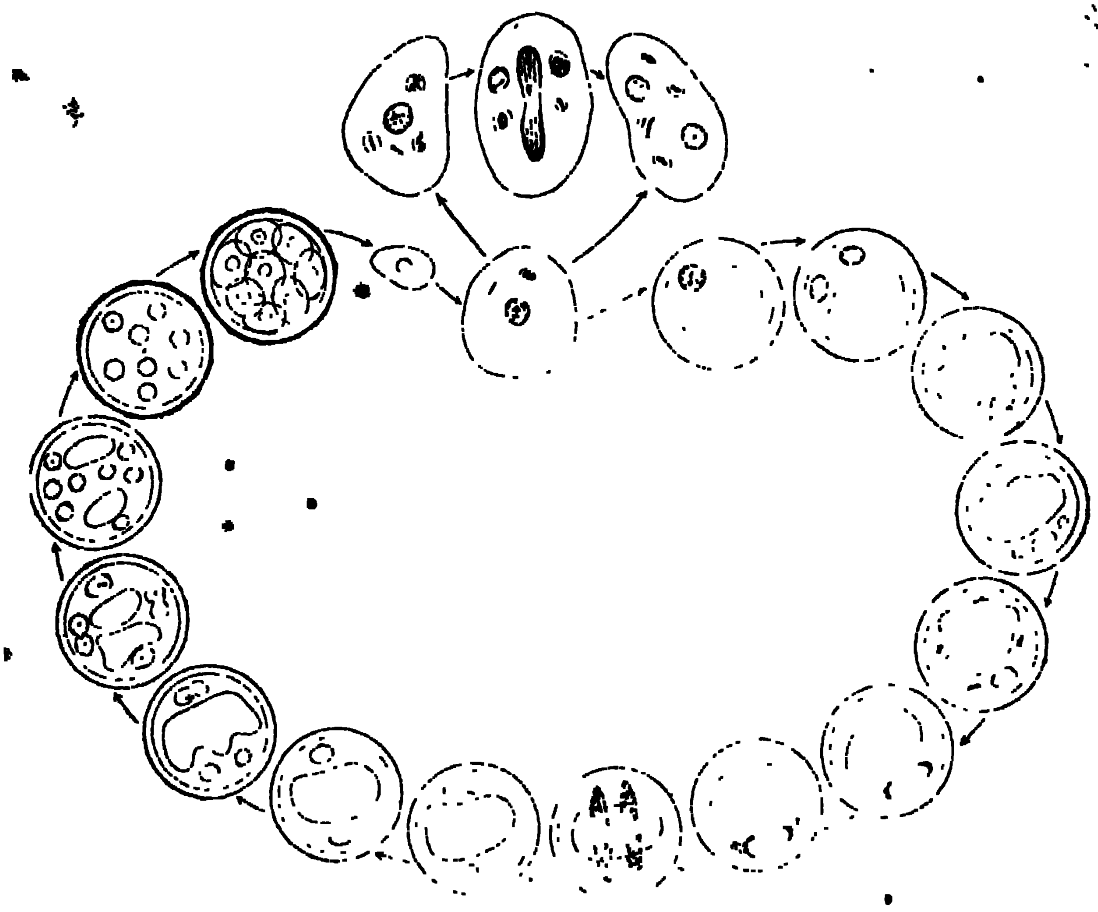

FIG. 49.—DIAGRAM OF THE LIFE-CYCLES OF *L. muris* GRASSI (CONSTRUCTED FROM WENYON'S DRAWINGS).

Each pair then fused to form one nucleus, and then almost immediately divided to form four nuclei, and these again to form eight nuclei.

During this process the soft gelatinous cyst wall of the precystic stage is converted in a tough resistant envelope, inside which an inner membrane is formed (compare *Amœba proteus*). The outer cyst wall becomes tough and irregular in the fæces.

Method of Infection.—The cysts now escape from the intestine in the normal fæces, in which the amœbæ are not seen, these being only found in diarrhœal motions. Cysts were used to infect by feeding a mouse, which was apparently free from infection, and in about three to four weeks cysts appeared for the first time in the fæces.

Wenyon did not see the cysts burst and the amœbæ escape.

Wenyon says: 'When we take into account the striking similarity of these two amœbæ (*L. muris* and *L. coli*), both in the free condition and in their encysting process, it is difficult to avoid the conclusion that they are identical'

In 1917 Wenyon and O'Connor published exceedingly valuable researches on the diagnosis of *L. coli* and on the house-fly as a carrier of the cysts.

We therefore see that while a great deal is known as to the structure, life-history, and method of infection, there is still much to be observed. Are Schaudinn and Wenyon correct in their description of autogamy, or does *L. coli* really form gametes like *Entamœba blattæ*? Is there any true schizogony?

After this rather long history, we will not enter fully into the structure of *L. coli*, but will only present a very condensed account.

Morphology. In diameter it measures as a rule 20 to 40 μ, although forms as small as 10 μ and even 5 μ have been described. The cytoplasm is vacuolated and contains bacteria, and extremely rarely one red corpuscle. The ectoplasm is not visible until a pseudopodium is about to be protruded. The vesicular nucleus resembles that of the tetragena stage of *L. histolytica*, an account of which is given below, but the cyclic changes are not so well defined. The karyosome when present is small, and is composed of two chromidia united by a chromatic substance. At the commencement of a cycle this karyosome is a round compact mass of chromatin connected with the periphery by a linin network with few chromatinic granules. This karyosome breaks up, its chromatin increasing in amount, the linin network becomes thicker, and there are more chromatin granules at its nodes, and this goes on until all the chromatin is collected as blocks under the nuclear membrane and only a small granule is left in the centre, and then the cycle begins again by the growth of the granule into a large karyosome.

Life-History. The life-cycle comprises two phases: a binary division by promitosis takes place (and not by amitosis, as described by Schaudinn). The process of schizogony is described to take place by repeated division into two, forming two, four, and eight nuclei (*vide* Fig. 42, p. 292), which form eight little Loeschiæ which begin the asexual cycle again, but this is very doubtful. Encystment takes place, followed by division of the nucleus into two, four, and finally eight nuclei. During this stage a large vacuole exists in the cytoplasm, which disappears in the eight-nuclei stage. Contrary to Schaudinn, Hartmann and Whitmore believe that no zygosis takes place in the cyst, but that eight little amœbæ are formed which, on escaping from the cyst, they think may conjugate in pairs and form the synkaryon or zygote from which the vegetative forms arise after the manner described by Mercier in 1909 for *E. blattæ*. Sometimes the cysts have more than eight nuclei—*e.g.*, ten or twelve—which must be considered to be abnormal.

Bionomics.—*L. coli* lives in the lumen of the intestine, and feeds upon the contents of the bowel.

Diagnosis.—Amœbæ moving slowly with pale non-refractile pseudopodia, with a thin rim of ectoplasm and with an endoplasm containing all sorts of organisms and no red cells, and with a large distinct nucleus, are *L. coli*, and this diagnosis should be confirmed by the discovery of the cyst because—

1. The typical characters are liable to considerable changes, and the amœba may be very like *L. histolytica*, as will be emphasized below.
2. Wenyon and O'Connor's researches confirm that *L. coli* will not, as a rule at all events, ingest red blood-corpuscles.

With regard to the cysts, they measure from 13–38 microns, but the average is over 25 microns; the typical cyst has eight nuclei and the very large cysts sixteen. At times chromidial bodies may be present, making them look like *L. histolytica* cysts, from which they are to be distinguished by the number of nuclei, which in the motions is generally eight.

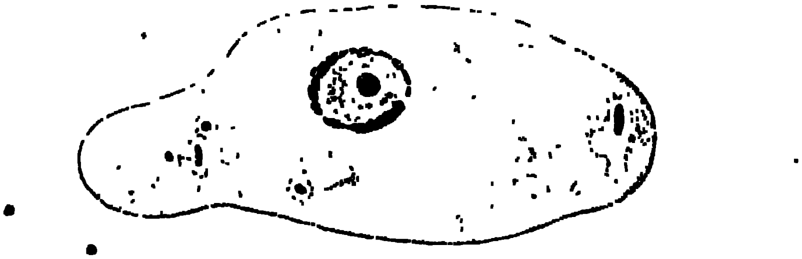

FIG. 50.—*Loeschia coli* SCHAUDINN, VEGETATIVE FORM, STAINED. (× 1050 DIAMETERS.)
(After James.)

Carriage by House-Flies. Wenyon and O'Connor, working in Egypt, have shown that *L. coli* and *L. histolytica* cysts can be ingested by house-flies (Musca, Fannia, Calliphora, and Lucilia) which have fed on fæces containing such cysts. These cysts can live in the gut of the fly so long as any fæcal matter remains there, but die after all the fæcal matter has been expelled, which takes place some twenty-four hours after the fæcal feed. The cysts may be seen in the droppings of the fly as early as five minutes and as late as twenty-four hours after the fæcal feed.

As to the conveyance of cysts on the exterior of the fly, the observations of Kuenen and Swellengrebel and Nicol show that flies do not move far until they have cleaned themselves, so that but little fæcal matter is left, and as this dries the cysts perish.

Method of Infection. The experiments of Calandruccio and of Wenyon and O'Connor have proved that infection takes place *per os*, and is due to the cysts; and that, further, these are introduced most probably by food contaminated by the cyst-laden fæcal matter of house-flies.

Distribution.—*L. coli* is found in both the tropics and the Temperate Zone. In the former it is especially common in the fæces of natives.

Pathogenicity.—*L. coli* is a non-pathogenic commensal found in man, and possibly in rats and mice, and perhaps in other animals. Views as to its pathogenicity have probably arisen through mistaking the tetragena phase of *L. histolytica* for *L. coli*. An Amœba resembling *L. coli* is found in monkeys in which an Amœba resembling *L. histolytica*, and called *L. nuttalli*, is also found.

Loeschia histolytica Schaudinn, 1903.

Synonyms.—*Amœba coli* Loesch, 1875; *Entamœba histolytica* Schaudinn, 1903; *Entamœba tetragena* Viereck, 1907; *E. africana* Hartmann and Prowazek, 1907; *E. minuta* Elmassian, 1909; and *Amœba dysenteriæ* Councilman and Lafleur, 1891. Among the many doubtful species of Amœbæ found in man there must be many names which are synonyms of *L. histolytica*, but comparisons are very difficult, as descriptions are often incomplete—*e.g.*, *Amœba urogenitalis* Baelz, and *Amœba pulmonalis* Artault.

Nomenclature.—The correct name is *Loeschia coli* (Loesch, 1875), as will be explained below.

Definition.—*Loeschia* with cytoplasm often containing red corpuscles and with four nucleate cysts.

Historical.—*Early Observations.*—Loesch discovered the amœba which he named *Amœba coli* in motions from a case of dysentery, and considered it to be pathogenic. It was by this name that Quinke and Roos in 1893 called the organisms found by them in dysentery. As already stated, Councilman and Lafleur called an amœba found in cases of dysentery *Amœba dysenteriæ*, and it is certain that this was Loesch's *Amœba coli*. An amœba somewhat similar to the 'tetragena stage' of *L. histolytica* was seen by Kruse and Pasquale in 1893.

We thus see that the correct name for the dysenteric amœba is *Loeschia coli*, as Dobell has pointed out, and that the correct name for the harmless amœba is *L. hominis*, because Casagrandi and Barbagallo called it *Entamœba hominis* in 1897, when it really had no name. Unfortunately Schaudinn did not utilize this name, and in his revision applied the term 'coli' to the non-pathogenic form, and invented the name *histolytica* for the pathogenic amœba, which is difficult to change at the present time, as there is no certainty that there is at present finality in this nomenclature.

Differentiation.—In 1902 Jürgens for the first time clearly differentiated the pathogenic amœba, and in the following year (1903) Schaudinn studied and compared the morphology and the life-cycles of his *L. coli* and his *L. histolytica*, and thus established their characters, and gave the following account:—

Morphology.—Its average measurement is 25 to 50 μ in diameter, and therefore the average is greater than that of *L. coli*. It consists of clear hyaline ectoplasm and granular endoplasm, in which can be seen red blood-corpuscles, vacuoles, bacteria, and other matters, but the nucleus is not clearly visible unless coloured by some preparation. When resting it is oval or spherical, but during movement it alters its appearance repeatedly, throwing out pseudopodia and creeping about. The nucleus is small, about 5 μ in diameter, and is poor in chromatin, and placed excentrically sometimes close to the periphery. The limiting membrane is difficult to define, and the amount of chromatin is relatively very small. A small karyosome can sometimes be seen in the centre of the nucleus.

Life-History.—It reproduces in three ways: (1) binary fission; (2) gemmation; and (3) sporogony.

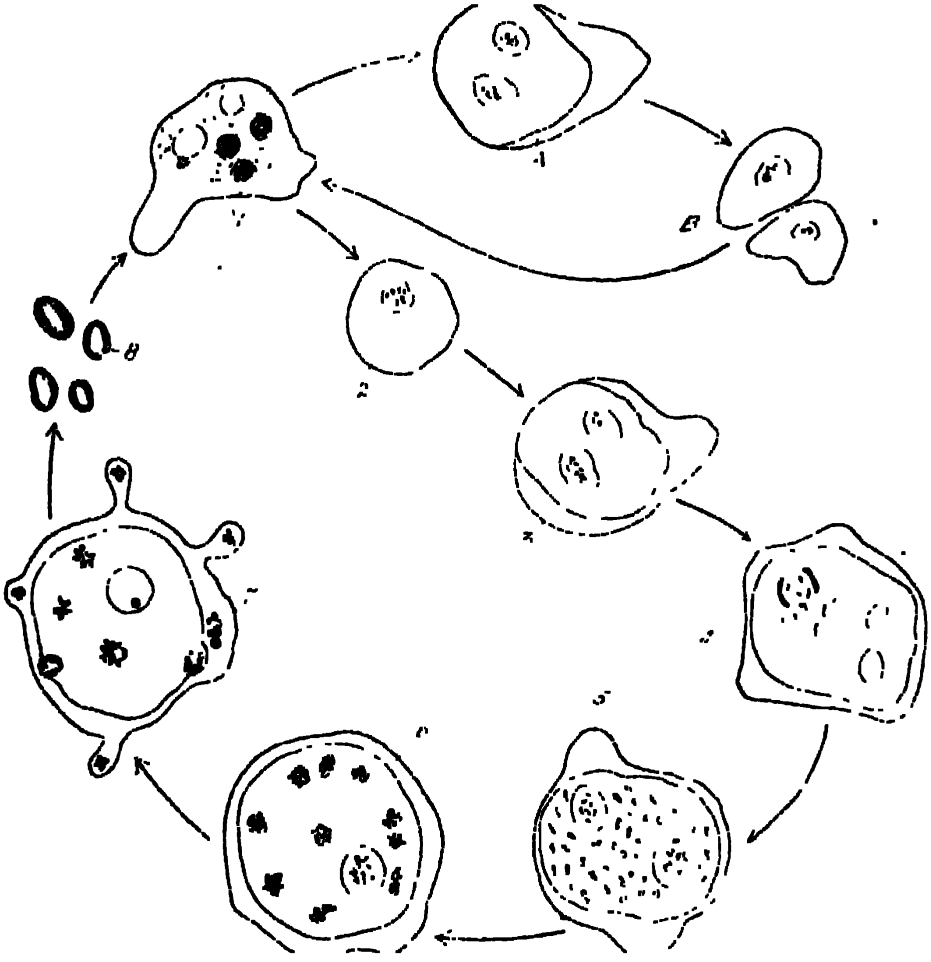

FIG. 51.—DIAGRAM OF THE LIFE-CYCLES OF *Loeschia histolytica* ACCORDING TO SCHAUDINN'S VIEWS.

(Constructed from Craig's drawings in the *Journal of Infectious Diseases*.)

A, B, Binary fission; 1-8, spore-formation.

1. *Binary Fission.*—This method was only discovered by Schaudinn on examining fresh specimens of the infected alimentary canal.

The nucleus divides by amitosis into two, and then the cytoplasm splits into two equal daughter cells.

2. *Gemmation.*—Gemmation, found more commonly than binary fission by Schaudinn, consists of the division of the nucleus by amitosis into two or more daughter nuclei, which, together with small portions of the cytoplasm, separate off from the mother cell, the daughter cell being smaller than the mother cell.

3. *Spore-Formation.*—In spore-formation, which only takes place under favourable circumstances, such as when [illegible] is taking place after an

attack of dysentery, the chromatin in and around the nucleus becomes diffused into the cytoplasm, and finally collects near the periphery, and the remains of the nucleus disappear, being either pushed out or absorbed. The ectoplasm forms small knobs, containing several chromidia in each. These knobs and their chromidia become separated off as rounded bodies, which, becoming surrounded with a yellowish-brown envelope, form the spores for the infection of a new host, as has been shown by Schaudinn's feeding experiments on cats, which developed typical dysentery with the amœbæ in the motions, in the lumen, and in the wall of the alimentary canal. These experiments further proved that it was only by the spores that infection would be spread. The remaining portion of the amœba dies after the formation of the spores.

Recent Work.—Modern researches tend to confirm Schaudinn's morphological description as well as his binary fission, but not the amitotic form of division, while the bud formation (Fig. 52) has been proved by James and others to be artificial, and the spores are regarded as not belonging to an Amœba, but to some other organism in the fæces.

In 1905 Craig in the Philippine Islands confirmed Schaudinn's morphological characters, and called attention to the rapid movements of *L. histolytica* and to the greenish tint which it often assumes in motions containing much blood.

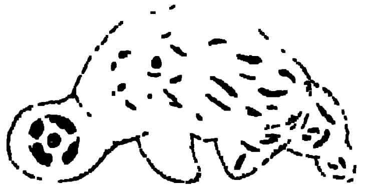

FIG. 52.—ARTIFICIAL BUDDING IN *Loeschia histolytica* SCHAUDINN, IN MOIST CHAMBER PREPARATIONS. (After James.)

In 1907 Viereck stated that there were more than one pathogenic amœba in man. The second one, which he named *Entamœba tetragena*, looked like *L. coli*, but had only four-nucleate cysts, and this, he thinks, is the type seen by Quincke and Roos and by Kruse and Pasquale. In the same year Hartmann and von Prowazek found an entamœba in patients coming from Africa, which could be differentiated by its nuclear structure from *L. coli* and *L. histolytica*, and this they named *E. africana*; but later Hartmann, finding quadrinucleate cysts, concluded that it was the same as *E. tetragena*, which is an accepted fact.

In 1908 Craig, drawing attention to variations in *L. histolytica* and in *L. coli*, emphasized the difficulty in differentiation between these organisms, and in the same year Werner confirmed the existence of *L. histolytica* and of *E. tetragena*.

In 1909 Hartmann states that Schaudinn knew about *E. tetragena*, and that of the three, *L. coli*, *L. histolytica*, and *E. tetragena*, *L. histolytica* is the smallest, and has ectoplasm differentiated from endoplasm even at rest. Its nucleus is excentric, can be distorted, and does not possess a double contoured achromatic membrane, while its lack of chromatin is characteristic, there being only a little karyosome and a condensed layer of chromatin at the margin of the nucleus, while nuclear cyclical changes are rare. In the same year Noc wrote a paper mainly of an epidemiological nature, but also dealing with this amœba, and Elmassian described

E. minuta, which is to-day generally considered to be a stage of *L. histolytica*.

In 1911 there appeared a valuable paper by Walker, in which he distinguished only *L. coli* and *L. histolytica*, but the latter was considered to have 'a tetragena stage,' a fact accepted to-day. He said that *L. histolytica* was hyaline, feebly refrangent, with active motility, feebly staining cytoplasm, and an indistinct nucleus, with a relative paucity of chromatin, which was present as a barely perceptible layer on the inner surface of the nuclear membrane, with or without a few fragments scattered in the nuclear network (histolytica stage), or as a more extensive but loose peripheral granular layer and a loose central karyosome (tetragena stage). All cysts were quadrinucleate.

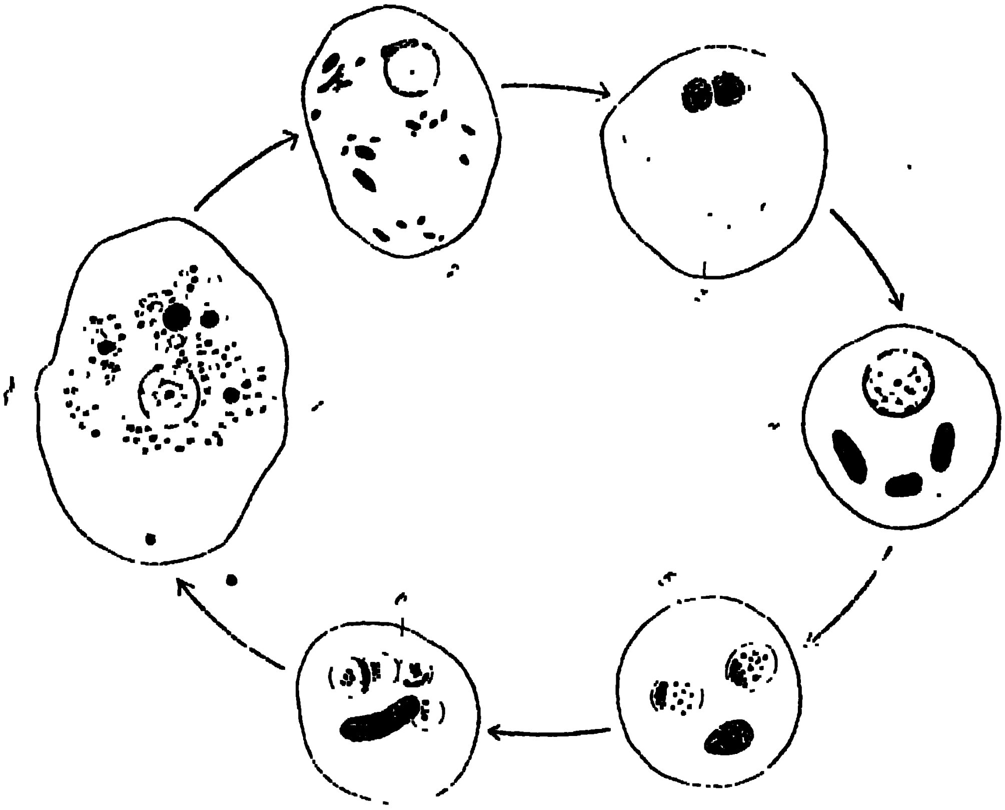

FIG. 53.—DIAGRAM OF THE LIFE-CYCLES OF *Loeschia histolytica* SCHAUDINN.

(Constructed from Hartmann's drawings in the *Archiv für Schiffs- und Tropen-Hygiene*.)

1. Fully grown parasite; 2-6, stages in encystment and nuclear division.

In the same year Whitmore and Akashi published contributions.

In 1912 Hartmann came to the conclusion that there really was only one pathogenic amœba in man, and that this was *E. tetragena*, the morphology and development of which he studied.

This was the view which we adopted in our second edition, and Hartmann's observations may be gathered from the following account:—

Morphology.—It is usually about 25 to 40 μ in diameter, but may be as small as 20 μ, 10 μ, or even 5 μ. When at rest it is spherical, but varies in shape when in motion. The ectoplasm is usually well defined, and in pseudopodia is seen to consist of hyaline highly refractive protoplasm, but this differentiation is sometimes difficult to define. The endoplasm is greyish in colour, and usually contains red blood-corpuscles as well as other matters. The vesicular nucleus is clearly visible, and has a well-defined membrane on which chromatic granules are distributed. In the centre there is a karyosome surrounded by a clear area, and containing a centrosome. A cycle of changes is constantly proceeding in the nucleus: first chromidia break away from the karyosome and pass outwards into the nucleus, and this proceeds until little but the centrosome is left, when it ceases, and chromatin begins to accumulate again around the centrosome, until the karyosome is re-formed, when the cycle begins again.

Life History.—Asexual reproduction is by promitosis. Sporogony is rare, and when it occurs tends to cyst formation, before which the amœbæ become small, and their chromidia form three to six masses. The cyst sometimes contains a large vacuole. Nuclear division takes place until four nuclei are formed. The further life-history is unknown.

In 1912 Calkins gave his account of the Genera and Species of Amœbæ, Hassall his valuable bibliography, Crawley his list of Parasitic Amœbæ, Craig his relationship of Parasitic Amœbæ to Disease, Darling his identification of Pathogenic Panama Amœbæ, and von Prowazek the structure of the nucleus of parasitic Amœbæ, while James contributed two papers on the clinical identification of the Entamœbæ and on infection with *E. tetragena*. In the latter of these papers it is stated that the *histolytica phase* is found in *infections with acute symptoms*, while the *tetragena phase* is found in more *chronic infections*. Craig formulates a life-history for *L. histolytica* as follows:—

1. *Vegetative Stage:* Histolytica-phase in acute dysentery; tetragena-phase in chronic dysentery.
2. *Precystic Stage:* Amœbæ decrease in size (minuta-phase), and the nucleus is intermediate in type between the other two phases.
3. *Cystic Stage:* Cysts 7-20 microns quadrinucleate.

In 1913 Whitmore gives an account of his own and the work of Viereck, Hartmann, and Huber. In 1914 there appeared a most important paper by James detailing historical matter, morphology, and classification and technique, with regard to the Entamœbæ of man. In 1917 Craig gave an excellent summary of the Amœbæ parasitic in man.

We thus see that although *L. coli* and *L. histolytica* are distinct, it is difficult to effect a diagnosis in the *trophozoite phase*, and that histolytica, tetragena, and perhaps minuta, are phases of one and the same organism.

In the same year there appeared papers by Wenyon and O'Connor on the 'Human Intestinal Protozoa in the Near East,' detailing the characters of *E. histolytica*, and by Chalmers and O'Farrall with regard to its presence in the urinary tract, which brings in the synonym *Amœba urogenitalis* Baelz, 1883.

Wenyon and O'Connor consider that no infection can be ascribed to *L. histolytica* unless some amœbæ with included red corpuscles are present or unless typical cysts are present in the stool. An amœba with refractile ectoplasm, and indistinct nucleus and active movement, is most likely to be *L. histolytica*, but these characters alone will not distinguish the organism.

For the diagnosis of Amœbæ they lay down the following rules:--

1. Amœbæ containing red blood-corpuscles are *L. histolytica*, whether the stool is dysenteric or not; and, further, they indicate an active dysentery. These cases urgently require emetine treatment.
2. Amœbæ, none of which contain red blood-corpuscles, occurring in a dysenteric motion are indicative of *L. coli* or of *L. histolytica* in a carrier, while the cause of the dysentery is not an amœba; and these cases should be watched for a few days, without treatment, with a view to finding the cysts.
3. Amœbæ, none of which contain red blood-corpuscles, occurring in non-dysenteric motions may be *L. coli* or *L. histolytica*, and diagnosis has to be made by finding the quadrinucleate cysts, perhaps, after several days' observation.

In 1918 Dobell showed, by experimental infection of tadpoles, that *L. histolytica* and *L. ranarum* were distinct species, and with Jepps drew attention to the existence of diverse races of *L. histolytica*, which could be distinguished by the dimensions of the cysts.

The above does not complete the history, but is as full as space permits, and we will now turn to the morphology.

Morphology.--*Vegetative Stage. Young Trophozoite Phase*.--This phase may also be termed the *histolytica phase*, as defined above.

It occurs when active dysenteric processes are proceeding in the bowel, and is represented as a rule in the fresh condition by large amœbæ measuring from 30-90 microns in diameter, but exceptionally being present in small size. As a rule its motility is very marked, often starting with such a rapid action as to be worthy of the name explosive. The pseudopodia are broad, and may be solely ectoplastic, or be composed of endoplasm as well. The ectoplasm may be clearly distinguishable from the endoplasm even when the amœba is at rest, but often there is no such distinction.

The cytoplasm may have a well-defined light green colour, or more usually this colour is wanting. It may contain a number of vacuoles, or it may not. It often possesses a number of ingested red blood cells, but at times these are wanting. It may be vacuolated, or it may be granular.

The nucleus in the fresh specimen is usually difficult to see. It is excentric, poor in chromatin, and easily altered by internal pressure. It possesses a very delicate membrane, with a few peripherally arranged grains of chromatin.

In stained specimens there is rarely any differentiation of the ectoplasm from the endoplasm. The cytoplasm may contain vacuoles, erythrocytes, and perhaps the phagocyted nuclei of other cells. The nucleus, unless distorted, is roundish, possesses a delicate nuclear membrane, under which a thin band or a few grains of chromatin may lie. The centre of the nucleus is occupied by a karyosome, which may contain a very minute centriole. The space between the karyosome and the nuclear membrane sometimes shows a delicate, poorly staining network, at the nodes of which lie fine granules of chromatin. The cyclical changes described by Hartmann for the next stage are not visible.

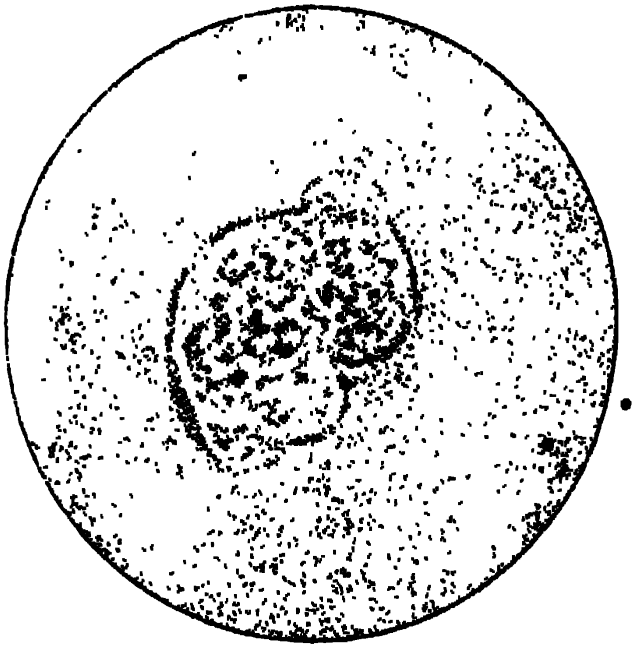

FIG. 51.—PHOTOMICROGRAPH OF THE LIVING AND RAPIDLY MOVING *Loschia histolytica* SCHAUDINN, IN THE YOUNG TROPHOZOITE STAGE OF ACUTE DYSENTERY. (× 1,500 DIAMETERS.)

(From the *Journal of Tropical Medicine.*)

James has pointed out that when stained by Hastings' and Giemsa's method the nucleus takes on a light blue colour, and contains a delicate network of blue threads, and a number of fine red coloured threads and bars scattered irregularly over this network, composed of a substance which he calls '*erythrochromatin*,' to distinguish it from the true chromatin.

Old Trophozoite Phase.—This is the phase so carefully described by Hartmann under the heading *E. tetragena*, and often called the *tetragena phase*. It resembles the *histolytica phase* in many particulars, but differs therefrom in the fact that the nucleus is usually clearly visible as a well-rounded globular vesicle plainly set off from the cytoplasm by a stout double contoured membrane and showing in the middle a small karyosome, surrounded by a clear structureless zone, between which and the nuclear membrane there is a linin network on which granules of chromatin are distributed.

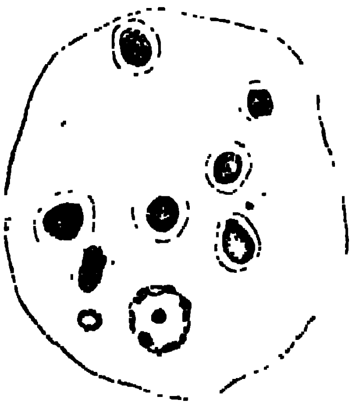

FIG. 55. *Loeschia histolytica* SCHAUDINN, YOUNG TROPHOZOITE, FIXED AND STAINED SHOWING NUCLEUS AND PHAGOCYTED RED BLOOD CELLS. (× 1,050 DIAMETERS.)

(After J.)

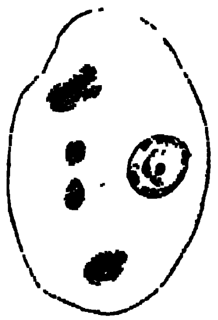

FIG. 56. *Loeschia histolytica* SCHAUDINN, OLD TROPHOZOITE OR TETRAGENA PHASE, STAINED PREPARATION (× 1,050 DIAM-

This nucleus undergoes cyclical changes, but in a given preparation, as a rule, all the amœbæ show the same appearance. The cyclical changes are:—

1. Large blocks of chromatin under the nuclear membrane, a very definite karyosome containing a centriole (Fig. 57, *a*, and 58, *a*).
2. Many small granules of chromatin scattered under the membrane and at the margin of the karyosome (Fig. 57, *b*).

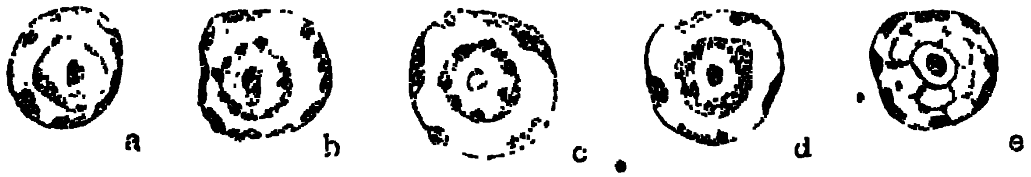

FIG. 57.—NUCLEUS OF *Loeschia histolytica* SCHAUDINN, OLD TROPHOZOITE PHASE. STAINED PREPARATIONS. (× 1,050 DIAMETERS.)

(After James.)

Note the cyclical changes described in the text.

3. Chromatin more concentrated under the nuclear membrane and at the karyosome margin, while a clear zone is appearing around the centriole (Fig. 57, *c*).
4. Chromatin under the membrane and at the karyosome margin (Fig. 57, *d*).

5. Chromatin has left the karyosome margin and passed over the linin network towards the nuclear membrane (Fig. 57, *e*).

6. The centriole swells and re-forms the karyosome, and so the cycle begins again or the amœba divides (Fig. 58, *b*).

Life-History.—*L. histolytica* may reproduce by binary fission during the vegetative stage, or it may encyst.

The first is the method by which it increases its numbers in a given host, and the second is for the purpose of passing from one host to another.

There is no sure evidence of schizogony.

Simple Division.—The centriole divides into two parts, each of which travels to opposite sides of the karyosome and are connected by a thread, the *centrodesmose*. The further stages require study.

Encystment—*Precystic Phase.*—All the amœbæ present in a given case reduce in size (*L. minuta*), but their numbers are augmented. The amœbæ become sluggish and have a clear ectoplasm, but the nucleus is not easy to see, and chromidia may or may not be present in the cytoplasm. The nucleus is spherical, with a thick regular membrane and with chromatin granules near the periphery. The karyosome shows no centriole.

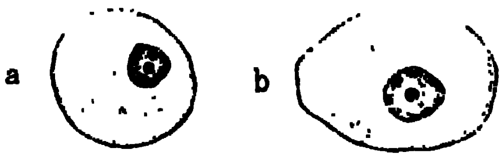

FIG. 58.—*Loeschia histolytica* SCHAUDINN OLD TROPHOZOITE PHASE SHOWING THE FIRST AND LAST STAGES OF THE CYCLICAL NUCLEAR CHANGES. (× 1,050 DIAMETERS.) (After James.)

Cystic Phase.—Different strains produce cysts of different sizes—*e.g.*, small cysts 7-10, medium 9-12, large 12-18 microns in diameter. Chromidia are formed in the cytoplasm, and may be derived from the nucleus, and may function as food material. The cytoplasm becomes granular and the nucleus swollen and elongated. An intranuclear spindle is formed between two centrioles situate at each end. The chromatin forms rows of granules extending from pole to pole. The nucleus divides and the daughter nuclei enter the resting stage, in which they remain for a long time. Each of these subsequently again divide, giving rise to the typical quadrinucleate cysts. Penfold, Woodcock, and Drew have brought evidence to show that, as a rule, the amœba escapes undivided from the cyst. No one has so far seen any flagellate forms or any gametes.

Infection.—Darling in 1913 showed that only the cysts were infective, and that they are ingested with food, and must not have been passed out of the original host longer than two or three days.

Wenyon and O'Connor in 1916 have proved that, as in the case of *L. coli*, house-flies can ingest the cysts, which are subsequently passed on to human food, and so the infection carried from man to man.

These researches clearly prove that the method of infection is by cysts passed in fæcal matter entering the flies, and so reaching human food, as direct fæcal contamination is not so likely, though, of course, it may also be a method of infection.

Further, these cysts are spread abroad by the fæcal matter of *human carriers—i.e.*, persons who have recovered from amœbic dysentery, and even those who have never suffered in this manner. These carriers are the *human reservoir* of the parasite.

Diagnosis.—Amœbæ present in human fæces and containing red blood-corpuscles are, as a rule, *L. histolytica*. Amœbæ without red corpuscles require differentiation by the cysts, which must be sought during several days. Quadrinucleate cysts belong to *L. histolytica*, others are doubtful or definitely negative.

Cultivation.—Since the days of Auerbach in 1856 attempts have been made to cultivate pathogenic amœbæ in pure or contaminated cultures. With regard to *L. histolytica* all such attempts were failures until Cutler apparently succeeded, in 1918, on Dean and Monat's egg medium, to which a few drops of blood had been added, and on blood-clot medium. The media were inoculated with blood and mucus from motions passed not longer than three hours, and were incubated at 28°-30° C. In culture the amœbæ varied from 8-30 microns in size, with homogeneous but often vacuolated cytoplasm containing ingested red blood cells and moving typically like *L. histolytica*. Uninucleate and binucleate forms were seen. Cysts were obtained by ceasing to subculture for two to three days and then placing the culture for two hours in an ice-chest.

Cysts from the culture produced typical dysenteric lesions in cats by feeding and by inoculation high into the rectum by means of a catheter.

Strains.—*Vide* historical section (p. 313).

Pathogenicity.—*L. histolytica* is the cause of amœbiasis in man and animals, causing amœbic dysentery and amœbic abscesses in the liver and other parts of the body.

Loeschia gingivalis Gros, 1849.

Synonyms.—*Amœba gingivalis* Gros, 1849; *A. buccalis* Sternberg, 1862; *A. dentalis* Grassi, 1879; *A. dentalis* Braun, 1883; *Entamœba buccalis* Prowazek, 1904; *A. maxillaris* Kartulis, 1906.

Definition.—Loeschia with cysts containing only one nucleus, cytoplasm often containing red blood-corpuscles, ectoplasm only visible during motion as a clear highly refractive layer. Nucleus as a rule not visible. Reproduction only by simple fission.

History.—This amœba, which occurs in the mouth in healthy and diseased conditions, was first described by Gros in 1849, and was afterwards studied by Sternberg, Grassi, Prowazek, and mentioned by Braun, and is probably the same as Kartulis' organism.

Morphology.—Its size varies from 7-35 microns, the average being 12-20 microns.

The ectoplasm is only well defined during movement, which is quite active, and takes place by short blunt or long tapering pseudopodia. The endoplasm is granular, containing non-contractile food vacuoles and often red blood-corpuscles. The nucleus as a rule is not distinct.

Life-History. Reproduction apparently only takes place by simple fission, while cyst formation, which has been observed, is believed to be purely protective, as they contain only one nucleus. The cysts may measure from 8 10 or more microns.

Animal Experiments. All attempts to produce dysentery in animals by means of this amœba have so far been failures.

Pathogenicity. It has been accused, without sufficient proof, of being the cause of pyorrhœa alveolaris.

Doubtful Species.

The species to be now described are not considered as 'good' by many authorities, but we give a brief account of them for the sake of completeness.

Loeschia tropicalis Lesage, 1908.

Lesage, from his studies of tropical dysentery, has come to the conclusion that, just as there is a *Loeschia coli* Loesch parasitic, but non-pathogenic, in the intestine of man in warm and temperate countries, so there is another amœba parasitic, but non pathogenic, in the intestine of man in the tropics. This parasite he names *L. tropicalis*.

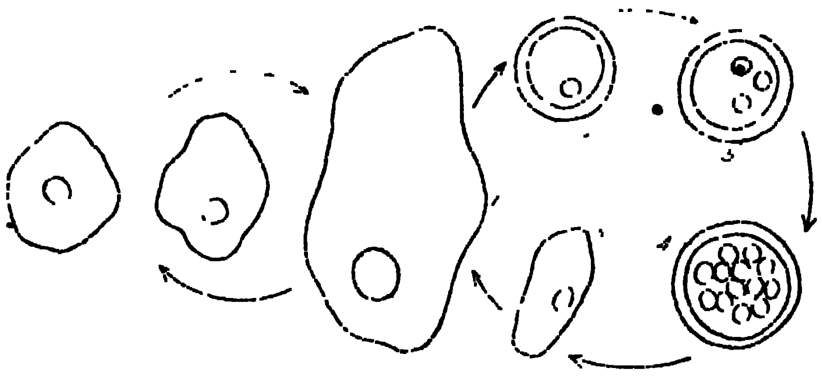

FIG. [illegible].—*Loeschia tropicalis* LESAGE, 1908: DIAGRAM OF THE LIFE-CYCLES CONSTRUCTED FROM LESAGE'S DRAWINGS.

(Constructed from Lesage's drawings in the *Bulletin de la Société de Pathology Exotique*, showing binary fission and spore formation.)

It resembles *L. coli* by having a nucleus which contains much chromatin and by becoming encysted, but it differs from the same in having a clearly visible ectoplasm, by the small size of its cysts, and by the fact that the nucleus of the cysts breaks up into a number of nuclei, which are from three to several (he draws thirteen in one cyst). This entamœba can be cultivated along with bacteria, but is non p[illegible]nic to animals.

[illegible] considers this to be the same amœba which was studied and cultivated by Musgrave and Clegg, and thinks that the production of dysenteric symptoms in their experiments was due to contamination with the minute spores of *Loeschia histolytica*. Walker in 1908 describes as a new species, *E. hominis*, which may perhaps be the same as *L. tropicalis*.

Pathogenicity. It is a harmless commensal in the alimentary canal of man.

Culture. It can be cultivated in symbiosis with bacteria.

Loeschia undulans Castellani, 1905.

Synonym.—*Entamœba undulans* Castellani, 1905.

This amœba was found in fæces from persons suffering from diarrhœa in Ceylon, together with other intestinal protozoa—*e.g.*, Cercomonata and Trichomonata. A somewhat similar amœba has been found by Gauducheau in dogs.

It varies in size, being from 12 to 30 μ in diameter, but there may be much smaller individuals. It has no flagella, but possesses an undulating membrane, and long straight pseudopodia, which are rapidly emitted and retracted, only one pseudopodium being protruded at a time. There is no marked differentiation into ectoplasm and endoplasm, and a non-contractile vacuole is usually to be seen. The cytoplasm, which is finely granular, often contains bacteria. Castellani is inclined to consider this parasite as a developmental stage of *Cercomonas hominis*, as was his original opinion. Perroncito long ago described an amœboid stage of *Cercomonas hominis*. Wenyon considers it to be a stage of a Cercomonas.

FIG. 90.—*Loeschia undulans* CASTELLANI, 1905.

Loeschia phagocytoides Gauducheau, 1908.

Synonym.—*Entamœba phagocytoides* Gauducheau, 1908.

Loeschia phagocytoides was discovered by Gauducheau in Indo-China in a case of dysentery. It is very small—only 2 to 15 μ in diameter—very actively motile, and possessing a well developed ectoplasm. It can be easily cultivated on ordinary agar-agar inoculated with *Bacillus typhosus* or other bacteria, which it readily engulfs and digests. Some individuals show in their ectoplasm peculiar spirochæte-like bodies.

Loeschia minuta Elmassian, 1909.

Synonym.—*Entamœba minuta* Elmassian, 1909.

This amœba, found by Elmassian in a case of chronic dysentery in South America, resembles *L. tetragena*, but is much smaller, rarely exceeding 14 μ in diameter. There is no differentiation between the ecto- and endo-plasm. The nucleus is invisible in fresh preparations, and when stained is rich in chromatin. Encysted forms contain four nuclei.

Loeschia nipponica Koidzumi, 1909.

Synonym.—*Entamœba nipponica* Koidzumi, 1909.

This entamœba was found by Koidzumi in the motions of cases of dysentery and in healthy people in Japan. In the former case it is associated with *L. histolytica*, which it resembles in size (15 to 30 μ) and in the marked difference between the ecto- and endo-plasm. The pseudopodia are never spinose; the endoplasm is vacuolated, and more granular than in *L. histolytica*. The nucleus is well defined (5 to 7 μ), and rich in chromatin. This amœba reproduces by fission, schizogony, and sporogony.

Loeschia hartmanni Prowazek, 1912.

Found in man in Savaii. It is 4 to 13 μ in diameter; nucleus vesicular, 2 to 3·3 μ; cysts small, quadrinucleate, characterized by a thin, bacteria-like arrangement of chromidia.

Loeschia williamsi Prowazek, 1911.

This Loeschia is considered to be identical with *L. coli* Loesch.

Loeschia brasiliensis H. Baurepaire Aragao, 1912.

Resembles *L. coli*. Cysts 7 to 15 μ in diameter, with eight nuclei and a double contour membrane. The cysts are characterized by the presence of a certain amount of siderophile substance which divides the cysts into two portions of nearly equal size.

Loeschia butschlii Prowazek, 1912.

Synonym. *Entamœba butschlii* Prowazek 1912.

Found in a boy in the Caroline Islands. It varies in size from 10 to 24 μ; coarse alveolar cytoplasm; nucleus vesicular; round karyosome and centriole; cysts roundish said to differ from those of *L. coli*.

Loeschia mortinatalium Smith and Weidman, 1910.

Synonym.- *Endamœba mortinatalium* Smith and Weidman, 1910, and perhaps *Amœba pulmonalis* Artault, 1898.

Definition. Loeschia of large size, 22-38 × 20-25 microns, with nucleus 10 microns in diameter, with well-defined membrane, large karyosome, and occasionally a centriole.

Remarks.- Somewhere about 1800 Ribbert found amœbæ in the kidneys and parotid glands of infants. In 1898 Artault observed amœbæ with a nucleus and a vacuole in a lung cavity. Brumpt has seen similar amœbæ and R. Blanchard has found some in the lungs of sheep, which may or may not be the same as the *Entamœba ovis* Swellengrebel, 1914, found in the gut of sheep.* This latter measures 12-14 × 11-12 microns. Its cysts are 8 microns in diameter, uninucleate, with a glycogen vacuole. In 1904 Jesionek and Kiolemenoglou found amœbæ in the kidneys, liver, and lungs of an eight months syphilitic fœtus. In 1910 Smith and Weidman found an amœba in the kidneys, liver, and lungs of stillborn full-term fœtus, and in 1914 they found their *L. mortinatalium* again in the lungs of a two-months old child which was syphilitic and died of pneumonia. Athey and Chalmers have observed amœbæ in the sputum and in the lungs of a case of pneumonia in the Anglo-Egyptian Sudan unassociated with any known history of dysentery, which they thought were possibly *L. histolytica*. Time must show what these amœbæ really are.

Loeschia minutissima Brug, 1917.

Synonym. *E. minutissima* Brug, 1917.

A very small amœba, 4·11 - 4·8 microns. Usually 6·5-7 × 5-6 microns.

Loeschia tenuis Kuenen and Swellengrebel, 1917.

This amœba, which was described as *Entamœba tenuis*, measures 6-9 microns in diameter, with cysts 6-8 microns, and one to four nucleated, is very like *E. nana* of Wenyon and O'Connor and the *E. minuta* of Woodcock and Penfold, which latter, however, is said to be the same as *E. histolytica*.

Loeschiæ in Animals.—Though somewhat beyond the bounds of the present work, we may mention that amœbæ, believed to belong to the genus Loeschia, but requiring restudy in the light of recent researches, occur in several vertebrates—*e.g.*, *L. nuttalli* Castellani, 1908, found in liver abscesses and dysentery in monkeys in Ceylon; *L. cobayæ* in guinea-pigs, *L. enterica* in cats, etc., *L. muris* Grassi in mice, considered by Wenyon to be *L. coli*, *L. fecalis* in several animals, *L. intestinalis* in horses, etc., *L. galloparvæ* in turkeys, *L. ranarum* Grassi in frogs, and many more.

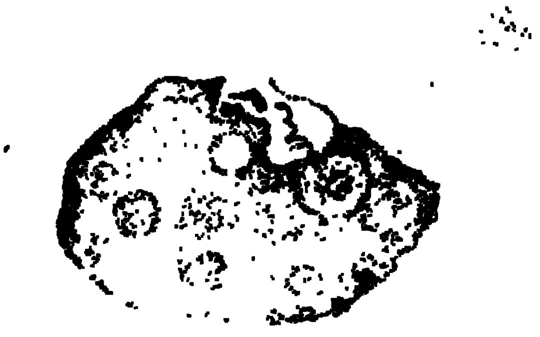

FIG. 61.—*Loeschia nuttalli* CASTELLANI, 1908 CONTAINING RED BLOOD CELLS.

Genus Vahlkamfia Chatton and Lalung-Bonnaire, 1912.

Definition. *Gymnamœbida*, with vesicular nucleus (protokaryon) having one large karyosome with or without a centrosome, with little peripheral chromatin, with division by promitosis. Cysts typically uninuclear.

Remarks.—Practically all cultivable amœbæ isolated from human stools and potable water by various observers belong to this genus. Cropper has grown a peculiar amœba belonging to this genus in citrate solution.

Type.—*Vahlkamfia limax* Dujardin, 1841, *emendavit* Vahlkamf, 1904.

Vahlkamfia punctata Dangeard, 1910.

This amœba was found in Indo-China in the motions of a case of diarrhœa. The ectoplasm is rarely visible, and the endoplasm is very basophile, while the method of division is by promitosis. The cysts are 8 to 12 μ in diameter, with a thin wall showing a double contour ornamented with punctations, and always uninucleate.

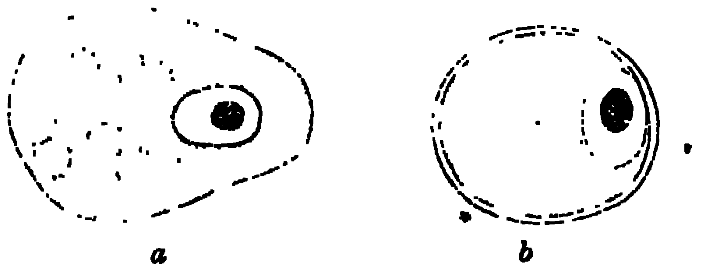

FIG. 62.—AMŒBA AND CYST FOUND IN HUMAN FÆCES AND POSSESSING THE LIMAX TYPE OF NUCLEUS. (*a*) TROPHOZOITE, (*b*) CYST. (× 1,950 DIAMETERS.)

(After James, from the *Annals of Tropical Medicine and Parasitology*.)

Vahlkamfia lobospinosa Craig, 1912.

Synonym.—*Amœba lobospinosa* Craig, 1912; *V. withmorei* Hartmann, 1912.

This amœba was cultivated from a dysenteric stool from a patient in Manila in 1905, and first described by Musgrave and Clegg. In 1912 it was studied by Craig and called *Amœba lobospinosa*, also by Williams and Calkins, by James, by Liston, and by Wells.

James, in the Canal Zone, obtained this amœba for a considerable period from the fæces of a patient which were guarded against contamination, and hence it must be admitted that it can live for a time in the intestine of man, but it is probably non-pathogenic.

On the other hand, in all the other reported cases it has occurred as an aerial contamination of the fæces or pus in which it has been found. It was first cultivated by Musgrave and Clegg.

OTHER SPECIES.

In 1917 Kuenen and Swellengrebel divided the species of *Limax amœba* into three types, the *Limax*, the *Endolimax*, and the *Pseudolimax*; but taking *V. limax* Dujardin, 1841, *emendavit* Vahlkampf, 1904, as the type species, and allowing that *V. lacustris* Naegler, 1909, is the same species, the following are known:

A. *Small forms, 3-15 microns*:—
Cysts 1·5 microns in diameter—*V. limax* Dujardin, 1841, *emendavit* Vahlkampf, 1904.
Cysts over 7 microns in diameter.
(*a*) Karyosome surrounded by a peripheral row of chromatin granules—*V. lacertæ* Hartmann, 1907.
(*b*) Karyosome not so surrounded—*V. froschi* Hartmann and Prowazek, 1907.

B. *Medium-sized forms, 15-30 microns*.—
(*a*) Trophozoite binucleate—*V. diploidea* Hartmann and Naegler, 1908.
(*b*) Trophozoite uninucleate:
1. Contractile vacuole present—*V. tachypodia* Glaeser, 1912.
2. Contractile vacuole absent—*V. polypodia* Schutze, 1875.

C. *Large forms reaching to 50 microns*:—
(*a*) Trophozoite binucleate—*V. binucleata* Gruber, 1884.
(*b*) Trophozoite uninucleate:—
1. Ectoplasm like a lamella—*V. lamellipoda* Glaeser, 1912.
2. Ectoplasm not so distinct:—
(1) Nuclear division promitotic—*V. albida* Naegler, 1909.
(2) Nuclear division mesomitotic—*V. guttula* Dujardin, 1912.

V. binucleata may be a stage in the development of Pelomyxa, which appears to be impossible to Jepps and Dobell, while Alexeieff places it in a genus Hartmannella with a type *H. hyalima* Dangeard, which Jepps and Dobell say is quite different. It probably requires a new genus creating for itself. *V. diploidea* was obtained by Hartmann and Naegler in cultures from lizard fæces, and has been found by Jepps and Dobell in human fæces which had been kept for some time. Alexeieff proposes to place it in *Sappinia* Dangeard, 1896. *V. pædophthora* Caullery, 1910, is like *V. limax*, but is parasitic in the eggs and embryos of a crab, belonging to the genus Peltogaster.

Vahlkamfia nana Wenyon and O'Connor, 1917.

Synonym. *Entamœba nana* Wenyon and O'Connor, 1917; *Vahlkamfia nana* Brug, 1917.

Definition. -*Vahlkamfia* of small size (5-10 microns), moving slowly, with blunt ectoplasmic pseudopodia, nucleus with membrane and large central karyosome, cysts 7-8 × 8-10 (when elongated) microns with one to four nuclei, without chromidial bodies.

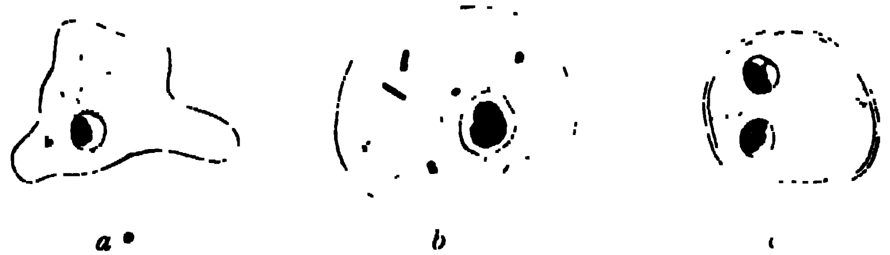

FIG. 63.—*Vahlkamfia nana* (WENYON AND O'CONNOR, 1916).
(*a*) Trophozoite, fresh conditions; (*b*) trophozoite stained preparation; (*c*) cyst with two nuclei.
(After Wenyon and O'Connor, from the publications of the Wellcome Bureau of Scientific Research.)

Remarks.- This amœba was found by Wenyon and O'Connor in Egypt, and we have seen it in the Anglo Egyptian Sudan and Southern Italy. It has been confused with *E. coli*, *E. histolytica*, and *V. limax*. *V. nana* has not been cultivated.

Time will be required to show definitely its generic position. Provisionally we have placed it under Vahlkamfia, though its cyst is binucleate.

Genus Dientamœba Jepps and Dobell, 1918.

Definition.- -*Gymnamœbida* of small size, without a known flagellate stage, and typically binucleate, with both nuclei of the same size and structure.

Type Species.- *Dientamœba fragilis* Jepps and Dobell, 1918, found in man. It is the only known species at present.

Dientamœba fragilis Jepps and Dobell, 1918.

Definition.- --*Dientamœba* with the generic characters.

Historical.- -This amœba was first detected by Jepps and Dobell in 1917 in a native of the British Isles who had never been abroad, but was suffering from slight diarrhœa, attributed to a chill. It was found in British soldiers who had been to Salonika, and in natives of New Zealand serving as soldiers. In all it has been seen in seven cases.

Morphology.—It is a very small active organism, measuring when rounded some 3·5-8-10-12 microns in diameter, and moving about by means of extremely thin, hyaline, leaf-like pseudopodia composed of sharply defined ectoplasm. The rest of the body is often rounded, and consists of granular endoplasm, and is situate posterior to the pseudopodia, thus giving a snail like appearance during active movement.

The cytoplasm is alveolar and contains bacilli and cocci. There is no contractile vacuole, but there are diffuse brown-stained patches indicative of glycogen in iodine-stained preparations. The amœba is binucleate in about 80 per cent. of the forms examined, and these nuclei are usually invisible in the living organism. In stained preparations they are 2 microns in diameter, and each contains a large central karyosome surrounded by a clear zone, which is traversed by a few very fine radiating linin threads, and which separates the karyosome from the extremely delicate nuclear membrane, on which there is no chromatin. There is sometimes a separate granule to be seen lying in the centre of the karyosome, which is the centriole of many authors.

Life-History.—No signs of division or cyst formation have been observed.

Habitat.—The intestine of man, probably in the colon.

Food.—Small bacteria and yeasts living in the intestinal contents.

Pathogenicity.—It is believed to be non-pathogenic.

Cultivation.—So far all attempts at cultivation have failed.

Binucleate Amœbæ.—We have already noted under the genus Vahlkamfia two binucleate amœbæ in addition to *V. nana*—viz., *V. diploidea* Hartmann and Naegler, 1908, with occasional uninucleate forms, and *V. binucleata* Gruber, 1884, and have shown that they probably are not *Vahlkamfia* and equally they are not *Dientamœba*. Another binucleate form may be *Amœba mira* Glaeser, 1912, about which there appears to be much doubt as to whether the name was given to a binucleate or uninucleate form. Schaudinn's *Paramœba* is a marine binucleate amœba, and forms a genus in which Janicki in 1912 placed some of Grassi's parasitic amœbæ found in Sagitta. In these amœbæ the two nuclei are dissimilar, one being a nucleus and the other a Nebenkoerper. Craigia (*vide infra*) may also possess two dissimilar bodies, one a nucleus and the other like a Nebenkoerper.

Genus Craigia Calkins, 1912.

Definition.—*Gymnamœbida*, free swimming or parasitic, with a uniflagellate swarm stage, and with or without an extranuclear Nebenkoerper-like body in the endoplasm. Ectoplasm seen on movement; size 10-25 microns.

History.—In 1896 Schaudinn described the life-history of *Paramœba eilhardi* Schaudinn, 1896, which possessed a cytoplastic extranuclear body, which he called a 'Nebenkoerper.' Reproduction was by simple fission and by cyst formation, in which the parasite broke up into a number of spores, each of which contained a piece of the nucleus and a piece of the Nebenkoerper. Each of these spores develops two flagella, and breaking out of the cyst forms the swarm stage. Finally the flagella are lost, after longitudinal division, and the spores become small amœbae.

In 1906 Craig found a parasite resembling that described by Schaudinn in the fæces of patients suffering from chronic dysentery in the Philippine Islands. He considered that they were the pathogenic agent of the symptoms from which the patients suffered, and because of their similarity to Schaudinn's organism called them *Paramœba hominis* Craig, 1906, and as such we described them in the first two editions of this work.

In 1912 Calkins considered that Craig's parasite could not be classified in the genus Paramœba, because its swarm spores have only one and not two flagella, while its extranuclear body is apparently different from that in Paramœba. He therefore gave it the name *Craigia hominis* (Craig, 1906), which Jepps and Dobell consider a non-existent organism and the genus a *nomen nudum*.

In 1915 Barlow discovered a new species, which he called *Craigia migrans* in Honduras.

Craig thinks that probably infections with this parasite are widespread, and that they may be often confounded with Cercomonads, etc.

Species.—There are four known species—viz., two parasitic in marine worms and two parasitic in man. The latter are distinguished as follows:—

A. Small accessory extranuclear body present in larger forms. Flagellate forms multiply by longitudinal division—*Hominis*.

B. Small accessory extranuclear body absent. Flagellate forms do not divide—*Migrans*.

Craigia hominis Craig, 1906.

Synonym.—*Paramœba hominis* Craig, 1906.

Definition.—Craigia in which the accessory nuclear body is present in the larger forms, and the swarm spores divide longitudinally, the accessory body and the motile organ participating in this division.

History.—It was discovered in 1906 by Craig, in the Philippine Islands, in cases of chronic diarrhœa, and in 1915 by Barlow, in Honduras, where it not only causes a form of chronic diarrhœa, but also severe ulcerative conditions of the intestine, resembling those of amœbic dysentery. Barlow fully confirmed Craig's observations.

Morphology.—In the *amœba stage* it measures from 15-25 microns, and possesses an ectoplasm which is clearly visible during motion, but not while at rest. The endoplasm is granular, and contains a nucleus which is distinct and composed almost entirely of chromatin. There is also an extranuclear body which is of an accessory nature.

Life-History.—The amœba can reproduce by binary division for some time, at the end of which it encysts, surrounding itself with a double contoured envelope, and divides into a number of small, spherical bodies, each of which contains a piece of the nucleus and a portion of the accessory body. The cyst now ruptures and the spores escape as uniflagellate swarm spores, some 3-20 microns in length. This is the *flagellate stage*. These little pear-shaped flagellates divide by longitudinal fission, in which the accessory body and the flagellum take part. Later the flagellates cease to move, lose their flagella, and become amœbæ, thus completing the cycle of the life-history.

Cultivation.—We are not aware of any attempts at artificial cultivation.

Pathogenicity.—It causes chronic diarrhœa and dysentery in man.

Craigia migrans Barlow, 1915.

Definition.—Craigia in which the accessory nuclear body is absent and in which the swarm spores do not divide longitudinally before becoming amœbæ.

History.—It was discovered by Barlow in fifty-one infections in Honduras, where it caused a severe dysenteric condition in the lower bowel and sometimes liver abscess. Barlow notes that it may be necessary to place this species in a genus distinct from Craigia.

Morphology.—The amœba measures some 12-30 microns, the average being 20 microns. The endoplasm is granular and contains a nucleus, but no accessory nuclear body.

Life-History.—The cysts measure 18 microns, and the flagellates, of which there are forty or more in a cyst, about 3.5 microns. These flagellates do not divide, but pass directly into the amœba stage.

Pathogenicity. It causes severe dysenteric lesions and liver abscess in man.

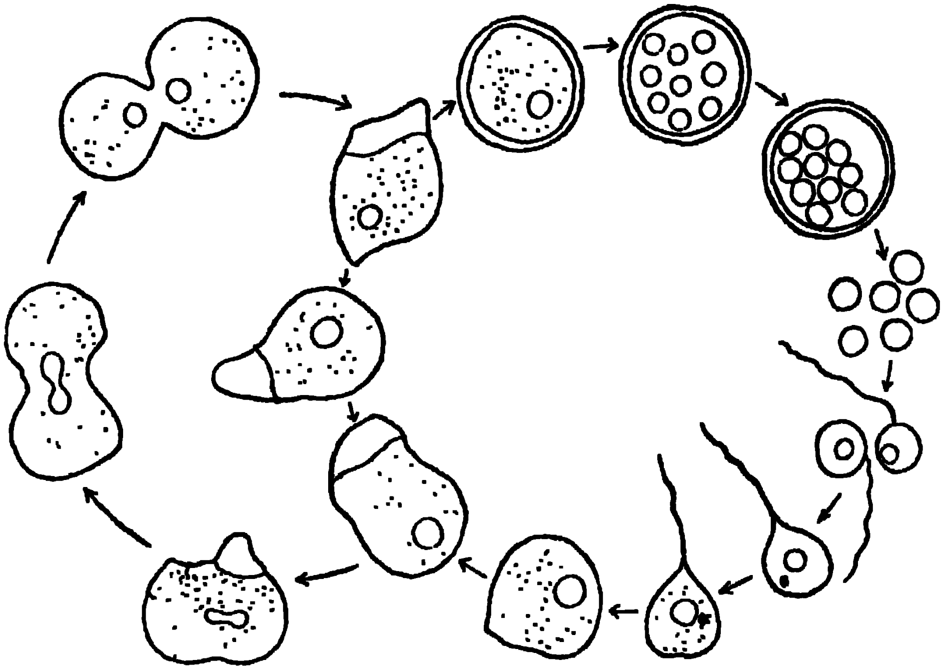

FIG. 64.—DIAGRAM OF THE LIFE-CYCLES OF *Craigia hominis* CRAIG. (After Craig, from the *American Journal of Medical Sciences.*)

ORDER II. THECAMŒBIDA.

Synonyms.—*Filosa* Leidy, 1879; *Testacea.*

Definition.—Amœbæ with a shell composed of different materials cemented on a chitinous base. Through the single opening in this shell pseudopodia, which may be lobose or branched but which never anastomose, project.

FAMILY GROMIIDÆ Eimer and Fickert, 1899

Definition. Thecamœbida with simple shell, composed for the most part of chitin, without calcareous deposits and single chambered.

Genus Chlamydophrys Ehrenberg.

Type Species. *Chlamydophrys enchelys* Ehrenberg.

Chlamydophrys enchelys Ehrenberg.

Synonym.—*Chlamydophrys stercorea* Cienkowsky, 1876, *Leydenia gemmipara* Schaudinn, 1896.

This rhizopod (Fig. 66), which is believed to be parasitic in man in one stage of its life-history, can be found growing in human fæces, as well as in those of the cow, the rabbit, the mouse, and the lizard. It is oval in form, enclosed by a shell, except anteriorly, where the filiform pseudopodia project. The body of the parasite is divisible into an anterior portion, in which lie the contractile and food vacuoles, and a posterior, with the nucleus. Reproduction is by 'bud-fission,' by which is meant that half the protoplasm protrudes at the mouth and forms a new shell, and then separates from the other half, which retains the old shell. If two forms reproduce by 'bud-fission' close together, the daughter cells may partially coalesce (plasmogamy), forming large colonies of twenty or more individuals. The parasites may become encysted.

The sexual process starts by the extrusion of all foreign substances and the collection of the remainder of the plasma and the chromidia into the shell.

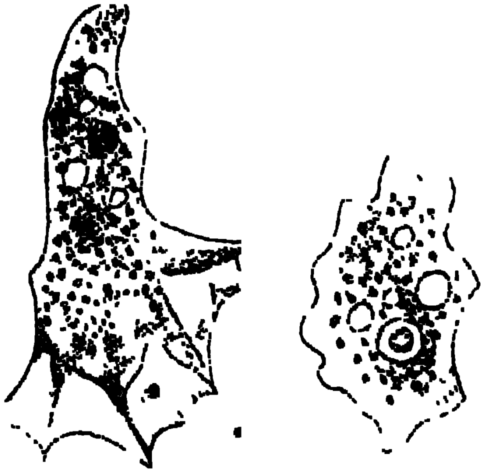

Fig. 65. *Chlamydophrys enchelys* (Leydenia Stage) Ehrenberg. (After Schaudinn.)

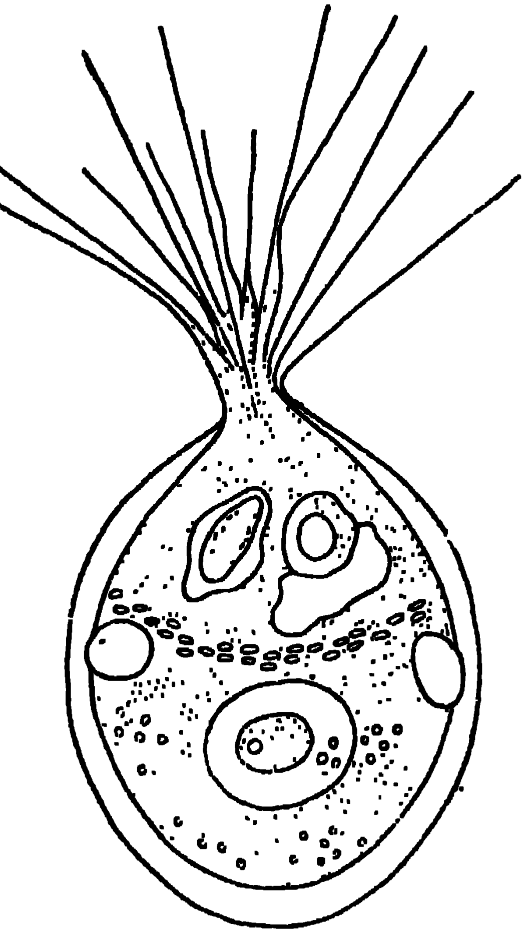

Fig. 66.—*Chlamydophrys enchelys* Ehrenberg. (After Cienkowsky.)

The chromidial mass breaks up into a number of nuclei, never more than eight, around which the plasma divides, forming swarm cells, which, developing two flagella at one pole and escaping from the cell, conjugate with the swarm cells of another individual, and then become encysted. When the cyst ruptures under favourable circumstances, a little amœba escapes, which speedily forms a shell, and becomes in due course an adult Chlamydophrys. If, however, it enters man it may remain in the amœboid stage, and as such was formerly called *Leydenia gemmipara* by Schaudinn. They were, however, originally observed by Lieberkühn in ascitic fluid taken from persons suffering from a malignant growth, but he did not determine their true nature. Leyden, again observing these cells in two similar cases, caused them to be examined by Schaudinn. Lauenstein and Behla have also seen them in a case of cancer.

They are spherical or irregularly polygonal, 3 to 36 μ in diameter, with knobs projecting from the surface. They possess a distinct ectoplasm with hyaline pseudopodia and a large vascular nucleus. Development takes place by binary fission and gemmation (Fig. 65).

Classification.—We have retained the old classification for the organism, and have not placed it in the Foraminifera, as is done by many authors.

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CHAPTER XVIII

MASTIGOPHORA AND PROTOMONADINA

Mastigophora—Euflagellata—Protomonadina—Monozoa—Oicomonadidæ—Bodonidæ—Cercomonadidæ—Tetramitidæ—References.

MASTIGOPHORA Diesing, 1866.

Definition.—Plasmodromata with one or more permanent flagella which serve as organs of locomotion, and at times for the capture of food.

Morphology.—The Mastigophora are usually microscopical in size, but have a tendency to colony formation.

The ectoplasm is present in the form of a sheath called the periplast, a term which is really botanical in its meaning. The periplast contains contractile elements called myonemes. The flagellum may be situate anteriorly (tractellum) or posteriorly (pulsellum); there may be but one (monomastigote), two, or four of equal length (isomastigote), one long and one short (paramastigote); one anterior and one posterior (heteromastigote); several flagella placed together (polymastigote), or numerous flagella scattered over the body (holomastigote).

The typical flagellum consists of an elastic axial core more or less enclosed in a contractile sheath from which the 'end-piece' projects. It takes its origin from a granule situated in the cytoplasm, and apparently forming only a swelling at its base. The swelling is, however, a centrosome, to which various names have been applied, such as basal granule or blepharoplast. Sometimes this centrosome is contained in a special nucleus which is called a kinetonucleus. The centrosome-blepharoplast may be single, when there is only one flagellum; or multiple, when there are many flagella. The flagellum may, however, penetrate deeper into the cytoplasm, until it reaches the nucleus. This prolongation is called the rhizoplast, which may represent the central spindle (centrodesmose) of the achromatic elements of the dividing nucleus, and which connects the divided portions of the original centrosome; or it may have arisen simply as an outgrowth from the blepharoplast. Thus, the various parts of the flagellum may be rhizoplast, blepharoplast, sheath or envelope, and end-piece.

If the centrosome is single, it may be intra- or extra-nuclear, and in either case is a centrosome-blepharoplast; if multiple, the portion connected with the nucleus is the centrosome, and that connected with the flagellum is the blepharoplast.

The periplast in the heteromastigotes may be drawn out into an undulating membrane which helps locomotion.

When the periplast is thin or absent the body-form may still be preserved by an internal stiff rod—as, for example, the axostyle of Trichomonas.

There is a difference of opinion as to which is the anterior end of the mastigote. We believe, with Sambon, that the non-flagellate end should correctly be considered as the anterior end, but several authorities hold quite different views, and our anterior end will correspond with many other writers' posterior. Very often there is a depression somewhere on the surface of the animal, generally near the base of the flagellum, which is intended for the reception of food, and is called the mouth or cytostome; more rarely there is an œsophagus leading into the interior of the cell. Nutrition may be holozoic or holophytic, but this hardly concerns us, as the forms to be described are all parasitic, and live in fluids from which they absorb nourishment by their whole surface.

In the cytoplasm there is a nucleus, and in certain forms two nuclei: a trophonucleus for nutrition, and a kinetonucleus for movement. The character of these nuclei will be dealt with in detail in the section Trypanosomidæ. The cytoplasm may also contain food vacuoles, contractile vacuoles, chromatin particles, and metaplastic granules.

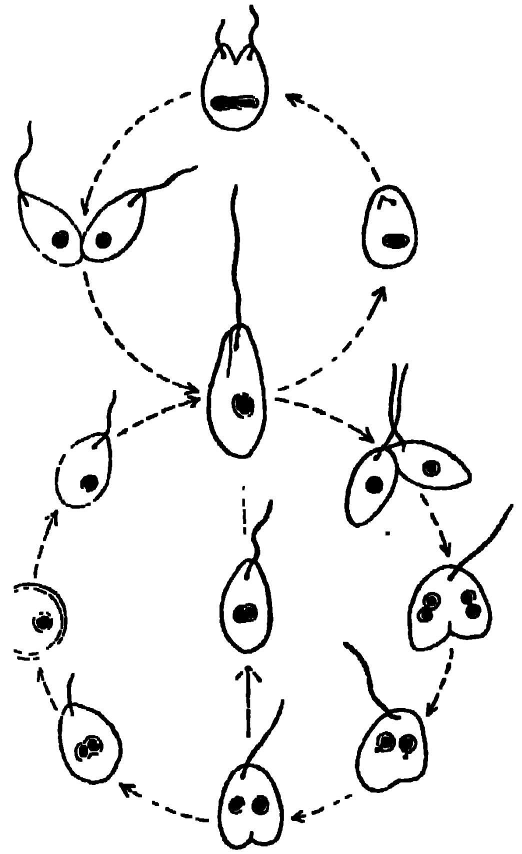

Fig. 97. Diagram of the Life-Cycles of a Mastigote (*Copromonas subtilis* Dobell).

The upper cycle demonstrates simple fission and the lower sporogony.

(After Dobell, from the *Quarterly Journal of Microscopical Science*.)

Life-History.—Reproduction takes place asexually by simple division. Latent or encysted forms are also known.

The whole subject of the structure and life history of the parasitic Mastigophora requires much further research, which, indeed, is being rapidly carried out all over the world—in fact, so rapidly that it is hardly possible to write anything on the subject as a whole which will not quickly be out of date.

Classification.—The Mastigophora may be divided into subclasses as follows:—

A. *Body inflated with gelatinous substance*—Subclass 1, *Cystoflagellata* Haeckel, 1873.

B. *Body not so inflated* :—

I. Periplast markedly thickened, with two flagella arising in the middle of the body, one trailing and one lying in the transverse groove—Subclass 2, *Dinoflagellata* Bütschli, 1885.

II. Periplast thin, with a variable number and arrangement of flagella—Subclass 3, *Euflagellata* Cohn, 1887.

Only the third subclass concerns us.

SUBCLASS EUFLAGELLATA Cohn, 1887.

Definition.—Mastigophora without body inflated with gelatinous substance, and possessing a thin periplast and a variable number and arrangement of flagella.

Classification.—The Euflagellata may be classified into orders as follows :—

A. *Chromatophores often present* :—

I. With cellulose envelope—Order 1, *Phytomonadina* Blochmann, 1895.

II. Without cellulose envelope :—

A. Small forms without oesophagus or vacuole system—Order 2, *Chromomonadina* Klebs, 1892.

B. Large forms with oesophagus and vacuole system—Order 3, *Euglenoidina* Bütschli, 1884.

B. *Chromatophores absent* :—

I. Amoeboid forms in which the food is captured by pseudopodia—Order 4, *Rhizomastigina* Bütschli, 1884.

II. Non-amoeboid forms in which the food is usually captured by flagella—Order 5, *Protomonadina* Blochmann, 1895.

We are only concerned with Order 5, Protomonadina.

ORDER V. PROTOMONADINA Blochmann, 1895.

Definition.—Euflagellata in which chromatophores are absent and in which the individuals are non-amoeboid and usually capture their food by flagella.

Remarks.—As defined above, the Protomonadina is a large order, and includes the Polymastigina of Bütschli and Blochmann, as well as the Binucleata of Hartmann, both of which were treated as separate orders in our previous editions. We, however, foreshadowed a return to Doflein's method of classification, and discussed the whole subject on pp. 282 and 283 of the second edition.

Classification.—So large is this order that, for convenience' sake as well as for morphological reasons, it may advantageously be divided into two suborders after the method of Hartmann and Chagas, which is as follows:—

A. No tendency to bilateral symmetry in undividing forms—Suborder 1, *Monozoa* Hartmann and Chagas, 1911.

B. More or less tendency to bilateral symmetry in undividing forms—Suborder 2, *Diplozoa* Hartmann and Chagas, 1911.

SUBORDER I. MONOZOA Hartmann and Chagas, 1911.

Definition.—Protomonadina without tendency to bilateral symmetry in undividing forms. The anterior flagella vary from one to many, in addition to which a trailing flagellum or undulating membrane may be present.

Classification.—This suborder can be divided into some ten families as follows:—

DIAGNOSTIC TABLE OF THE MONOZOA.

A. *One flagellum present*:—
  I. With a collar—Family 1, *Craspedomonadidæ* Stein, 1878.
  II. Without a collar:—
    (*a*) Kinetonucleus not separate from the nucleus—Family 2, *Oicomonadidæ* Senn, 1900.
    (*b*) Kinetonucleus separate from the nucleus—Family 3, *Trypanosomidæ* Doflein, 1901.
B. *Two flagella present*:
  I. Both anterior:—
    (*a*) Unequal—Family 4, *Monadidæ* Stein, 1878, *emendavit* Senn, 1900.
    (*b*) Equal—Family 5, *Amphimonadidæ* Kent, 1880, *emendavit* Bütschli, 1884.
  II. One anterior and one trailing flagellum:—
    (*a*) Trailing flagellum free:—
      1. In horny sheath and with lip or proboscis-like process—Family 6, *Bikœcidæ* Stein, 1878.
      2. Without sheath or process—Family 7, *Bodonidæ* Bütschli, 1884.
    (*b*) Trailing flagellum in part attached to the body—Family 8, *Cercomonadidæ* Kent, 1880, *emendavit* Bütschli, 1884.
C. *Three to six anterior flagella*, with or without one trailing flagellum (except *Embadomonas* with one anterior and one cytostomic flagellum)—Family 9, *Tetramitidæ* Kent, 1880.
D. *Numerous anterior flagella*—Family 10, *Callimastigidæ* da Fonseca, 1915.

Of these ten families we are concerned with only five, of which one, the Trypanosomidæ, because of its importance, we shall leave till the next chapter; so that at present we will consider the following families only:—

Family 2. Oicomonadidæ.
Family 7. Bodonidæ.
Family 8. Cercomonadidæ.
Family 9. Tetramitidæ.

FAMILY OICOMONADIDÆ Senn, 1900.

Synonym.- *Cercomonadina* Saville Kent, 1880, *pro parte*.

Definition.- -Monozoa with a single flagellum, no collar and no kinetonucleus.

Remarks. This family was formed by Senn for Oicomonas, several allied forms of which are to-day classified in the Trypanosomidæ.

Type Genus. --*Oicomonas* Saville Kent, 1880.

Classification. The various genera of this family may be differentiated as follows:-

A. Without definite nucleus. Chromatin diffuse-- -*Selenomonas* (*Selenomastix*).
B. With definite nucleus: -
  I. *Rhizostyle: not known to be present* :- -
    (*a*) Flagellum anteriorly directed:
      Body oval or roundish *Oicomonas*.
    (*b*) Flagellum trailing or posterior:- -
      1. Body long spindle-shaped -*Ancyromonas*.
      2. Body three-cornered bowed leaf-shaped- - *Phyllomonas*.
  II. *Rhizostyle present* :- -
      Body 6-11 × 3·5 microns. Flagellum springs from a small basal granule, and is continued backwards into the body by a dark staining filament, the rhizostyle *Rhizomastix*.

Only the first genus concerns us.

Genus Oicomonas Saville Kent, 1880.

Synonym. *Cercomonas* Davaine, 1860, *pro parte nec* Dujardin, 1841.

Definition. --Oicomonadidæ, with oval or roundish body and one anteriorly directed flagellum

Remarks.- In 1841 Dujardin formulated the genus Cercomonas, which Wenyon has placed upon a firm basis.

In 1860 Davaine described two varieties of flagellates which he found in cholera motions. The first and larger of these, which he calls A, is without doubt *Chilomastix mesnili*, while the second and smaller is an Oicomonas. Unfortunately Davaine called both these parasites *Cercomonas hominis*, but the genus was one of his own construction, and most assuredly was not the Cercomonas of Dujardin.

In 1880 Saville Kent formed the genus for uniflagellate free-swimming forms, which are capable of temporarily fixing themselves to any object by extending a sarcode thread, which can be withdrawn when they start to swim.

This sarcode thread was the only point of distinction from the genus which Saville Kent called Monas, but which Stein in 1878 had improved, so that it came to be defined as possessing two anterior flagella, one long and one short, while the posterior end was capable of forming a filiform pseudopodium. In view of this, and as the filiform pseudopodium is not an essential character, Oicomonas came to be looked upon as including forms with a single anteriorly directed flagellum, and as such requires investigation by modern cytological methods. In this genus must come all those organisms which resemble Form B of Davaine's *Cercomonas hominis*, as this is not a Cercomonas, and they must include *Monas pyophila* Blanchard.

With regard to the flagellate called *Monas lens* Müller, 1786, and reported as being present in man, it is not a Monas, but was classified by Saville Kent as a Heteromita. It may be a Bodo or a Prowazekia.

Type Species.—*Oicomonas mutabilis* Saville Kent, 1880, found in vegetable infusions.

The more important parasitic species which concern us are:

Oicomonas pyophila R. Blanchard, 1895,
Oicomonas hominis Davaine, 1854,
Oicomonas vaginalis Castellani and Chalmers, 1909,

and these may be differentiated as follows:—

A. With thick cuticle—*Pyophila*.
B. Without thick cuticle, in human intestine—*Hominis*.
C. Without thick cuticle, in vaginal mucus—*Vaginalis*.

Oicomonas pyophila R. Blanchard, 1895.

Synonym. *Monas pyophila* R. Blanchard, 1895.

Definition.—Oicomonas with a thick cuticle.

Historical.—Grimm found this flagellate in the sputum and pus of a pulmonary and of a hepatic abscess occurring in a Japanese woman living in Sappho. The organism requires reinvestigation by modern methods.

Morphology.—The flagellate measures 30-60 microns in length and is heart-shaped, being enclosed in a thick cuticle which extends into the cytoplasm, dividing it into three parts, and is continued along the flagellum for a considerable distance. At its tip the flagellum is free.

Life-History.—Nothing is known as to this.

Oicomonas hominis (Davaine, 1854), *emendavit* Castellani and Chalmers, 1918.

Synonyms.—*Cercomonas hominis* Davaine, 1854, *pro parte*—*i.e.*, Form B.

Definition.—Oicomonas with a thin cuticle.

History.—In 1854 Davaine described two forms, A and B, under the heading *Cercomonas hominis*. Form A is *Chilomastix mesnili*, while Form B is *Oicomonas hominis*.

Morphology.—*O. hominis* is a round or pear-shaped parasite averaging from 8 to 10 μ in diameter, with a long flagellum projecting from the more pointed end. There is no undulating membrane. The nucleus is small, indistinct, and usually situated near the flagellar extremity.

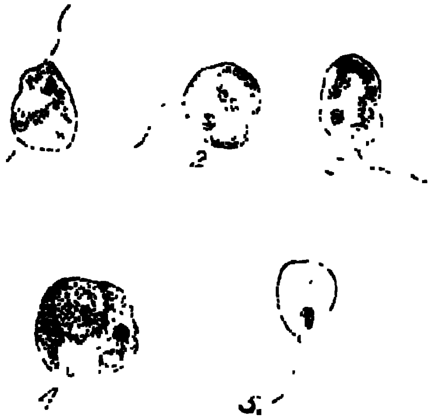

Fig. 68.—*Oicomonas hominis* (Davaine).

1-3, and 5, Flagellate forms; 4, encysted form.

Life-History.- Reproduction is by binary fission, and Perroncito and Piccardi have described encystment.

Habitat.- According to our experience at autopsies, the parasite may live not only in the small intestine, as generally stated, but also in some cases in the large intestine. Oicomonas is readily killed, as observed by Castellani and Willey, by a solution of methylene blue (1 in 3,000).

Oicomonas vaginalis Castellani and Chalmers, 1909.

Synonym.- *Cercomonas vaginalis* Castellani and Chalmers, 1909.

This is a pear-shaped or rounded parasite, measuring 5 to 12 μ in its maximum diameter, and provided with one flagellum, a small nucleus, and food vacuoles, but without a pulsating vacuole. It is not uncommon in the vagina of native women in Ceylon.

Oicomonas perryi Castellani, 1907.

Synonym.– *Cercomonas perryi* Castellani, 1907.

Found by Castellani in Ceylon in monkeys (*Macacus pileatus* and *Semnopithecus priamus*) suffering from diarrhœa. It is morphologically extremely similar to *O. hominis*, being roundish or pear-shaped, 8 to 12 μ in diameter. There is one flagellum originating from the pointed end. The nucleus is situated near the flagellar end. Reproduction seems to be by binary fission, but cysts can be seen

Other Species.- *O. anatis* Davaine, in the alimentary canal of ducks; *O. canis* Gruby and Delafond, in dogs; *O. gallinarum* Davaine, in fowls.

Bodonidæ Bütschli, 1884, *emendavit* Doflein, 1901.

Definition.- Monozoa, free living or parasitic, with one anterior and one posterior (or trailing) flagellum, with or without a kinetonucleus and an undulating membrane.

Nomenclature. In part, at all events, this family represent the Heteromitidæ of Saville Kent, as *Heteromita* Dujardin, 1841, is in part Bodo and in part Cercomonas.

Type genus.- *Bodo* Stein, 1878.

Classification.—The following is a poor attempt to differentiate the genera of the Bodonidæ known to us:- -

A. With an undulating membrane:- -
  I. Kinetonucleus well marked—*Trypanoplasma*.
  II. Kinetonucleus poorly marked—*Trypanophis*.

- B. Without an undulating membrane, but a kinetonucleus may or may not be present:—
  - I. While swimming all flagella are posterior. (Genera with which we are not concerned, as yet not found in man.)
  - II. While swimming all flagella are not posterior:—
    - (*a*) Body with antero-posterior groove—*Colponema.*
    - (*b*) Body without such a groove:—
      - 1. Food believed to enter anteriorly:—
        - (1) Kinetonucleus absent—*Bodo.*
        - (2) Kinetonucleus present—*Prowazekia.*
      - 2. Food believed not to enter anteriorly. (Genera with which we are not concerned, as not yet found in man.)

Trypanoplasma Laveran and Mesnil, 1901, *emendavit*, 1904.

Definition.—Bodonidæ living in the blood and alimentary canal of vertebrates with two flagella—one projecting anteriorly and the other running posteriorly, and raising the periplast into an undulating membrane. Kinetonucleus almost as large as the trophonucleus. Sporogony in the Hirudinea.

Remarks.—This genus, which was first described by Laveran and Mesnil, is interesting, first, because it shows definitely an anterior flagellum, which has disappeared in most trypanosomes, and a posterior flagellum, which, like all trypanosomes, carries the undulating membrane; secondly, because, according to Léger and Keysselitz, members of this genus are parasitic in the alimentary canal of fish, and not in the blood.

Morphology.—The body of a trypanoplasma is flattened, and often curved, with a concave side, thicker than the convex, to which the undulating membrane is attached. The body is soft and of changing form. At the junction of the anterior and middle thirds of the body can be seen two masses of chromatin. The one on the convex side is the trophonucleus, and the other on the concave side the elongated kinetonucleus, in front of which are two small chromatic granules, one of which gives rise to an anterior flagellum which becomes free at once, and the other to a posterior, which, turning backwards, runs the whole length of the cytoplasm, raising the periplast into an undulating membrane.

Life-History.—Division is longitudinal, the kinetonucleus dividing first, and then the flagella.

Often Trypanoplasmata show seasonable variation, the infection being more intense in hot weather. They are evidently pathogenic, producing anaemia associated with serous fluid in the peritoneum, pericardium, and œdema of the organs.

The parasite appears to be spread by leeches, in which the sexual forms conjugate by a fusion of nuclei, after reduction, and of the cytoplasm, from which results an ookinete possessing a trophonucleus and a kinetonucleus.

These ookinetes give rise to male, female, and indifferent forms, which multiply abundantly. Parthenogenesis may occur.

Brumpt infected fish by the bite of leeches, but Keysselitz failed with *Pisciola geometra*, and it is hardly surprising, for he describes the leech as becoming ill, with swelling of the clitellar region, alteration in colour and activity, and finally death, thus showing that this leech could hardly be the usual definitive host. He has already noted the initial stages in *Hirudo medicinalis*. Another genus of leech which spreads these parasites is *Hemiclepsis*.

Classification.—Crawly considers that the generic name should be *Cryptobia* Leidy, but the diagnosis of this genus is vague. With regard to classification, Keysselitz is of the opinion that all so far described species should be considered to belong to one species—*Trypanoplasma borreli* L. and M.

Type Species.—*Trypanoplasma borreli* Laveran and Mesnil, 1901.

Trypanoplasma borreli Laveran and Mesnil, 1901.

In the blood of *Leuciscus erythrophthalmus* (the rudd) and *Phoxinus lævis* (the minnow), and in the alimentary canal of the leech *Piscicola geometra,* and perhaps in *Hirudo medicinalis.*

Trypanoplasma cyprini Plehn, 1903

In *Cyprinus carpis.*

Trypanoplasma (Cryptobia) dendrocœli Fantham and Porter, 1910.

This parasite measured 20 to 40 *μ* in length, with a large and often curved kinetonucleus. It lives in the alimentary canal of *Dendrocœlum lacteum,* and was the first trypanoplasma to be found in the Platyhelminthes.

Trypanoplasma intestinalis Léger, 1905.

This trypanoplasma is very important, because it was found in the œsophagus and anterior part of the stomach of *Box boops*, a salt-water fish.

It is the first trypanoplasma described as existing outside the blood. In addition to typical form, Léger describes globular parasites with three anterior flagella and a rudimentary undulating membrane, which reminds one of *Trichomonas.*

These he considers to be female forms, and says that he has seen conjugation with male forms.

Trypanoplasma ventriculi Keysselitz, 1906

Synonyms.—*Heteromita dahlii Apstein = Diplomastix dahlii.*

This is found in the intestine of *Cyclopterus lampus*, and is apparently a typical trypanoplasma. Discovered by Dahl in 1857.

Trypanoplasma varium Léger, 1904.

In *Cobitis barbatula* (loach), and in *Hemiclepsis marginata.*

Trypanoplasma guernei Brumpt, 1905.

In *Cottus globio,* and develops in *Piscicola*

Trypanoplasma barbi Brumpt, 1905.

In *Barbus fluviatilis*, and in the leech (*Piscicola*).

Trypanoplasma abramidis Brumpt 1905

In the bream (*Abramis brama*) and the leech (*Hemiclepsis*).

Trypanoplasma truttæ Brumpt, 1905.

In *Salmo fario*, and perhaps in *Pisciola.*

Other Species.

T. keysselitzi Minchin, 1909, in the tench; *T. gurneyorum* Minchin, 1909, in the pike; *T. clariæ* Mathis and Léger, 1911, in *Clarias macrocephalus*, *T. congri.*

Trypanophis Keysselitz, 1904.

Bodonidæ in *Cœlenterata*, with two flagella, an anterior and a posterior. The kinetonucleus is situated anteriorly, and is much smaller than the trophonucleus. According to Floyd, a blepharoplastic granule gives rise to the free flagellum. The attached flagellum arises near the basal granule of the free flagellum, and gives rise to a narrow undulating membrane.

Trypanophis grobbeni Poche, 1903.

In the gastro-vascular system of different Siphonophora—*e.g.*, *Halistemma ergestinum.* The parasite is curved somewhat, like a trypanosome.

Genus Prowazekia Hartmann and Chagas, 1910.

Definition.—*Bodonidæ* with a kinetonucleus.

Type.—*Prowazekia cruzi* Hartmann and Chagas, 1910.

The separation of the old genus *Bodo sensû lato* into *Bodo sensû stricto* and *Prowazekia* is not at present generally accepted; for example, Alexeieff and others oppose it, stating that the generic name for all the species included under *Prowazekia* should be *Bodo*, while that for the only species at present under Bodo—viz., *B. lacertæ* Grassi, 1881—should be *Prowazekella* (new genus) *lacertæ* Grassi, 1881. Nor is this the only confusion with regard to *Prowazekia*, for one species—*P. urinaria* Hassall, 1859—has been found in urine which has been passed for six hours or more in the Temperate Zone; and three species—*P. asiatica* Castellani and Chalmers, 1910, Ceylon; *P. cruzi* Hartmann and Chagas, 1910, Brazil; *P. weinbergi* Mathis and Léger, 1910, Indo-China—are found in fæces; while one form—*P. parva* Naegler, 1910—lives in slime on stones at Lunz.

All observers are agreed that these flagellates are non-pathogenic, but the question which is debated is whether they are accidental contaminations of the urine and fæces after being passed out of the body, and the urine problem is further complicated by the question as to whether it was contaminated by the fæces.

With regard to the urinary species, it has been found by Hassall in 1859, Salisbury in 1868, Kunstler in 1883, and Stinton in 1912. He obtained it only twice from the same patient, who was in a hospital ward in Liverpool, and in none of the other patients in the ward; it was not found in the fæces, nor in a vessel of water exposed to the air of the ward, nor in the water-supply. It was not present in later observations taken aseptically, and cultures died rapidly at 37° C. It is therefore concluded to be an accidental contamination.

The intestinal forms are not so easily dismissed, as we have found them in stools collected in sterile petri-dishes, and Mathis and Léger found their species in the fæces of persons in good health and suffering from diarrhœa, even when taken with aseptic precautions. It is possible, therefore, that some, at all events, of the intestinal forms are harmless occasional parasites of man.

Classification. The species may be differentiated as follows:—

A. Posterior flagellum free:—
  I. *Large forms.* More than 8 microns in length as a rule:—
    (*a*) Shape oval:—
      1. Rhizoplast present:—
        (1) Cytostome present—*Urinaria.*
        (2) Cytostome absent—*Asiatica* and *vaginalis*.
      2. Rhizoplast absent—*Cruzi.*
    (*b*) Shape pyriform:—
      Apex sharp—*Weinbergi.*
  II. *Small forms.* Not exceeding 8 microns in length—*Parva.*
B. Posterior flagellum attached to the body for a short distance—*Javanensis.*

Prowazekia urinaria Hassall, 1859.

This species has several times been found in human urine which has been passed some hours.

Morphology. The flagellate appears in three forms—a sausage-shaped form, 10 to 25 μ in length by 2·5 to 6 μ in breadth; a round or oval form, varying from 4 μ in diameter to 15 by 10 μ in measurement; a carrot shaped form, varying from 6 by 3 μ to 25 by 4 μ. The cytoplasm contains a large number of small, highly refractile granules, and contains a trophonucleus and a kinetonucleus, which latter is a relatively large pear shaped body. The body is enclosed by a thin periplast, and possesses two flagella, a shorter anterior and a longer lateral, which arise from blepharoplasts (basal granules), which are connected by rhizoplasts to the kinetonucleus. There is a cytostome situate near the root of the short flagellum.

Bionomics. It moves in a jerky manner, with the short flagellum directed forwards and the long flagellum backwards. The small flagellum is also useful in capturing food, such as bacteria. Food enters by means of the cytostome and forms the usual food vacuoles, which accumulate at the aflagellar end. A contractile vacuole is seen in large flagellates, and may measure 1 to 3 μ in diameter. It is situate near the base of the cytostome, to which it is joined by a minute canal. It contracts every 15 to 30 seconds at a temperature of 20° C. It is thought to be the dilated fundus of the cytostome.

Life-History. It divides in two by binary fission, the blepharoplast apparently dividing first and forming two new flagella, after which the cell nuclei and the cell divide. It can lose its flagella, and can form round or oval cysts 5 to 7 μ in diameter, inside from which after a time it again becomes flagellate, and escapes in its typical form.

Cultivation. In association with bacteria it grows well in urine, on salt agar, nutrient agar, serum agar, blood agar, peptone, salt solution, nutrient broth, and diluted blood-serum at a temperature of 20° C., but is killed by a temperature of 37° C. in one or two hours. It has not been cultivated free from bacteria.

Prowazekia asiatica Castellani and Chalmers, 1910.

Synonym. *Bodo asiaticus* Castellani and Chalmers, 1910.

This flagellate was found in 1909 by Castellani and Chalmers in the stools of cases of ankylostomiasis suffering from diarrhœa in Ceylon. It was studied in detail by Whitmore in 1911, and assigned to the new genus *Prowazekia*, which Hartmann and Chagas had differentiated from the old genus *Bodo*

Morphology. *P. asiatica* is found in the motions in two forms—either as a long, slender flagellate measuring 10 to 16 μ in length by 5 to 8 μ in breadth or as a more rounded form, which has a transverse diameter of 8 to 10 μ. The cytoplasm is alveolar in structure, containing food vacuoles, but no contractile vacuole. The trophonucleus is usually situate in the flagellar third of the cytoplasm, and consists of a nuclear membrane a widish space for the enchylema, and a central karyosome, with usually a centrosome. The kinetonucleus is situate nearer the flagellar extremity, and is connected by a long strand with a small piece of chromatin situate near the aflagellar extremity, and by another strand with one of the two blepharoplasts which lie adjacent to the flagellar extremity. These blepharoplasts are united together, and, as already stated, to the kinetonucleus by strands. Usually there are two, which may lie side by side or one over the other. From these blepharoplasts the two flagella take origin, and quickly pass to the exterior.

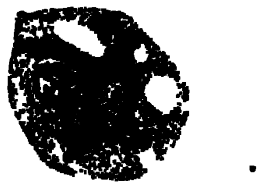

FIG. 69.—*Prowazekia asiatica* CASTELLANI AND CHALMERS: FROM FÆCES.

Reproduction.—Asexual reproduction takes place by metamitosis, but sexual reproduction is unknown. Cyst formation has been observed, resulting in rounded bodies 6 to 7 μ in transverse diameter, possessing tropho- and kineto-nuclei, and enclosing the remains of the flagella.

Culture.—*P. asiatica* is readily cultivated in liquid and in the water of condensation of solid media in symbiosis with bacteria. The most suitable medium is the condensation water of nutrose agar (2 to 4 per cent.), or maltose agar, on which a few drops of albumin-water have been placed, when it can be subcultured and grown indefinitely if the tubes are kept uncapped and subcultures are made twice a week.

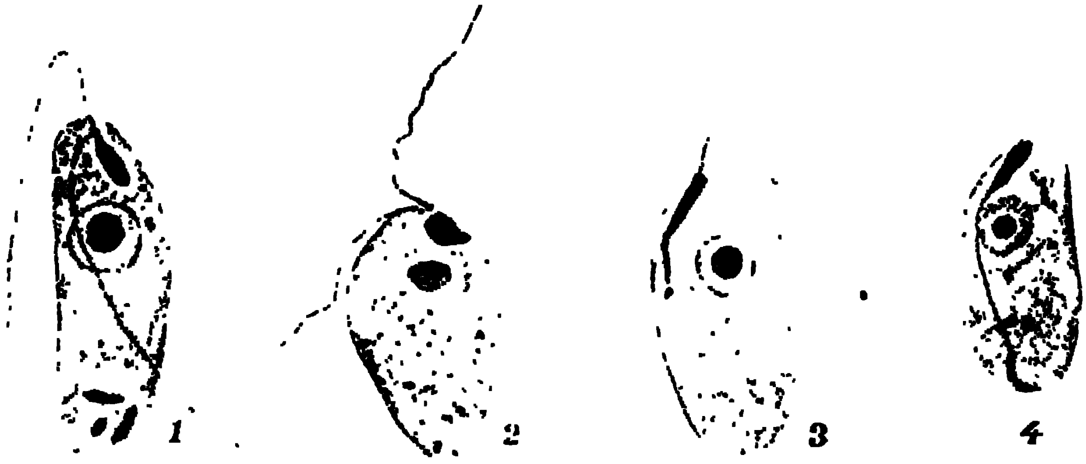

FIG. 70.—*Prowazekia asiatica* CASTELLANI AND CHALMERS: FROM CULTURES. (After Whitmore.)

Pathogenicity.—Probably nil.

Prowazekia cruzi Hartmann and Chagas, 1910.

Oval to pear-shaped forms; length 8 to 12 μ; breadth, 5 to 6 μ, with the flagella at the narrow end. Found in Brazil. Differs from *P. asiatica* by the absence of the strand which originates from the kinetonucleus and terminates into a chromatin granule. Martin has found in human stools in Tsingtau a *Prowazekia* which he believes to be identical with *P. cruzi*.

Prowazekia weinbergi Mathis and Léger, 1910.

Pear-shaped, but rather drawn out into a point; length, 8 to 15 μ; breadth, 4 to 6·5 μ. Flagella at broad end. Found frequently in the motions of men in Tonkin.

Prowazekia parva Naegler, 1910.

Characterized by its small size, the longest forms being 5 to 8 μ. The cysts do not contain flagella.

Prowazekia javanensis Flu, 1912.

Definition. Prowazekia in which the posterior flagellum is attached to the body for a short distance.

Remarks.- Flu believes that there is only one species of Prowazekia. He obtained his variety from an agar culture of human fæces in the Dutch East Indies.

Prowazekia vaginalis Castellani and Chalmers, 1918.

Definition. Prowazekia living in the vaginal mucus.

Remarks. Morphologically identical with *P. asiatica* found in motions, but the investigated strains of the latter will not live in vaginal mucus.

Genus Bodo Stein, 1875.

Definition.- Bodonidæ without undulating membrane or kinetonucleus, but with a rhizoplast. While swimming one flagellum is anterior and the other trailing, without antero-posterior groove.

Bodo stercoralis Porter, 1918.

Discovered in human fæces by Miss Porter. Body measures from 14 μ to 19 μ long and is from 6 μ to 9 μ broad, with large nucleus

Bodo lens Muller, 1786.

Synonyms.—*Monas lens*, *Heteromita lens*.

Remarks.--Usually free living, but said to be found in man once (*vide* 'Animal Parasites of Man,' by Fantham, Stephens, and Theobald).

Genus Toxobodo Sangiorgi, 1917:

Definition.- Bodonidæ of semilunar shape.

Type and only Genus.- *Toxobodo intestinalis* Sangiorgi, 1917.

Toxobodo intestinalis Sangiorgi, 1917.

A flagellate organism semilunar in shape, 6-9·6 × 1·6-4·8 microns, found in the human intestine and grown for ten generations in culture media (peptone water). It has two flagella, and resembles a Bodo, except in shape.

Genus Heteromita Dujardin, 1841.

Bodonidæ round or oval, with two flagella, one at each pole.

Heteromita zeylanica Castellani and Chalmers, 1910.

This flagellate is elongated, 8 to 15 μ in length by 3 to 4 μ in breadth, with single flagellum at each pole, and a nucleus fairly rich in chromatin. No undulating membrane or pulsating vacuole, but with chromidia in the cytoplasm. It is not cultivable. This flagellate we classify provisionally under the genus *Heteromita*. It was found in the stools of persons suffering from ankylostomiasis in Ceylon.

ORDER CERCOMONADIDÆ Saville Kent, 1880, *emendavit* Bütschli.

Definition.—Monozoa with elongate or oval forms, possessing one free anterior flagellum and one trailing flagellum.

Type Genus.—*Cercomonas* Dujardin, 1841, *emendavit* Wenyon, 1910.

Remarks.—It appears to us that this is the only genus which can be classified in this family at the present moment.

Genus Cercomonas Dujardin, 1841, *emendavit* Wenyon, 1910

Synonyms.—*Heteromita* Dujardin, 1841, *pro parte nec Cercomonas* Davaine, 1860, *nec Oicomonas* Saville Kent, 1880.

Definition.—Cercomonadidæ, pear-shaped, with a protokaryon type of nucleus situate near the flagellar extremity, with a basal granule or blepharoplast from which a sort of rhizoplast may run to the margin of the cytoplasm, at which it divides into the two flagella, one of which is anterior, while the other is posterior and closely attached to one side of the body, at the posterior end of which it becomes free.

Type Species.—The type species of the properly defined family is certainly *Cercomonas longicauda* Dujardin, 1841, *emendavit* Wenyon, 1910, even though the first species in Dujardin's description is *C. detracta*, because this latter has never again been described, and has therefore never been examined by modern methods.

Certainly Dujardin's genus Heteromita agrees in description and illustration with many of the features of *C. longicauda*, and therefore we consider it to be a synonym.

There are a number of species described by Dujardin, but until they have been examined by modern methods it is impossible to define them. They are all free-living forms.

Cercomonas longicauda Dujardin, 1841, *emendavit* Wenyon, 1910.

Synonyms.—*Cercomonas parva* Hartmann and Chagas, 1910

Definition.—*Cercomonas* elongate 8-15 × 3-4 microns, with very marked long posterior flagellum.

History.—This flagellate was first discovered by Dujardin in 1841 in an old infusion, and was next described by Wenyon in 1910, being found in cultures made from human fæces. In the same year

Hartmann and Chagas met with it in Brazil. Since then it has only been recorded once.

Morphology. The body is pear shaped, measuring on an average 8-15 microns in length by 3-4 microns in breadth, but Wenyon has met with small forms measuring only some 2-3 microns in greatest length.

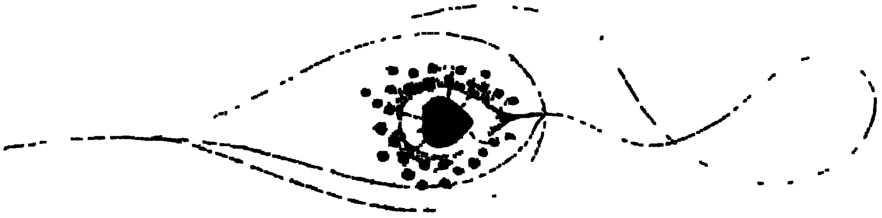

Fig. 71.—*Cercomonas longicauda* Dujardin, 1841.
Type with granules around the nucleus; compare this with Fig. 74.
(After Wenyon, from the *Quarterly Journal of Microscopical Science*.)

The cytoplasm is alveolar and contains a large anteriorly situate nucleus, which has a nuclear membrane enclosing a clear space, in which lies a large karyosome. The nuclear membrane may be drawn out into a cone, at the apex of which lies the granule - blepharoplast- from which either the flagella spring directly or a single rhizoplast passes to the periphery and then divides into the two flagella. In any case, the flagella arise from the anterior broader end, and while one is directed forwards, the other passes posteriorly over the surface of the body, to which it is attached until it reaches the posterior end, when it becomes a free posterior flagellum. The cytoplasm also contains a number of bright refractile granules.

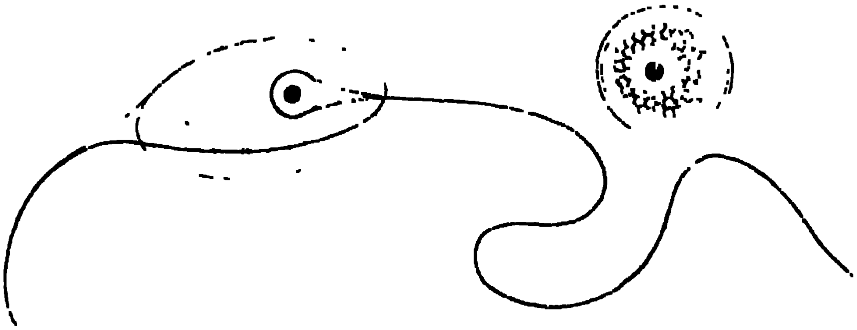

Fig. 72.—*Cercomonas longicauda* Dujardin, 1841.
Type without granules and Cyst.
(After Wenyon.)

Life-History.—Simple fission, with division of the nucleus by promitosis, takes place, while cyst formation is also known.

The cysts measure some 6-7 microns in diameter. They are slightly brownish spherical bodies containing a spherical central nucleus surrounded by bright refractile granules.

Pathogenicity.—It is believed to be non-pathogenic, and to be accidentally present in the fæces.

Cercomonas parva Hartmann and Chagas, 1910.

This is probably the same as *C. longicauda*.

FAMILY TETRAMITIDÆ Kent, 1880, *emendavit* Chalmers and Pekkola, 1917.

Definition.—Monozoa with three to six anterior flagella (with the exception of Embadomonas, which has only two visible flagella, one anterior and one posterior), with or without a rhizoplast, with or without a posterior or trailing flagellum, which may, or may not, form an undulating membrane, with or without an axostyle or a cytostome. Habitat, free living and parasitic.

Type Genus.—*Tetramitus* Perty, 1852.

Classification.—The family may be divided into three subfamilies as follows:—

A. *Without an axostyle*:—
  (*a*) With three flagella—Subfamily I., *Embadomonadinæ* Chalmers and Pekkola, 1918.
  (*b*) With four to six flagella—Subfamily II., *Tetramitidinæ* Chalmers and Pekkola, 1917, *emendavit* 1918.

B. *With an axostyle*—Subfamily III., *Trichomonadinæ* Chalmers and Pekkola, 1917.

SUBFAMILY EMBADOMONADINÆ Chalmers and Pekkola, 1918.

Definition.—Tetramitidæ with or without a cytostome, but without an axostyle and with three flagella only. (Only two are visible in Embadomonas.)

Classification.—The known genera of the subfamily Embadomonadinæ may be recognized as follows:

A. *Without cytostome*:—
  I. With three anterior flagella—(1) *Enteromonas* da Fonseca, 1915.
  II. With one anterior and two posterior flagella—(2) *Dallengeria* Saville Kent, 1880.
  III. With two anterior and one posterior flagella—(3) *Dicercomonas* Chalmers and Pekkola, 1919.

B. *Cytostome present or probably present* (*as a groove*):—
  I. With one anterior, one cytostomic and then free, and one free trailing flagellum—(4) *Trimastix* Saville Kent, 1880.
  II. With one anterior and one posterior flagellum which is generally cytostomic, and with a large cytostome with siderophilous, often folded, border—(5) *Embadomonas* Mackinnon, 1911.

The genera in which we are interested are Enteromonas, Dicercomonas and Embadomonas.

Genus Enteromonas da Fonseca, 1915.

Definition.—Embadomonadinæ without a cytostome or trailing flagellum and with three anterior flagella.

Type and only Species.—*Enteromonas hominis* da Fonseca, found in Brazil.

Enteromonas hominis da Fonseca, 1915.

Definition.—Enteromonas with the characters of the genus.

Remarks.—This parasite was first found by da Fonseca in Brazil in 1915, and subsequently by Chalmers and Pekkola, in the Anglo-Egyptian Sudan, in Europeans and natives.

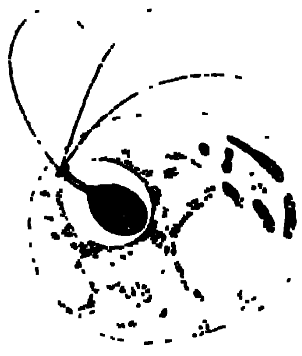

FIG. 73.—*Enteromonas hominis* DA FONSECA, 1915.

Morphology.—The parasite is roundish or oval, without a tail, and with a diameter varying from 5-6 microns. The periplast is not rigid, and encloses an endoplasm, often with inclusions such as bacteria. Situate anteriorly lies the protokaryon type of nucleus, from which a rhizoplast runs to a blepharoplast, from which three anterior flagella arise.

Life-History.—Da Fonseca records longitudinal division.

Pathogenicity.—The flagellate probably causes diarrhœa.

Genus Embadomonas Mackinnon, 1911.

Synonym.—*Waskia* Wenyon and O'Connor, 1916.

Definition.—Embadomonadinæ, with a cytostome and one anterior and one posterior flagellum, and with a siderophilous, often folded, cytostomic margin.

Type Species.—*Embadomonas agilis* Mackinnon, 1911.

Other Species.—The type and the other species may be recognized as follows:—

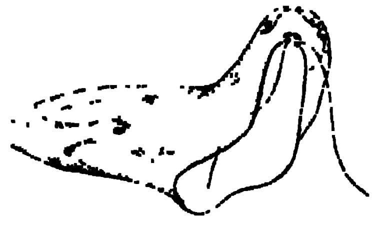

FIG. 74.—*Embadomonas agilis* MACKINNON, 1911.

(After Mackinnon, from the *Quarterly Journal of Microscopical Science*.)

A. *Habitat. intestine of Trichopterous and Tipula Larvæ in British Isles:*—

(*a*) Cytostomic borders feebly siderophilous, cytostomic flagellum exceedingly delicate and inconspicuous—

Size: 4-11 × 1·5-3 microns. Cysts: about 4 × 3 microns. (1) *Agilis*.

(*b*) Cytostomic borders markedly siderophilous, cytostomic flagellum well developed. Size: 7-16 × 5-9 microns. Cysts: 5-6 × 4-5 microns. (2) *Alexeieffi*.

B. *Habitat: intestine of Man in Alexandria*:—

Anterior flagellum long and thin, cytostomic flagellum shorter and stouter.

Size: 4-9 microns long, but with variable width 2-4 microns in narrow forms. Cysts: 4·5-6 microns in length. (3) *Intestinalis.*

Only *Embadomonas intestinalis* Wenyon and O'Connor, 1916, concerns us.

Embadomonas intestinalis Wenyon and O'Connor, 1916.

Synonym.—*Waskia intestinalis* Wenyon and O'Connor, 1916.

Definition.—Embadomonas found in the intestine of man in Alexandria. Size 4-9 microns in length, but with variable width, some 3-4 microns in narrow forms. Cysts 4·5-6 microns in length.

Remarks.—This flagellate was found by Wenyon and O'Connor in two cases in the Orwa-el-Waskia section of the 19th General Hospital in Alexandria.

Morphology.—The flagellate is pear-shaped, with a cytostome at the anterior end, from which (or slightly nearer the cytostome) a thin anterior flagellum takes origin, while a second stouter and shorter arises from the inner part of the anterior wall of the cytostome, from which it projects for a considerable distance.

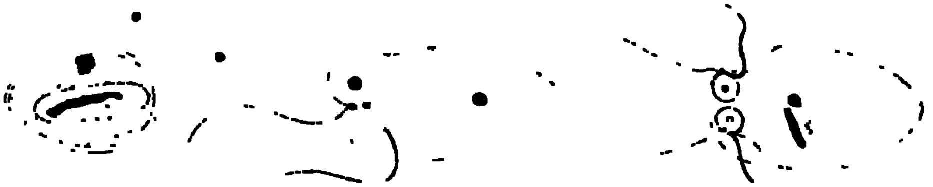

FIG. 75.—*Embadomonas intestinalis* (WENYON AND O'CONNOR, 1916). Showing dividing form, flagellate, and cyst. (After Wenyon and O'Connor.)

The cytoplasm is pale, frequently vacuolated with an anteriorly situate nucleus, which has a nuclear membrane and a central karyosome. On the surface of the nuclear membrane there are two granules from which the flagella arise.

Life-History.—Forms with two cytostomes and four flagella have been seen, indicative of division.

The cysts are pear-shaped bodies of a pearly-white appearance, and quite structureless unless stained, when certain nuclear structures can be made out.

Pathogenicity.—There is no evidence that it is pathogenic.

SUBFAMILY TETRAMITIDINÆ Chalmers and Pekkola, 1918

Definition.—Tetramitidæ with or without a cytostome with four to six flagella, but without an axostyle.

Classification.—Eight genera belong to the subfamily—viz.:—

Tetramitus Perty, 1852.
Callodictyon Carter, 1865.
Costiopsis Senn, 1900.
Chilomastix Alexeieff, 1911.
Tetrachilomastix da Fonseca, 1915.
Copromastix Aragão, 1916.
Tricercomonas Wenyon and O'Connor, 1917.
Protetramitus Chalmers and Pekkola, 1918.

And they may be differentiated as follows:—

A. *Without cytostome:*—
   1. With rhizoplast. (1) *Protetramitus* Chalmers and Pekkola, 1918.
   2. Without rhizoplast (2) *Copromastix* Aragão, 1916.
      (3) *Tricercomonas* Wenyon and O'Connor, 1917.

B. *Cytostome probably present:*
   At all events there is a deep ventral longitudinal furrow—
   (3) *Callodictyon* Carter, 1865.

C. *Cytostome present:*—
   I. Trailing flagellum is free:—
      (*a*) Body dorso-ventrally compressed, ventral surface with deep depression which serves as a sucker and contains the cytostome and two short free flagella; the two thick long trailing flagella issue from this depression—(4) *Costiopsis* Senn, 1900.
      (*b*) Body more or less symmetrical and not compressed or arranged as above, with three anterior and one free trailing flagellum—(5) *Tetramitus* Perty, 1852.
   II. Free trailing flagellum absent:—
      (*a*) Three anterior flagella—(6) *Chilomastix* Alexeieff, 1911.
      (*b*) Four anterior—(7) *Tetrachilomastix* da Fonseca, 1915.

Of these genera we are only concerned with Copromastix, Tricercomonas, Chilomastix, and Tetrachilomastix.

Genus Copromastix De Beaurepaire Aragão, 1916.

Definition. Tetramitidinæ without cytostome and rhizoplast.

Copromastix prowazeki Aragão, 1916.

Found in cultures of human fæces in Brazil.

Genus Tricercomonas Wenyon and O'Connor, 1916.

Definition.—Tetramitidinæ without cytostome and with three anterior and one trailing flagellum.

Remarks.—This genus is like Cercomonas in many ways, but cannot be classified in the family Cercomonadidæ; and as it shows a resemblance to Protetramitus, we place it here.

Type Species.—The type and only species is *Tricercomonas hominis* Wenyon and O'Connor, 1916.

Tricercomonas hominis Wenyon and O'Connor, 1916.

Definition.—Tricercomonas of small size and active movements, with spherical or ovoid body distinctly flattened on one side and with the posterior end drawn out and terminating in a flagellum, which can be traced forwards along the flattened side to the anterior end of the body, where three anterior long flagella take origin. Habitat, the intestine of man in Egypt.

Morphology.—In addition to the characters given above, the body, which measured 4–8 microns in length, is seen to be somewhat grooved along the course of the posterior flagellum. No definite cytostome could be seen. The cytoplasm contains bacilli and cocci, a nucleus with a central karyosome, and a nuclear membrane, which is drawn out into a cone-like elevation, from the summit of which the flagella take their origin.

Life-History. As forms with two nuclei have been seen it is presumed that binary division may take place. The cysts are oval, 6–8 microns in length and about half this breadth, containing one to four nuclei of the same type as the flagellate.

Pathogenicity. It is believed to be non-pathogenic.

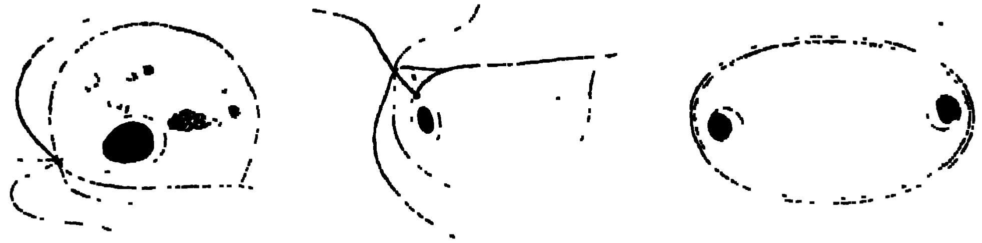

FIG. 70.—*Tricercomonas intestinalis* WENYON AND O'CONNOR, 1915.
Two flagellate forms (compare side view with Fig. 71) and one cyst
(After Wenyon and O'Connor, from the publications of the Wellcome Bureau of Scienti[illegible]ch.)

Genus Chilomastix Alexeieff, 1911.

Synonyms.—(1) *Cercomonas* Davaine, 1880, *pro parte nec* Dujardin, 1841; (2) *Trichomonas* Roos, 1893, *nec* Donné, 1837; (3) *Monocercomonas* Epstein, 1893, *nec* Grassi, 1879; (4) *Macrostoma* Alexeieff, 1909, *nec* Latreille, 1825; (5) *Fanapepea* Prowazek, 1911; (6) *Tetramitus* Brumpt, 1912, *nec* Perty, 1852; (7) *Difämus* Gäbel, 1914; (8) *Cyathomastix* Prowazek and Werner, 1914.

Definition.—Tetramitidinae with large cytostome, three anterior flagella, but no free trailing flagellum.

Type Species.—*Chilomastix caulleryi* Alexeieff, 1909. *Synonym*: *Macrostoma caulleryi* found in the intestine of tadpoles.

Other Species.—*C. mesnili* Wenyon, 1910; *C. motella* Alexeieff, 1912; *C. bittencourti* da Fonseca, 1915; *C. capræ* da Fonseca, 1915; *C. cuniculi* da Fonseca, 1915.

These species may be differentiated as follows:—

A. *Characters known to us* :—

I. *Size large ; 20-25 microns in length* :—

Flagella easily seen in cysts which resemble *C. mesnili* cysts in size and appearance—(1) *Caulleryi*.

II. *Size medium* ; 11-18 *microns in length* :—

(*a*) Cytostome long; cysts about 7 × 5·6 microns in which the anterior flagella are difficult to see—(2) *Mesnili*.

(*b*) Cytostome very short; cysts large, about 8 × 6 microns, in which the anterior flagella are very distinct—(3) *Bittencourti*.

III. *Size small* ; 7-12 *microns in length* :—

(*a*) Nucleus with a central karyosome connected to the blepharoplast by a rhizoplast; size 9-12 microns in length—(4) *Capræ*.

(*b*) Nucleus without a central karyosome and without a rhizoplast; size 7-9 microns in length—(5) *Cuniculi*.

B. *Characters unknown to us* :—

Found in species of *Motella*—(6) *Motellæ*.

Chilomastix mesnili Wenyon, 1910.

Synonyms.—(*a*) *Cercomonas hominis* Davaine, 1860, *pro parte* ; (*b*) *Monocercomonas hominis* Epstein, 1893, *nec* Grassi, 1879; (*c*) *Trichomonas intestinalis* Roos, 1893, *pro parte nec* Leuckart, 1879; (*d*) *Macrostoma mesnili* Wenyon, 1910; (*e*) *Fanapepea intestinalis* Prowazek, 1911; (*f*) *Tetramitus mesnili* Brumpt, 1912; (*g*) *Difāmus tunensis* Gabel, 1914; (*h*) *Cyathomastix hominis* Prowazek and Werner, 1914; (*i*) *Tetramitus bocis* Brumpt, 1912; (*k*) *Chilomastix intestinalis* Kuczynski, 1914.

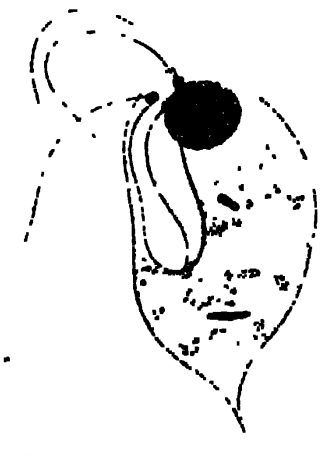

FIG. 77.—*Chilomastix mesnili* WENYON 1910.

Note the membrane raised by the cytostomic flagellum.

Definition.—Chilomastix of medium size, with long cytostome and with cysts about 7 × 5·6 microns, in which the anterior flagella are difficult to see.

Historical.—This flagellate appears to have been first noted by Davaine in 1860, being called Form A of *Cercomonas hominis*. After this it was noted by Roos in 1893, and by Epstein in the same year. It was rediscovered and properly described by Wenyon in 1910, and later noted by Prowazek in 1911, Nattan-Larrier in 1912, Brumpt in 1912, Gaebel in 1914, Chatterjee in 1915, Wenyon in 1915, Da Fonseca in 1915 and 1916, Fantham and Porter in 1915, Archibald, Hadfield Logan, and Campbell in 1916, Wenyon and O'Connor in 1917, Castellani in 1917, and Chalmers and Pekkola in 1918.

Remarks.—The parasite is widely distributed all over the world.

Morphology.—Its shape varies, but it is generally pear-shaped, measuring some 11-18 microns in length if the caudal appendage is included, and some 1·6-4·0 microns less if this is excluded. There is a large cytostome situate anteriorly. The cytoplasm contains a large, roundish, oval or slightly irregular chromatic nucleus, anterior to which lies two or three granules, from which the three anterior flagella take their origin. No rhizoplast can be seen. The margins of the cytostome are thickened, and appear to contain a fourth or *posteriorly directed flagellum* in the inner siderophilous rim, while the outer rim appears to be homologous with a *parabasal*.

Life-History.—Reproduction takes place by binary fission and cyst formation. The cysts are usually egg-shaped, measuring 7 × 5·6 microns. The cyst wall is separated from the parasite by a clear space, while the cytoplasm contains a nucleus, a blepharoplastic mass, and at times the mouth margins can be seen. Division forms with two nuclei have been noted.

Pathogenicity.—There is a difference of opinion. Some observers consider it to be non-pathogenic, while others hold that it is may cause diarrhœa.

SUBFAMILY TRICHOMONADINÆ Chalmers and Pekkola, 1917.

Definition.—Tetramitidæ with an axostyle.

Classification.—The ten genera belonging to this subfamily may be differentiated as follows:—

DIAGNOSTIC TABLE OF TRICHOMONADINÆ.

A. *Cytostome absent*:—
I. Three anterior flagella—(1) *Protrichomonas* Alexeieff, 1911.
II. Four anterior flagella—(2) *Monocercomonas* Grassi, 1879.

B. *Cytostome present*:—
I. Without undulating membrane:—
(*a*) *Without trailing flagellum*:—
1. Periplast thickened in places; four anterior flagella—(3) *Polymastix* Bütschli, 1884.
2. Periplast not thickened; six anterior flagella—(4) *Hexamastix* Alexeieff, 1912.
(*b*) *With trailing flagellum*:—
1. Three anterior flagella:—
(1) Without parabasal—(5) *Eutrichomastix* Kofoid and Swezy, 1915.
(2) With parabasal wound around the axostyle—(6) *Devescovina* Foà, 1905.
2. Four anterior flagella—(7) *Tetratrichomastix* Mackinnon, 1914.

II. With undulating membrane:—
  1. Three anterior flagella—(8) *Trichomonas* Donné, 1837.
  2. Four anterior flagella—(9) *Tetratrichomonas* Parisi, 1910.
  3. Five anterior flagella—(10) *Pentatrichomonas* Chatterjee, 1915.

Of these genera, Trichomonas, Tetratrichomonas, and Pentatrichomonas concern us.

Genus Trichomonas Donné, 1837.

Definition.—Trichomonadinae with a cytostome, an undulating membrane, and three anterior flagella

Remarks.—In his work 'Recherches microscopiques sur la nature du mucus,' Donné (1837) described and figured an organism which he found in innumerable quantities in vaginal mucus.

He considered that it possessed a single flagellum which at times was bifurcated distally, a series of three to five cilia with very rapid rotatory movement, and that at times it was elongated posteriorly into a tail. The name was first spelt Tricomonas but afterwards altered to Trichomonas.

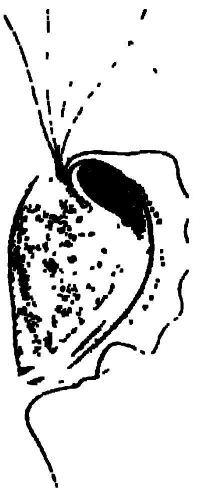

FIG. 78.—*Tetratrichomonas gallinarum* (Martin and Robertson, 1912). (× 2[illegible] Diameters.)

Dujardin (1841) described *T. limacis* from *Limax agrestis* in much the same terms, and so did Perty (1852) with regard to *T. batrachorum*, though he depicted the axostyle, but Stein's figures of Perty's organism show clearly the three anterior flagella, the undulating membrane the posterior free flagellum the axostyle the nucleus and the cytostome, and in this way was laid the foundations upon which the main features of the genus were placed.

Returning now to the type *T. vaginalis*, this was restudied in 1884 by Blochmann, who illustrated the three anterior flagella, the undulating membrane, the axostyle and the nucleus, but in the same year Kunstler produced a much better illustration showing four anterior flagella taking their origin from a blepharoplast from which the undulating membrane also arose, while this shows a trace of a parabasal. The nucleus is also represented, while the axostyle shows exceedingly clearly. He also saw the cytostome. Bensen (1910) figured two blepharoplasts, one of which is connected with the nucleus by means of a rhizoplast, and he also gave an illustration of a cyst. Thus the type species *T. vaginalis* was brought into line with the results of researches upon the species found in animals, of which a number have been carefully described and drawn by Dobell, Alexeieff, Martin and Robertson, Kuczynski, and by Kofoid and Swezy.

The only difficulty is with the type *T. vaginalis*. Does it possess three anterior flagella or four? If the latter, then the genus Trichomonas has as a synonym Tetratrichomonas, and a new name must be found for the forms with three anterior flagella.

Type Species.—*Trichomonas vaginalis* Donné, 1837.

Morphology.—The essential points in the general morphology are the pear-shaped body, the small anterior and ventrally situate cytostome without siderophilous lips, and the three anteriorly springing flagella arising (according to Wenyon) from the anterior of the two granules into which the blepharoplast is divided. From the posterior granule arises a posterior flagellum, which, passing backwards, forms the undulating membrane and finally terminates in a free posterior portion. From the same granule arises another stiff rod-like structure, the *parabasal*, which serves as a support for the undulating membrane, and often there is a row of granules lying parallel to this rod. Springing from the blepharoplast and directed posteriorly over the nucleus is a peculiar body, clear, with bounding lines, which projects from the posterior end as a spine and often contains chromatinic granules. This organella is the axostyle, called also the *baguette interne*. It may be a supporting structure, but it may also be concerned in movement. It does not stain with nuclear stains, and therefore appears clear, while in the living organism it is a refractile rod.

The nucleus is usually more or less oval, and possesses a membrane, inside which the chromatin is distributed in the form of granules.

Two chromatinic granules (axoplasts) are often found where the axostyle leaves the cytoplasm.

Life-History.—Binary division with its nuclear changes have been carefully studied by Kofoid and Swezy. Multiple fission has also been described. Transference from host to host is by the typical cysts

Classification.—A very large and increasing number of species of doubtful value are in existence: e.g., *T. bactrachorum* Perty, 1852, in frogs; *T. suis* Gruby and Delafond, in pigs; *T. limacis* Dujardin, in snails; *T. lacertæ* Blochmann, in lizards; *T. caviæ* Davaine, in guinea-pigs; *T. perroncili* Castellani, 1907, in monkeys; *T. columbarum*, in pigeons. Plimmer and others have also recorded a Tetratrichomonas in the blood of snakes (Fig. 79), and this probably came as an infection from the alimentary canal. Martin and Robertson have also described forms in fowls, and Kuczynski has contributed an elaborate paper on the morphology of the genus.

Four species are said to occur in man—*T. vaginalis*, *T. hominis*, *T. dysenteriæ*, and *T. pulmonalis*.

While some differences do exist in the animal forms, still there is nothing of a specific nature to be found in the human and it is quite possible that they are all one species, and that they are the same as that found in the rat—viz., *T. intestinalis*, with three anterior flagella, unless, indeed, *T. vaginalis* really possesses four flagella, but on this point we are not certain; moreover, Künstler was often wrong with regard to the number of flagella (*vide Polymastix melo-*

dontha, which he said had six flagella, and *T. intestinalis*, which he depicted with four flagella).

There is, however, a peculiar matter which must be referred to. Schaudinn stated that trichomonas becomes an ameba, and that two of these amebae, after giving off reduction bodies, became encysted together and conjugated. The zygote divided into several portions, leaving a considerable *nucleus de reliquat*. Gauducheau has described ameboid forms becoming a trichomonas, but such observations have failed to meet with confirmation so far, and are therefore *sub judice*.

Trichomonas vaginalis Donné, 1837.

Synonym.—*Trichomonas irregularis* Salisbury 1868.

This parasite lives in the vagina when the reaction of the mucus is acid. It is found in Europe, and we have observed it in Ceylon and in equatorial Africa. It has also been reported to occur in the urethra in men, after cohabitation with women infected with the parasite.

It is not transferable to rabbits, guinea pigs, or dogs. It has not been cultivated, nor is it understood how women become infected.

T. vaginalis is fusiform or pear-shaped in appearance, length from 15 to 25 μ, and breadth from 7 to 12 μ. The non-flagellate extremity is pointed and the flagellate extremity rounded. The parasite is generally considered to be harmless but we have, however, found it much more frequently in women suffering from vaginitis than in normal women.

Trichomonas hominis Davaine, 1854.

Synonyms. *Cercomonas hominis* Davaine, 1854; *C. intestinalis* Lambl, 1875; *T. intestinalis* Leuckart, 1879; *Monocercomonas hominis* Grassi, 1882; *Cimaenomonas hominis* Grassi, 1883.

The utmost confusion has existed between this species, *Oicomonas hominis* and *T. vaginalis*. It has been found in cases of diarrhea in Europe, India, and Ceylon but in small numbers may be found also in the intestine of individuals apparently healthy; it has also been reported from the mouth cavity and stomach. It seems to prefer to live in alkaline mucus.

T. hominis is pear-shaped, with a breadth of from 18 to 25 μ, with three flagella at its broadest end, and an undulating membrane. The cytoplasm contains a rather indistinct nucleus, and one or several non-pulsating vacuoles.

It has not been transmitted to animals, nor has it been cultivated. It can reproduce by longitudinal division, but forms are to be seen indicating encystment and conjugation. Alexeieff considered at one time the bodies described as trichomonas cysts to be in reality an ascomycetes fungus, which he called *Blastocystis enterocola* and Brumpt used the term *Blastocystis hominis*.

Trichomonas dysenteriæ Billet 1907.

This *Trichomonas* was first found by Billet in the fæces, and later in 1912 by Gauducheau, who believes that it becomes an amœba in one stage of its life-history. The latter observer divides the life-history of a *Loeschia* into—(1) Stage of parasitism in the tissues; (2) stage of saprophytism in the lumen of the bowel or in cultures when it lives on bacteria; (3) stage of free existence when it is a flagellate. He considers that *Loeschia undulans* Castellani 1904, is allied to this species, although Castellani is inclined to believe that it is a stage of an *Oicomonas*.

Trichomonas pulmonalis Schmidt 1895.

This form has been found by Schmidt and St. Artault, Leyden and Jaffé, in the sputum and lungs of persons suffering from phthisis, gangrene, and putrid bronchitis.

Other Species. *T. batrachorum* Perty, 1852, in the cloaca of *Rana temporaria*, *R. esculenta*, *Bufo vulgaris*, and *Hyla arborea*, in Germany and Italy; *T. suis* Gruby and Delafond, in the alimentary canal of pigs; *T. limacis* Dujardin, in the gut of *Limax agrestis*; *T. lacertæ* Blochmann in the cloaca of *Lacerta agilis*, *T. caviæ* Davaine, in the large bowel of guinea-pigs; but this last may perhaps be separated off into a separate genus, *Trichomastix*, with one long flagellum directed across the body. *T. perronciti* Castellani, 1907, in monkeys suffering from diarrhœa, is very similar morphologically to *T. hominis*. *T. columbarum* Prowazek and Aragao, 1909, is found in the buccal mucosa of pigeons. Plimmer has shown that flagellates of the type of *Trichomonas* can be found in the blood of snakes.

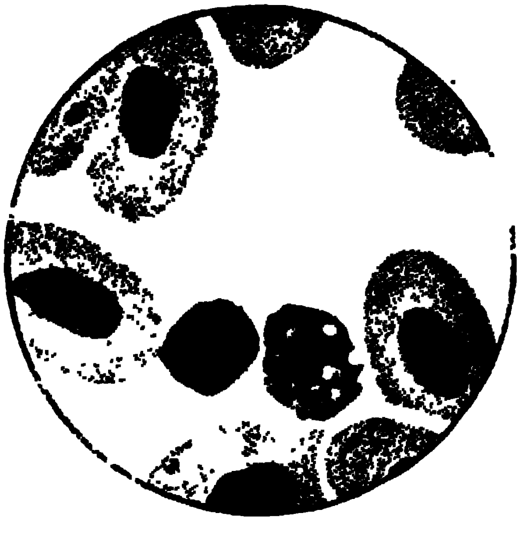

FIG. [illegible] OF TRICHOMONAS TYPE FOUND IN THE BLOOD OF A LEOPARDINE SNAKE.

(After Plimmer.)

Tetratrichomonas Parisi, 1910.

Definition.—Trichomonadinæ with a cytostome, an undulating membrane, and four anterior flagella.

Type Species.—*T. prowazeki* Alexeieff, 1909, found in salamanders and tritons.

Remarks.—Alexeieff (1909) found a trichomonas-like parasite in the terminal intestine of *Salamandra maculosa*, *Triton cristatus* and *Alytes obstetricans*, and subsequently in *Hæmopis sanguisuga*. This parasite, measuring 10 to 14 by 4 to 7 microns, possessed four free unequal anterior flagella and an undulating membrane thrown into long loose folds, as well as a thinnish axostyle and a nucleus rich in chromatin and bounded by a very definite membrane. He named this organism *Trichomonas prowazeki*, but as it possesses four and not three anterior unequal flagella, Parisi created a new genus with it as the type.

Tetratrichomonas vaginalis Castellani and Chalmers, 1919.

Künstler described *Trichomonas vaginalis* with four flagella, and we have seen forms in the human vagina with four flagella.

Tetratrichomonas intestinalis Chalmers and Pekkola, 1919.

Found in human fæces in Egypt by Wenyon and O'Connor, and later by Chalmers and Pekkola in the Sudan.

Genus Pentatrichomonas Chatterjee, 1915.

Definition.—Trichomonadinæ with a cytostome, an undulating membrane, and five anterior flagella.

Type Species.—*Pentatrichomonas ardindelteili* Derrieu and Raynaud, 1914, found in the intestine of man in Africa and India.

Remarks.—Chatterjee instituted this genus for a flagellate which he found in the intestine of man in Bengal, and which at the time he called *P. bengalensis*. This organism agrees in most particulars except measurement with that mentioned above under the heading *Hexamastix* Derrieu and Raynaud, and therefore Chatterjee's generic name takes the place of this Hexamastix, but Derrieu and Raynaud's specific name has priority, and the parasite becomes known as *Pentatrichomonas ardindelteili* Derrieu and Raynaud, 1914, until some definite difference between the two is established.

More recently Chatterjee states that he has found this organism to be present in thirty-two cases of chronic dysentery.

Pentatrichomonas ardindelteili (Derrieu and Raynaud, 1914).

This is the only species and hence also the type, and has the characters of the genus. It is found in man.

REFERENCES.

There is no one paper or book which deals at all adequately with the Mastigophora; the best we can recommend is Saville Kent's 'Infusoria,' Doflein's latest edition, and Fantham, Stephens, and Theobald's (1916) 'Animal Parasites of Man.' But none of these are any use without Dujardin, Davaine, and Stein, combined with Bütschli, Kunstler, Klebs, Wenyon, Dobell, Kofoid, and Swezy, etc. Chalmers and Pekkola have attempted statements with regard to the Tetramitidæ, with a view to clearing up the existing confusion.

For references, see Field, H. H. (1912), 'Bibliographia Protozoologica,' *Archiv fur Protistenkunde*, xxvi, p. 444. Jena.

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Minchin (1912) An Introduction to the Study of the Protozoa. London.

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Classification : Tetramitidæ and Chilomastix.

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Oicomonas.

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CHAPTER XIX

TRYPANOSOMIDÆ

Preliminary remarks—Trypanosomidæ—Herpetomoninæ—Trypanosominæ—Incertæ sedis—Leucocytozoön—Spirochætacea—References.

PRELIMINARY REMARKS.

In this chapter we complete the study of the Monozoa by considering the forms allied to Herpetomonas and to Trypanosoma, which have been gathered together into one family, the Trypanosomidæ of Doflein, and follow this by a description of Leucocytozoön and the Spirochætes, of which the classification is uncertain.

FAMILY TRYPANOSOMIDÆ Doflein, 1901.

Definition. Monozoa possessing one flagellum, without a collar and with the kinetonucleus separate from the nucleus.

Classification. This family may conveniently be divided into two subfamilies as follows:—

(*a*) Undulating membrane absent or rudimentary and the kinetonucleus on the flagellar side of the trophonucleus—Subfamily 1. *Herpetomoninæ* Castellani and Chalmers, 1919.

(*b*) Undulating membrane well developed and the kinetonucleus on the aflagellar side of the trophonucleus—Subfamily 2. *Trypanosominæ* Castellani and Chalmers, 1919.

SUBFAMILY HERPETOMONINÆ Castellani and Chalmers, 1919.

Definition. Trypanosomidæ in which the undulating membrane is either rudimentary or absent, and in which the kinetonucleus is situate on the flagellar side of the trophonucleus and remains there.

Type Genus.—*Herpetomonas* Saville Kent, 1881.

Classification. The various genera which used to be gathered together in the family Herpetomonidæ were:—

1. *Herpetomonas* Kent, 1881.
2. *Leptomonas* Kent, 1881.
3. *Crithidia* Léger 1902, *emendavit* Patton, 1908.
4. *Leishmania* R. Ross, 1903.

5. *Toxoplasma* Nicolle and Manceaux, 1908.
6. *Piroplasma* Patton, 1895.
7. *Achromaticus* Dionisi, 1898.
8. *Histoplasma* Darling, 1906.

Unfortunately, there has been much confusion with regard to these genera, due to lack of certain knowledge with regard to the morphology and life-histories of the type species. The controversy was keenest with regard to the points as to whether *Herpetomonas* and *Leptomonas* were or were not the same genus; whether *Herpetomonas* and *Crithidia* are good genera, or simply stages in the life-cycle of a trypanosome. Briefly, the position is this: In 1851 Burnett discovered a flagellate in the house fly, and called it *Bodo muscæ-domesticæ*, for which Kent created the genus *Herpetomonas* in 1881; but two pages earlier in his book Kent created the genus *Leptomonas* for a flagellate which Bütschli had found in the intestine of *Trilobus gracilis* in 1876. The only distinguishing features between these two genera are the presence of a contractile vacuole and the flexibility of the body in *Herpetomonas*, but modern research fails to confirm the presence of this contractile vacuole in *Herpetomonas*, and flexibility *per se* is insufficient to separate the two genera. Prowazek, however, in 1904, emended *Herpetomonas*, describing *H. muscæ-domesticæ* as possessing two flagella united by a membrane and arising from a flagellar situated diplosome; but Patton, in 1909, and Mackinnon in 1910, have demonstrated that this is merely a stage in the division of *H. muscæ domesticæ*; and Chatton and Léger, in 1911, demonstrated that there was an axostyle present in *Leptomonas drosophilæ*; and Chatton later showed that the diplosome of *H. muscæ-domesticæ* was merely the remains of this axostyle. Therefore it would appear that the two genera are indistinguishable, and might therefore be united, and, if so, the older name *Leptomonas* would by the law of priority come into use, to the exclusion of the name *Herpetomonas*; and this may happen, but it cannot be adopted at present, because the type species of the genus *Leptomonas*—namely, *L. bütschlii* Kent, 1881—has, as yet, been incompletely studied, and may eventually be found to be the same as, or different from, *Herpetomonas*; therefore we continue to retain the two genera *Herpetomonas* and *Leptomonas* in the same condition as in our last edition—that is to say, indistinguishable from one another.

With regard to the controversy as to whether there is a genus *Crithidia* or not, the answer is much simpler. There can be no doubt that crithidia like forms exist in the life-cycle of many trypanosomes; but the work of Patton, Porter, and Swingle has clearly shown that there is a separate genus, *Crithidia* Léger, 1902, emended Patton. Further, we believe that Miss Porter is correct when she states that *Crithidia* should be placed in the family Trypanosomidæ on account of the presence of an undulating membrane.

With regard to *Leishmania*, a better knowledge of the life-history has shown that this is merely a *Herpetomonas* or *Leptomonas*, but at the present time we retain it as a separate genus, as the full life-cycle has never been completely traced.

So far we have been considering genera in which there is no doubt that one stage of the life-cycle is flagellate; now we turn to the other genera, concerning which doubt is freely expressed as to whether they belong to the *Mastigophora* at all.

With regard to *Toxoplasma*, it was considered by some observers to be allied to *Leishmania*, but it contains only a single nucleus, without evidence of a kinetonucleus, and without the appearance of a flagellate stage on cultivation; and its life-cycle is little known, as is that of an apparently allied genus, *Elleipsisoma* França, 1911, while the relationship is further complicated by the genus *Toddia* França, 1911, which is said to arise from the infective granule. There appears to be more flagellate evidence for the genus *Globidium* Neumann, 1909. The so-called *Leucocytozoön piroplasmoides* Thiroux and Teppaz appears to be allied to *Toxoplasma*, having only one nucleus, and not developing any flagellate forms on cultivation. Finally, the work of Yakimoff and Kohl-Yakimoff indicates that *Toxoplasma* is related to the Hæmogregarines, especially as Splendore's flagellate stage has not been confirmed by Laveran's work.

The genus *Piroplasma* used to be classed with *Herpetomonas* because flagellate forms had been found by several observers, but these findings have been discredited because (1) they were discovered in the old faulty air-dried smears; (2) the possibility of their being intestinal flagellates of the genus *Prowazekia*, which entered the blood before death in diseased animals; (3) they are really trypanosomes, and not development stages of *Piroplasma* ; (4) the careful work of Nuttall and his collaborators have failed to demonstrate a flagellate stage.

Achromaticus was placed with the Herpetomoninæ because, according to Gonder, it always has a trophonucleus and a kinetonucleus, while Neumann maintains that it becomes flagellate in the bat mite, *Pteropus vespertilionis*. On the other hand, Yakimoff, Stolnikoff, and Kohl Yakimoff deny the presence of the double nucleus, and consider the parasite to be a typical *Piroplasma*.

According to Darling, *Histoplasma* becomes flagellated in the lungs, and therefore belongs to the Herpetomoninæ, though Rocha-Lima considers it to be a yeast, a view which we adopt.

Rhynchoidomonas belongs to the Trypanosominæ.

We therefore recognize the following as definitely belonging to the Herpetomoninæ:—

1. *Herpetomonas* Kent, 1881.
2. *Leptomonas* Kent, 1881.
3. *Crithidia* Léger, 1902, *emendavit* Patton, 1908
4. *Leishmania* Ross, 1903.
5. *Hæmocystozoōn* Franchini, 1913.

These five genera may be differentiated as follows:—

(*a*) Undulating membrane absent:—
  Genera: *Herpetomonas*, *Leptomonas*, *Leishmania*, *Hæmocystozoön*. (Probably all belong to one and the same genus, *Herpetomonas*.)

(*b*) Rudimentary undulating membrane present.—Genus *Crithidia*.

Morphology.—The flagellate stage of the Herpetomoninæ is usually an elongated spindle-shaped mass of cytoplasm composed of an inner granular endoplasm surrounded by a periplast (ectoplasm). In the cytoplasm lies a chromatinic mass, the trophonucleus, which, when properly treated, appears to be of the nature of a protokaryon. On the flagellar side of this lies another mass of chromatin called the kinetonucleus, and further back on the same side a minute bead—the blepharoplast—from which the flagellum passes through the cytoplasm, either directly, and so forming no undulating membrane and becoming a free flagellum, or it carries the cytoplasm with it, forming a rudimentary undulating membrane.

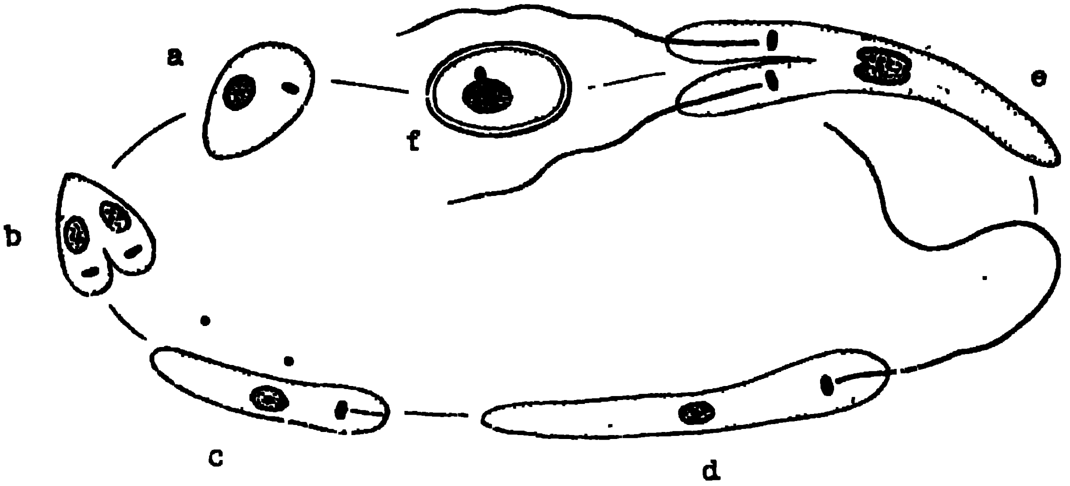


FIG. 80.—THE LIFE-HISTORY OF A HERPETOMONAS. (After Fantham.)

Life-History.—The flagellate forms are usually the inhabitants of the intestine of the arthropoda, but some live in plants.

They can multiply in their arthropodal host by longitudinal division of the flagellate stage, but this may become rounded binucleate cysts, which, passing from one host with the fæces, can infect a new host.

In the new host it appears as a non-flagellate binucleate rounded form, often called a Leishmania-like body, or the Leishmaniform stage, which develops in due course into the flagellate stage again.

Thus in the life-cycle there are the following stages:—

1. The flagellate stage.
2. The post-flagellate or encysted stage.
3. The Leishmaniform stage.
4. The flagellate stage again.

The Herpetomoninæ are distinct forms, and are not stages in the life-cycle of a trypanosome.

Hereditary Infection.—In an important paper O'Farrell in 1913 traced the infection of the ovum of the tick *Hyalomma ægyptium* by *Crithidia hyalommæ*. Usually the flagellate stage is passed in hæmocœlic fluid of the tick, but about the time of and during oviposition a considerable number of the flagellates enter the ovary, and some penetrate by their aflagellar extremity into the ova, where they become the Leishmaniform stage, which may form large plasmodial masses which break up into small resting forms. This flagellate is therefore strictly parasitic in the tick and its life-history

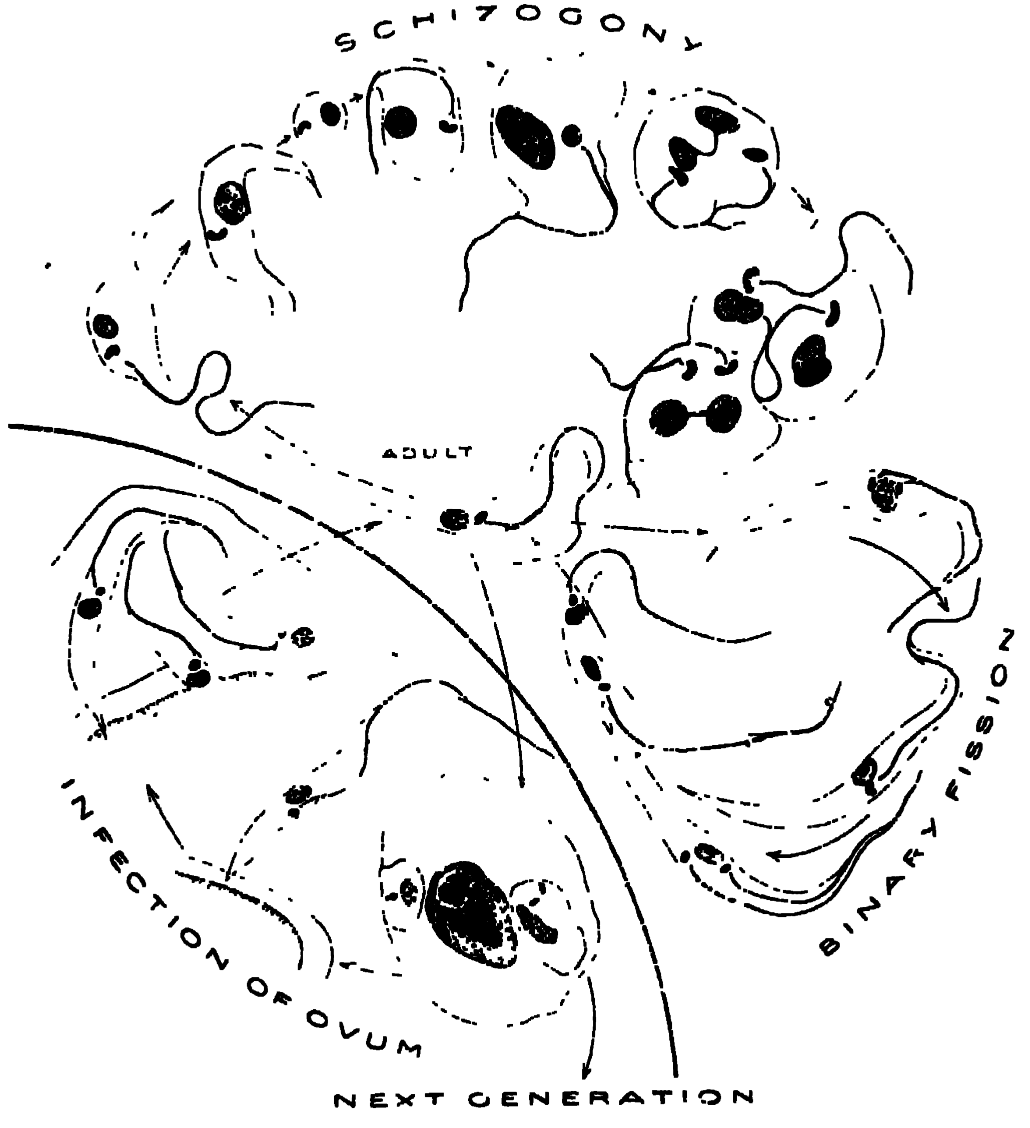


FIG. 81.—THE LIFE-CYCLE OF *Crithidia hyalommæ* O'FARRELL, 1913. (After O'Farrell.)

It demonstrates hereditary infection. The arrows in the infection of the ovum except the two on the right-hand side, are wrong. The left upper arrow should run from the adult to the ovum; the other two arrows should be omitted.

resembles that described by Porter for *Crithidia melophagia* in the fly *Melophagus ovinus*.

Pathogenicity.—In an able paper published in 1916 Fantham and Porter have shown that by feeding and by inoculation of various forms of herpetomonads and crithidias acute and chronic attacks of *herpetomoniasis* can be induced in vertebrates. Thus *Herpetomonas jaculum*, from *Nepa cinerea*, by feeding, produced the disease in mice, birds, a snake, frogs, newts, and fish; *H. stratiomyiæ* from *Stratiomyia chameleon* in a mouse; *H. pediculi* from *Pediculus corporis* in mice; *H. culicis* from *Culex pipiens* in birds; *H. ctenocephali* from a flea in a dog; *Crithidia gerridis* from *Gerris paludum* in dogs, lizards, mice, and frogs. In the infected animals both flagellate and Leishmaniform parasites were present.

These experiments are of great importance, and support the views expressed by Archibald that the method of infection of kala-azar in man is from aquatic insects and *per os*. Experimental herpetomoniasis is characterized by insidious onset followed by rapid illness, splenic and often hepatic enlargement, attacks of fever, emaciation, and often death.

Evolution of Herpetomoniasis.—As a result of the above-mentioned experimental work, Fantham and Porter have deduced the view that, in the case of the herpetomonads, disease is in the making to-day, and that as the result of change of habitat (brought about by ingestion or insect-faecal contamination of a bite), a herpetomonas may find itself in a vertebrate host, and there, taking on its Leishmaniform stage, becomes pathogenic, producing the disease *herpetomoniasis*, which may be acute or chronic. In the acute disease the flagellate forms abound, while in the chronic there are many more Leishmania-like forms.

Vertebrate Reservoir. As a variety of the chronic infection may be mentioned the vertebrate reservoir.

In 1914 Sergent, Lemaire, and Sanevet found herpetomonad flagellates in the blood and organs of a gecko in areas in Algeria in which Oriental sore was endemic, and suggested that the possible carrier was a phlebotomus. In the same year Chatton and Le Blanc found Leishmania-like forms in the red blood-cells of geckos in Tunis.

In 1915 Bayon found herpetomonas in the alimentary canal of *Chameleon pumilus* at Robbin Island, and also in a fly, *Scatophaga hottentota*, and suggested the possibility of infection of the vertebrate by swallowing a fly.

In 1914 Lindsey suggested that the oral Leishmaniasis of Paraguay might have its reservoir in rattlesnakes and its carrier in ticks or Simulium flies.

On the other hand, the very careful work carried out by Archibald in the Sudan has apparently excluded *domestic animals* as possible reservoirs of kala-azar in that region, where dogs are not readily susceptible to the virus, a fact which rather tends to differentiate the parasites of Sudan kala-azar from those of the Mediterranean.

Method of Infection.—As indicated above, the method of infection would be by swallowing the arthropod or some of its fæcal matter containing cysts, or by fæcal contamination of its cutaneous bite, or by both methods.

Archibald's evidence is against an insect as the infective agent of kala-azar in the Sudan, which he suggests is water-borne, in which case it might come from the fæces of insect larvæ or an aquatic arthropod.

Treatment of Infections.—Preparations of arsenic and of antimony are of great benefit in treating cases of herpetomoniasis or Leishmaniasis.

Prevention.—Dodds, Price, and Young seem to have had some success in segregating the infected human cases and removing the healthy to new abodes, and on theoretical grounds it would appear that if herpetomoniasis was endemic in any region, this should be examined for—

(*a*) Possible vertebrate reservoir;
(*b*) Possible arthropod carrier;

and if these are found, even if they are only possible, steps should be taken to protect the inhabitants from them.

Genus Herpetomonas Kent, 1881.

Synonyms.—*Bodo* Stein, *pro parte*; *Cercomonas* Dujardin, *pro parte*; and perhaps *Leptomonas* Kent.

Definition.—Herpetomoninæ elongated, rod-like, with a single flagellum. The kinetonucleus is situated near the posterior end, so that the flagellum is not attached to the side of the body, but becomes free at once and projects posteriorly. There is no undulating membrane. The contractile vacuole is situate quite close to the posterior extremity. The trophonucleus lies about the middle of the parasite, and possesses an achromatic substance with chromatic granules interspersed. The anterior end is tapering.

Type Species.—*Herpetomonas muscæ-domesticæ* Burnett, 1851.

History.—The genus *Herpetomonas* was created in 1881 by Saville Kent for Burnett's *Bodo muscæ-domseticæ*, and since then many flagellates have, rightly or wrongly, been classified under this genus. The life-cycles have been studied by Léger in 1903, Prowazek, 1904; Patton, 1907-08; Berliner, 1909; and Miss Porter, 1911. At the present time there are two different views concerning the characters of the genus: (*a*) Prowazek's view, supported by Chatton, Alilaire, and Berliner, that it is biflagellate; (*b*) Patton's view, supported by Miss Porter and others, that it is uniflagellate (a view which our observations support).

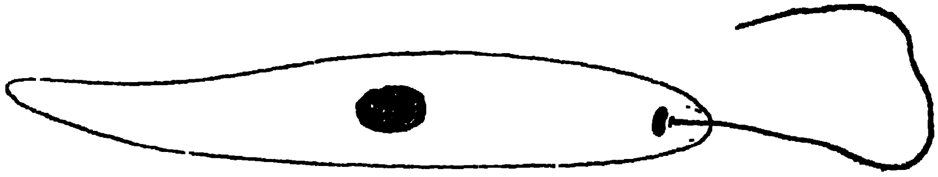


FIG. 82.—DIAGRAM OF A HERPETOMONAS.

Remarks.—The species of Herpetomonas, though not parasitic in human beings, are important to the student of tropical medicine, as they are parasitic in insects. Thus, *Herpetomonas muscæ-domesticæ* Burnett is parasitic in the intestinal canal of 8 per cent. of the house-flies (Prowazek), while others are found in fleas and bugs.

As already stated, there is considerable difference of opinion concerning the status of the Herpetomoninæ at the present moment. A number of observers, including Léger and Sambon, look upon them as merely stages in the life-history of trypanosomes; while others, such as Novy, McNeal, Ross, and Patton, hold that they are probably distinct from the blood trypanosomes. Woodcock, however, is correct when he says that those with trypaniform characters will probably be found to be stages in the life-cycle of trypanosomes, while the more typical herpetomonads will be found to be separate and distinct from these parasites.

In other words, some of the forms found in blood-sucking flies, leeches, etc., may be stages in the life-cycle of trypanosomes, while other forms, together, with those found in non-blood-sucking flies, and perhaps those found in larvæ, may (though it is open to question in the larvæ of blood-suckers) belong to a truly separate genus. The life-history of these forms has been mainly studied by Prowazek and Patton, whose results differ remarkably.

Herpetomonas muscæ-domesticæ Burnett 1851.

Synonyms.—*Bodo muscæ domesticæ* Burnett, 1851; *Cercomonas muscæ-domesticæ* Burnett, 1851; *Leptomonas muscæ-domesticæ* Burnett, 1851.

This flagellate is found in *Musca domestica* L., *Homalomyia scalaris* Fabricius, *Pollenia rudis* F., *Theicomyza fusca* Macquart, *Lucilia* sp.?, *Pycnosoma pulorum*, *Scatophaga lutaria* F., *Neuroctena anilis* Fallen, and *Homalomyia corvina* Verrall.

Miss Mackinnon has given a careful account of the morphology and life-history of *Herpetomonas muscæ-domesticæ* which is found in the house fly *Musca domestica* Linnæus.

Morphology.—The preflagellate stage takes place in the mid-gut, or more rarely the hind-gut, of the fly in the form of small round or oval bodies, 3 to 4 μ by 2·5 μ, which possess a circular trophonucleus and a rod-shaped kinetonucleus, while a rose-pink area in specimens stained by Giemsa, running from the kinetonucleus to the end of the cell, indicates the position of the future flagellum. This stage passes into the flagellate stage which takes place in the mid-gut when the Herpetomonad appears as a rather elongated (25 μ by 2·5 μ) body, which is blunt at the aflagellar end, and furnished with a flagellum which measures 30 μ, and arises from a blepharoplast situate near the kinetonucleus. The rhizoplast measures 4 μ, and is markedly thickened. The rod-shaped kinetonucleus is situate 6 μ from the flagellar extremity, and measures 2 μ by 0·8 μ. The trophonucleus is situate almost centrally, and measures 3 μ by 2 μ. The Doppelfaden of Prowazek is present as a line from the kinetonucleus via the trophonucleus far into the aflagellar end of the body.

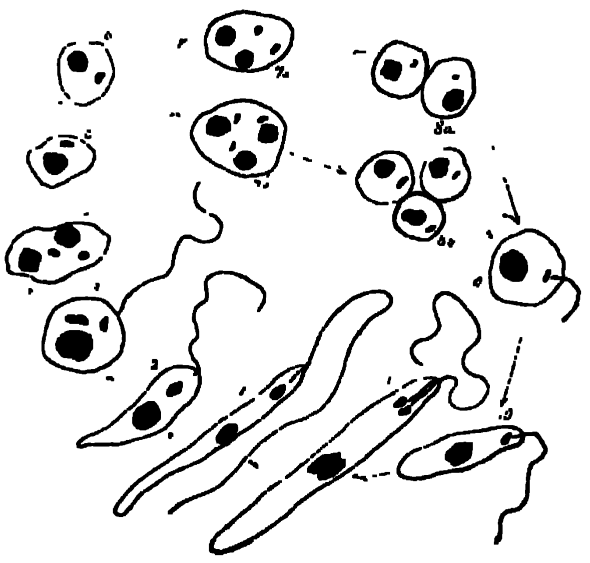


FIG. 83.—THE LIFE-CYCLE OF *Herpetomonas muscæ-domesticæ* BURNETT.

(After Patton.)

1, Fully developed parasite; 2-5, stages of encystment; 6, encysted or preflagellate form; 7a-8a, multiplication of the preflagellate form by simple division; 7b-8b, multiple division; 9, young flagellate stage; 10, other form; 11, longitudinal division commencing.

Life-History.—*Herpetomonas muscæ-domesticæ* multiplies by longitudinal division, in which the rhizoplast divides first, and each half is seen to have a separate blepharoplast, but there does not appear to be a splitting of the flagellum; on the contrary, Miss Mackinnon believes that the new flagellum grows out from one of the blepharoplasts, but for some time the two flagella lie close together, and this may last until the new flagellum has reached the length of the old flagellum. It is in this stage that *the deceptive appearances of a biflagellate organism* is produced. The kinetonucleus divides, and the trophonucleus also divides amitotically, the karyosome dividing first; after this the cytoplasm divides. Division takes place so rapidly that the organisms become smaller and smaller, and, attaching themselves to the epithelium of the hind gut, encyst—*i.e.*, pass into the post-flagellate stage of aflagellar cysts (3 to 4 μ by 3·5 to 2·5 μ), possessing tropho- and kineto-nuclei. These cysts pass out in the fæces, and are accidentally ingested by the fly along with food.

Hereditary Infection. No sign of hereditary infection could be found, nor of sexual reproduction.

Other Observations. Prowazek describes asexual reproduction by longitudinal division, in which the trophonucleus divides first, then the kinetonucleus, and lastly the flagellum, while Patton fails to find the division of the flagellum, and states that the second flagellum is developed as an outgrowth from the kinetonucleus. Prowazek has seen sexual conjugation, which Patton fails to find. Prowazek describes encystment, and considers that the infection is carried by the fæces, with which latter statement Patton agrees. Prowazek finds that the male and female parasites penetrate into the eggs of the fly, and undergo therein an autogamy by ethogenesis, in which the kinetonucleus carries out the development, by parthenogenesis, in which the trophonucleus is active, and by an indifferent type, in which both nuclei participate. There are, however, many transitional forms between these stages. Patton's description of the life-cycle is quite different, and resembles that which he has given for *Crithidia gerridis* (vide p. 369). He further supports this life-cycle by his previous description of a *Herpetomonas* in *Culex pipiens*.

Herpetomonas jaculum Léger, 1902

The parasite which was found in the alimentary canal of *Nepa cinerea* by Léger, has been studied in detail by Miss Porter.

Morphology. This *Herpetomonas* in the flagellate stage measures 15 to 33 μ in length by 1 to 4 μ in breadth, and is surrounded by a clear, flexible ectoplasm provided with myonemes, inside which is a granular endoplasm with granules arranged in such a way as to suggest a cytopharynx. The trophonucleus is oval, the kinetonucleus is fairly large, and chromidia are found widely separate from one another. A blepharoplast lies close to the well-developed flagellum.

Life-History. The flagellate attaches itself to the wall of the gut or to débris, and divides until small motionless forms result, which, shortening and encysting, form the 'post-flagellate stage.' It now escapes from its host as minute cysts in the fæces, which are deposited on the leaves of water plants. The fæces are eaten by the young *Nepa*, *i.e.*, there is contaminative or casual infection, and now the ingested cysts, which are small oval bodies, with tropho- and kineto-nuclei, form the preflagellate stage of the life-cycle, which passes into the flagellate adult stage.

Hereditary Infection. In addition, Miss Porter has seen flagellate forms pass through the wall of the gut near the ovaries, into which they penetrate and encyst, all of which is suggestive of hereditary infection.

H. bütschlii Saville Kent, 1881

In *Trilobus gracilis*, but it has not been perfectly studied.

H. pycnosomæ Roubaud, 1904

In *Pycnosoma putorium* Wiedmann, in Africa.

H. davidi Lafont, 1909

Described in *Euphorbia pilulifera* by Lafont, in Mauritius, Ceylon, and Réunion, East and West Africa, West Indies, Portugal, and India. We have often found this species in Ceylon. The parts of the plants affected are not healthy, and the disease is called 'flagellosis.' Miss Robertson has found a similar parasite in cotton plants in Uganda. It measures 10·5-16·5 × 1·5 microns.

Other Species.—*H. gracilis* Léger, 1902, in the Malpighian tubules of the larvæ of *Tanypus*; *H. lesnei* Léger, 1903, in the mid-gut, near the Malpighian tubules of *Dasyphora pratorum*. *H. subulata* Léger, 1903, in the gut of *Tabanus glaucopis* and *Hæmatopota italica* Meigen. *H. sarcophagæ* Prowazek, 1904, in the gut of *Sarcophaga hæmorrhoidalis*, *H. bombycis* Levaditi, 1905, *H. vespæ* Porter, 1911, in the gut of *Vespa crabro*, *H. ctenophthalmi* Mackinnon, 1909, in *Ctenophthalmus agyrtes*, *H. drosophilæ* Chatton and Alilaire, 1908, in *Drosophila confusa*.

Genus Crithidia Léger, 1902, *emendavit* Patton, 1907

Definition. Herpetomonidæ, in which the schizont is characterized by an attenuated posterior end, to which the flagellum is attached by a rudimentary undulating membrane. The kinetonucleus is situated close to the trophonucleus, either on the flagellar sides or slightly and rarely a little on the aflagellar aspect of this structure.

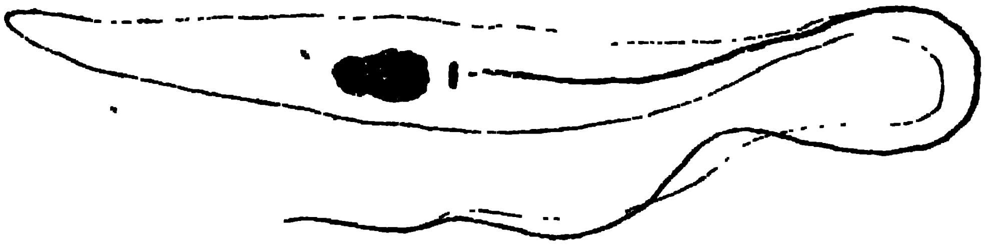


FIG. 81.—DIAGRAM OF A CRITHIDIA.

Remarks. In 1902 Léger created this genus for a flagellate organism which he found in the alimentary canal of *Anopheles maculipennis*, and in 1907 Patton worked out the life history of *Crithidia gerridis*.

Crithidia gerridis Patton, 1908.

This flagellate is a parasite in *Gerris fossarum Fabricius* and in a species of Microvelia, and in a water-bug allied to *Perittopus* found in Madras. The flagellate is found in the crop of the insect as a round, oval, or pear shaped body, 4 to 6 μ in length and 3 to 4 μ in breadth, in which lie a circular trophonucleus and a rod shaped kinetonucleus.

The parasite grows and becomes vacuolated, showing, when coloured, a small pink staining area between the kinetonucleus and the periphery, which later becomes a distinct pink rod, and is a rudimentary flagellum attached by a rudimentary undulating membrane to the cell. This membrane shows as a faint pink band between the flagellum and the body of the parasite.

Later the flagellum can be seen arising from an achromatic area, the blepharoplast, close to the kinetonucleus, and running along the periphery of the parasite.

The kinetonucleus increases in size, and the trophonucleus shows its chromosomes, while chromatic particles appear in the cytoplasm.

The kinetonucleus now approaches the trophonucleus, and elongates and divides, while the flagellum thickens and splits longitudinally, so that there are two kinetonuclei and two flagella.

The trophonucleus and the cytoplasm now divide, so that two daughter cells are formed, which in turn divide, forming rosettes of eight to forty or more cells, measuring 6 to 10 μ in length by 4 to 8 μ in breadth.

Eventually the rosettes break up, and the rounded parasite has a central nucleus and a kinetonucleus at one side, and from a point close to this a flagellum passes round its circumference, giving it an undulating contour. The parasite elongates, and the posterior end is drawn out along the flagellum; the length is now 15 to 45 μ and the breadth 2 to 4 μ. They are often found agglomerated together.

Longitudinal division now takes place rapidly, and the parasites pass down the intestinal tract and shorten, until they become round bodies with long flagella. A change then takes place, the flagellum becoming absorbed and

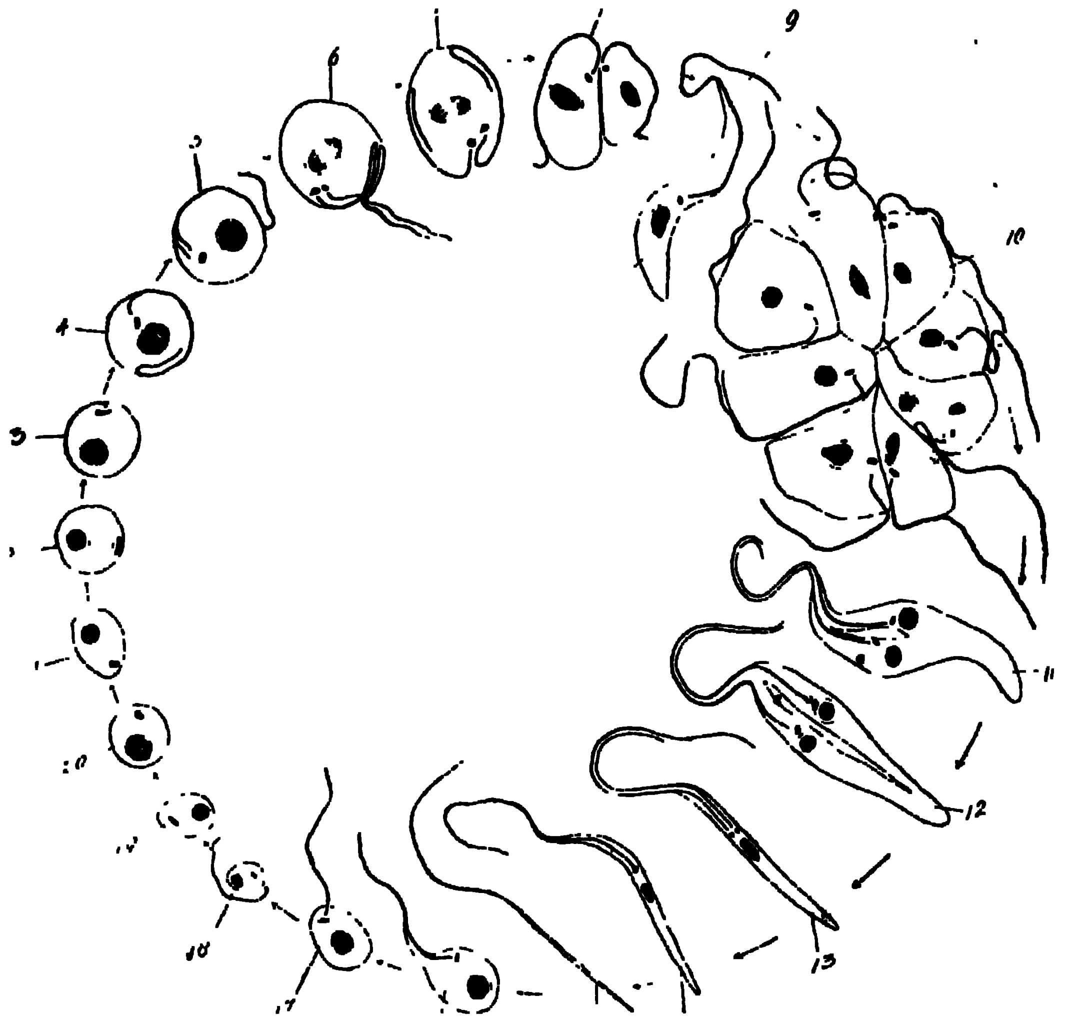


FIG. 85.—THE LIFE-CYCLE OF *Crithidia gerridis* PATTON.
(This is a diagram constructed from Patton's drawings.)

14, Crithidial form; 15, very slender forms; 16-18, rounded forms losing their flagella; 19-3, preflagellate round forms, gradually increasing in size; 4, 5, formation of the flagellum, 6-8, division; 10, agglomeration; 11-13, division.

finally detached, and the parasite appearing as a rounded body with a tropho- and a kineto-nucleus. The life-history is completed by the bodies being discharged with the fæces into the water, and so taken up by a new host. The ovaries and eggs were not infected. This is an excellent example of Minchin's contaminative method of infection.

Miss Porter has fully traced out the life-history of *C. gerridis* found in *Gerris paludum* in England, and confirms Patton's researches.

Crithidia melophagia Flu, 1908.

Flu has described *Crithidia melophagia* in *Melophagus ovinus*, a parasite of the sheep. He gives an account of asexual and sexual reproduction. The latter is characterized by a process of reduction, followed by conjugation with the formation of an oökinete and the infection of the eggs of the insect, which may cause a second generation of flies to carry the organism (Fig. 90).

Other Species.—*C. fasciculata* Léger, 1902, in the intestines of females of the species *Anopheles maculipennis* and in *Culex fatigans* Wied.; *C. campanulata* Léger, 1903, in the intestine of *Chironomus plumosus*; *C. minuta* Léger, 1903; this parasite is found in *Tabanus tergestinus*, and is characterized by having a thick rounded end; *C. cleti* Hindle and Lewis, 1912, in *Cletus varius* Dall, *C. pulicis* Porter, 1911, in *Pulex irritans* L., *C. hystrichopsyllæ* Mackinnon, 1909, in *Hystrichopsylla talpæ*, and a number unnamed by Miss Robertson in Hemiptera in Uganda; *Crithidia hyalommæ* O'Farrell, 1913.

Genus Leishmania R. Ross, 1903.

Synonyms. *Piroplasma* Laveran and Mesnil, 1903, *Helcosoma* Wright, 1903, *Herpetomonas* Rogers, 1904.

Definition. Herpetomoninae, living principally in endothelial cells, but also found in leucocytes and in the peripheral blood of mammals as small, oval, cytoplasmic masses with tropho- and kineto-nuclei, and developing into flagellate bodies in cultures.

Remarks.—Three species are known in man, morphologically similar, but pathogenetically different: *Leishmania donovani* Laveran and Mesnil, 1903, *L. infantum* Nicolle, 1908, and *L. tropica* Wright, 1903, and probably there are other varieties.

With regard to these species there is a general consensus of opinion that *L. tropica*, with its variety *americana*, is distinct from *L. donovani* and *L. infantum*. In respect to the two last-named forms it has been argued that they are identical because:—

I. Both attack adults and children.

II. A monkey immunized against *L. infantum* is refractory to *L. donovani*.

On the other hand, there are some differences, viz.:—

I. It is true that both attack adults and children, but the latter are much more easily infected by *L. infantum*.

II. *L. infantum* infects dogs readily, while these are more refractory to *L. donovani*.

III. *L. infantum*, according to one experiment by Nicolle and Manceaux, only produces a local cutaneous lesion when inoculated under the skin of a monkey, while *L. donovani*, under similar conditions, according to Row and Korke, produces a local cutaneous lesion, with or without a general infection, when inoculated into or under the skin.

For the present, we shall treat *L. donovani* and *L. infantum* as separate parasites.

The Sudan parasite is considered by Archibald to be distinct from *L. infantum* because:—

I. It behaves like *L. donovani* in that it does not readily infect dogs experimentally.

II. It behaves like *L. donovani* in that it produces a local cutaneous lesion, with or without a general infection, when inoculated into the skin of a monkey.

He further believes that it is a special variety of *L. donovani* because:—

I. It has signs of a coccal stage in its life-history. This has been objected to by Wenyon and Laveran, but has been confirmed by Smallman in two cases from Malta and by Statham and Butler in Sierra Leone.

II. Experimental evidence is not in favour of its being insect-borne. On the contrary, careful feeding experiments suggest that the method of infection is oral, while a study of the epidemiology and other facts make it probable that it is water-borne. The feeding experiments have been confirmed by Basile, though objected to by Laveran while the epidemiology supports facts noticed by Bousfield Thomson, and Marshall.

III. The local lesion produced by intracutaneous inoculations into monkeys does not exhibit any eosinophile leucocytes, which is different from the lesions produced by *L. tropica*, but it is not known whether this occurs or not in those due to *L. donovani* and *L. infantum*.

We therefore recognize it as *L. donovani varietas archibaldi*.

Leishmania donovani Laveran and Mesnil, 1903.

Definition.—*Leishmania*, producing in man the signs and symptoms of tropical kala-azar, in experimental monkeys general and local infections, but not readily infecting dogs.

History.—The history is fully given in Chapter XLVII., p. 1289, and it need only be remarked that the parasite discovered by Leishman in 1900 was described by himself and by Donovan in 1903; while Rogers, in 1904, cultivated the parasite at 22° C. and discovered the flagellate stage.

Christophers, in 1904, considerably added to our knowledge of these parasites, and Patton, in 1906 and 1907, showed that they were not merely found more commonly in the leucocytes of the peripheral blood than had been previously believed, but that they could develop into typical flagellates in the bed-bug, *Clinocoris rotundatus* Signoret, 1852 (which is the same as *C. macrocephalus* Fieb), but this is apparently more in the form of a natural culture than of a cyclic development.

Development in the Bug.—According to Patton, the parasites are ingested by the bug enclosed in the large cells or leucocytes, as just mentioned, and develop into fully flagellated forms without reference to the temperature of the external air.

The first change begins usually by an increase in size up to 4 to 7 μ and a vacuolation of the cytoplasm on the second day, but may be deferred for several days.

The single parasite may proceed directly to flagellation by the appearance of an area stained bright pink by Giemsa, and called 'the flagellar vacuole.' This vacuole, which has a dark centre, rapidly increases in size up to 1 to 3 μ, and, passing to the surface, sends out a small pink brush, which forms the flagellum by merely growing longer. There appears to be no doubt that the flagellum forms in this vacuole, and is not directly connected with the kinetonucleus.

The flagellate form has a dark blue, granular cytoplasm with a circular trophonucleus, which stains deeply in the centre, and a kinetonucleus lying

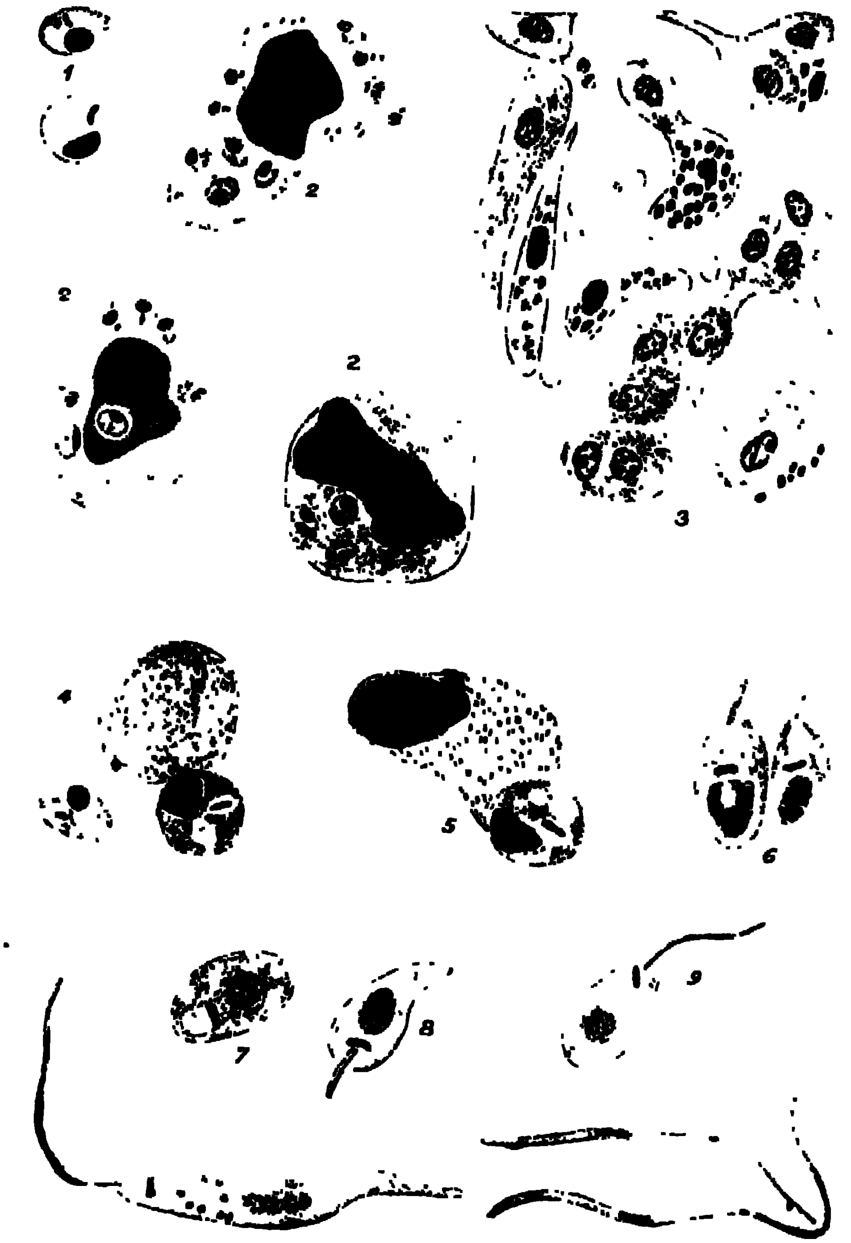


FIG. 86.—*Leishmania donovani* LAVERAN AND MESNIL

1, Free binucleate forms (after Christophers); 2, endothelial cell and leucocytes containing parasites (after Christophers); 3, capillary in the liver, showing endothelial cells containing parasites (after Christophers); 4, two parasites escaping from a leucocyte in the alimentary canal of the bug (after Patton); 5, further development in the bug (after Patton); 6, flagellate forms in the bug (after Patton); 7-11, culture forms (after Leishman); 7, 8, 9 show the development of the flagellum.

across the long diameter, and situated near the trophonucleus, and possessing a long flagellum consisting of a number of filaments adhering closely together, inserted into a pale area near the kinetonucleus. These parasites may divide into two equal or unequal flagellate forms, and apparently may go on so dividing for a length of time.

Instead of proceeding directly to flagellation, the parasite may show a division of its nuclei into two, with the formation of two flagella, and then division into two flagellate parasites, or the nuclei may multiply without division of the cytoplasm, so that forms containing four to eight nuclei may be found together, which eventually break up into separate flagellate forms. Patton has traced the development into the post-flagellate stage, and believes that if the bug is fed upon human or monkey's blood the flagellates are quickly destroyed, but if not so fed the cycle of development is completed in ten to twelve days after a single feed. He believes that this destruction of the flagellates by warm blood is the cause of the endemicity of the disease.

Donovan suggests that the true host may be *Conorhinus rubrofasciatus*, but Patton finds that the parasite in this bug degenerates and never flagellates.

Further, the evidence so far collected does not support the possibility of the bug, the flea, the mosquito, the phlebotomus, the domestic fly, the louse, or the tick as being the causal agent. It will be remembered that all these arthropods possess flagellates of their own, which the researches of Fantham and Porter, and Laveran and Franchini, have shown to be capable of producing disease and death in mammals when injected (*vide* p. 363).

As examples of flagellates occurring in bugs we may quote:-- *Herpetomonas lygæi* in *Lygæus militaris*, found in the Sudan and investigated by Archibald; *H. hospei* in *Lygæus hospes*; *H. aspongopi* Aders in *Aspongopus viduatus* (Sudan); *H. pyrrhocori* in *Pyrrhocoris aptera*; also Crithidia in *Cletus varius*, *Gerris fossorum*, *Conorhinus rubrofasciatus*, *Leptocoris trivittatus*; also a trypanosome in *Neotoma fuscipes*. It is therefore possible that the last word has not yet been said with regard to arthropods and their flagellates as the causal agent of kala-azar.

Archibald's experiments with the Sudan variety are very suggestive that the infection may be *per os*. The cycle may possibly be from man via the fæces to some water arthropod, from which it may escape also via the fæces into water, and so via the mouth into the alimentary tract and system of man, but this is not yet proved. With reference to this it should be remembered that Fantham and Porter infected young rats by feeding with *Nepea cinerea* containing *Herpetomonas jaculum*.

The present state of our knowledge with regard to this parasite is that it is the cause of the disease called kala-azar; and that it is probably spread by means of some arthropod, but the particular carrier is not known.

Geographical.—**The parasite is known to occur in India, Ceylon, China, Arabia, Egypt, and the Sudan, and many parts of Africa.**

Morphology.— **The parasite is round, oval, or pyriform in shape, measuring 2 to 3·5 μ in length by 1·5 to 2 μ in breadth, with a granular cytoplasm containing two chromatic masses. The larger, more rounded, stains slightly; the smaller, rod-shaped, stains deeply. From the latter a linear structure (Mesnil and Novy's rhizoplast) runs to the acute end. A vacuole is also often present.**

Distribution in the Body.—**The parasites are found sometimes in large numbers in endothelial cells in the capillaries of the liver, spleen, bone-marrow, lymphatic glands, and mucosa of the intestine, in the blood from the femoral, portal, and hepatic veins, and more rarely in the circulating blood shortly before death.**

Parasites liberated from the large cells are apparently taken up by mono-

nuclear, polynuclear, and rarely eosinophile leucocytes, and may be occasionally seen in films obtained from the finger even in early stages of the disease, though more frequently near the end.

Treutlein has stated that the parasite is to be also found in red blood cells, but probably they are merely lying in the concavity of the red corpuscle.

Life-History.—Multiplication in man takes place by simple binary fission and by multiple division into three or more bodies. Division begins at the broad end, but cytological details are still wanting, and the rest of the life-cycle is unknown.

Cultivation.—Cultures are obtained by adding the spleen-juice to a sterile sodium citrate solution and incubating at 22° C., as done by Rogers, or the N.N.N. medium may be used (p. 377).

Inoculation.—Monkeys, rats, and less readily dogs can be infected.

Pathogenicity.—*Leishmania donovani* is the cause of Indian kala-azar.

Archibald's Variety of **Leishmania donovani.**

Definition.—*Leishmania donovani*, which does not readily infect dogs experimentally, with signs of a coccal stage in its life-history. There is evidence that infection is by means of water. Habitat, Anglo-Egyptian Sudan.

Remarks.—This parasite has been investigated by Bousfield, who reported also a natural canine infection therewith (this, however, has not been confirmed by Archibald's many investigations), and also by Marshall, who infected monkeys and performed many careful experiments. Archibald's reasons for believing that this parasite is a variety of *L. donovani* are:—

1. *Coccal Bodies.*—Certain coccal bodies have been noted by Archibald in liver smears obtained from a case clinically simulating kala-azar. Material obtained by liver puncture from this case produced kala-azar when inoculated into a monkey, and Archibald suggests the hypothesis that these coccal bodies represent a stage in the life-history of the Leishman-Donovan parasite.

2. *Epidemiology.*—In the Sudan the evidence collected by Archibald does not suggest that the disease is insect-borne. This observer produced the disease in monkeys by carrying out careful feeding experiments, and suggests that the disease may be water-borne, a point which agrees with the observations of Bousfield, Thomson, and Marshall, that the disease exists more commonly in villages situate near water than in those farther away. A large number of domestic animals have been examined by Archibald, and none have been found to act as natural hosts of the virus; even experimental evidence shows that dogs are not readily susceptible to the virus—a fact which tends to differentiate the parasites of Sudan kala-azar from those of the Mediterranean.

Clinically the disease resembles that met with in other countries. As an aid to its diagnosis and as indication for splenic puncture being carried out, Archibald records the fact that peripheral blood films from suspected cases show evidence of blood destruction, leucopenia, and increase of large mononuclears and large lymphocytes, together with an absence of eosinophiles. The comparative or total absence of eosinophiles are suggestive of the disease; further, during the course of the disease an increase or diminution of the eosinophiles in the peripheral blood is some criterion as to whether recovery from kala-azar is likely to result.

Leishmania infantum Nicolle, 1908.

Synonym.—*Leishmania donovani* Laveran and Mesnil, 1903, *pro parte.*

History.—In 1904 Cathoire observed peculiar bodies in films from the spleen of a child who had died of an ill-defined malady in Goulette, in Tunisia. These bodies Laveran recognized as *L. donovani*. In 1905 Pianese announced his discovery of Leishmania bodies in large mononuclear cells in the smears from the liver and spleen of children dying from a type of infantile splenic anæmia, which he proposed to call infantile Leishmania anæmia in order to distinguish it from other forms of infantile splenic anæmia. In 1907 Nicolle and Cassuto observed the parasites in the spleen of a child in Tunisia suffering from irregular fever, splenomegaly, etc., and Nicolle named this disease infantile kala-azar, which is a most suitable name. After this it was described in Crete in 1907 by Aichel: in Sicily, Stromboli, and Calabria by Gabbi and Feletti; in 1910 it was found in Malta by Critien, in Lisbon by Alvares, while Gabbi proved that the disease 'ponos,' as seen in Spezzia, was the same disease; and Christomanos, Aravandinos, and Michaelides found it in the Grecian islands and Greece itself. In 1911 Christomonas found it in several places in Greece and Asia Minor, while Batinos found it in Corfu, Kefalinos in Patras, and it was found to be widely distributed in Southern Italy and Sicily. Martzinowsky has observed cases in Moscow, Tashim Ibrahim in Tripoli, Lemaire in Algiers, and Sluka and Zarfl in Tashkent in Turkestan. Marshall reports the disease among children of about twelve years of age in the Sennar province of the Sudan.

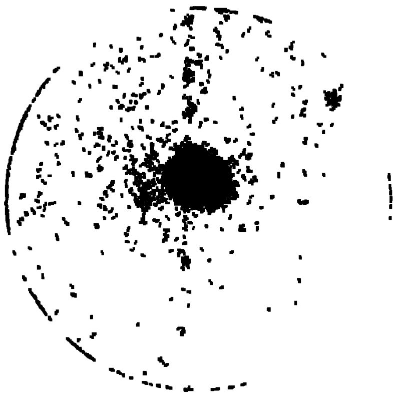


FIG. 87.—*Leishmania infantum* NICOLLE FROM THE LIVER OF A DOG EXPERIMENTALLY INFECTED.
(From a microphotograph by Basile.)

It is thus seen that *L. infantum* is mainly found around the Mediterranean basin, but may extend to Moscow and to Turkestan; probably its geographical distribution is but little known at present.

The study of the life-history began by the experiments of Nicolle, who in 1908 successfully inoculated a dog in Tunis intrahepatically and intraperitoneally with splenic blood from a case of infantile kala-azar, monkeys were also inoculated successfully.

Later, Manceaux, Comte, Laveran, Pettit, Jemma, Di Cristina, Cannata, Alvares, da Silva, Pulvirenti, and Tomaselli, successfully inoculated dogs, monkeys, and guinea pigs, and Volpino produced a purely local lesion somewhat analogous to Oriental sore by inoculating the cornea of a rabbit from an infected dog.

In 1908 Nicolle and Comte recorded the discovery of spontaneous kala-azar in dogs in Tunis, and eventually found 1·8 per cent. to be infected in the spring, but this percentage was raised by the Sergents to 7·2 per cent. in the summer in Algiers, and Sevenet has found that in Algiers 1·6 per cent. show infection in the spring and 8·8 per cent. in the summer. Basile, in an endemic region, Bordonaro, near Messina, found twenty-seven infected dogs out of thirty-three examined by trephining the head of the femur and making smears of the bone-marrow, and he obtained also a very important fact when he found infected dogs in *every* house where kala-azar had been found by Gabbi; and still more interesting is the observation that infected dogs were found in houses without cases of kala-azar, but subsequently a case has already occurred in one of these houses. Canine kala-azar has also been found in Catania, slightly in Rome, in 0·69 per cent. of dogs in Greece by Cardamatis, in 2·66 per cent. in Lisbon, also in Malta by Critien and Babington, and in a few dogs in Colombo by Castellani in 1911. It must be noted, however, that Colombo, being one of the greatest harbours of the world, some of the dogs found are in reality imported dogs. Negative results are reported by Donovan in Madras in 1,150 dogs, by Fülleborn in Hamburg in 50 dogs, by Wenyon in Bagdad in 110 dogs, by Jemma, Cristina, and Cannata in Palermo in 127 dogs, and by Archibald in the Sudan. For a long time cats were examined with negative results, but recently Ed. and Et. Sergent, Lombard, and Quillchini, have found a four-month-old kitten to be infected in Algeria. It will thus be seen that of all the endemic centres of infantile kala-azar, Palermo alone affords no evidence of natural canine kala-azar.

As the result of his work Basile, supporting Nicolle, has come to the conclusion that infantile and canine kala-azar are one and the same disease. He reared a number of dogs in the laboratory in Rome (where canine kala-azar is rare), and some of these he took to Bordonaro, where they contracted canine kala-azar and died. The parasites were found in the bone-marrow, spleen, and liver (Fig. 87), and also in *Pulex serraticeps*, taken from them during the last stages of the disease. The dogs in Rome were subsequently killed, and found to be free from *L. infantum*. *P. serraticeps* from a laboratory dog whose bone-marrow contained no Leishmania were isolated and kept at 22° C. in two glass vessels, and eventually one lot was fed on spleen-juice from a case of canine kala-azar, while the others were kept as controls. After a time the intestines of the fleas were dissected out and divided into two portions one was used for smears, and the other was made into an emulsion and injected subcutaneously into a young dog one month old, the bone-marrow of which had been shown to be free from Leishmania, while another dog was used as a control.

The smears from the infected fleas showed numerous specimens of Leishmania in a state of multiplication, while the control fleas were free. After fifteen days the dog became ill with fever and loss of appetite and dejection, and showed the parasites in the peripheral blood. In twenty-nine days the dog died, probably as a result of an operation to obtain bone marrow from the tibia. Natural infection by flea-bites was effected by introducing a sick dog covered with fleas into a cage containing a bitch and two thirty-day-old puppies, whose bone-marrow had been found free from infection. In thirty days these dogs were found to be infected, and subsequently the puppies died, but the other dogs lived, Controls were not infected. Basile found *P. serraticeps* in the bedclothes and mattresses of families who kept dogs in the house, and some of these fleas were brought to Rome from dogs or mattresses of people living in Bordonaro, and were fed upon laboratory-reared marrow-examined, clean dogs, whose peripheral blood and liver had also been examined for parasites with negative result. The dogs became ill and died, and the parasites were found in the bone-marrow, liver, and spleen. Control dogs were then killed and found healthy.

Basile concludes that *P. serraticeps* is the carrier of the disease. In Bordonaro he examined 1,000 fleas from dogs and the beds of families, but found only four infected with Leishmania. With regard to *P. irritans*, Basile finds that it is frequently a parasite of the dog, and that among specimens caught in the bed of a child suffering from kala-azar one was found to contain Leishmania. From experiments he believes that fleas are infective from December to March. There is one curious point noted, that Leishmania was found in spleen, liver, and bone marrow only a few days before death, though the fleas had bitten the dogs three months earlier.

With regard to the objections to this work, Gabbi has pointed out—

1. Canine and human fleas placed in contact with pure cultures of Leishmania on Nicolle's blood-agar show blood in the gut, but no Leishmania.
2. Leishmania in culture with intestinal bacteria from the flea or in culture with the juice from the same do not develop.
3. Starving fleas placed in contact with spleen-juice obtained by puncture from a child with kala-azar do not become infected with Leishmania.

Mazocchi in Piedmont finds that the fleas of dogs possess flagellate bodies of a crithidia-like nature, distinct from Basile's description of the Leishmania bodies found by him.

Alvares and Pereira da Silva's experiments with *Ctenocephalus serraticeps* support Basile, and they believe the infection to be contaminative via the fæces.

The main objection to Basile's experiments is that they were conducted in Rome, in which place dogs may acquire natural canine kala-azar; secondly, the question has to be solved as to whether the bodies seen in the flea are or are not Leishmania, and if not, whether they are some parasite naturally occurring in the flea.

Basile describes the forms found in the flea as follows:—

In the mid-gut Leishmania-like forms as oval, rounded, or pyriform bodies, 2 to 3 μ in length, with an excentrically-placed trophonucleus, and generally a kinetonucleus. Large forms, 4 to 6 μ by 2 to 3·5 μ, are also seen, and more posteriorly pyriform bodies, 6 to 8 μ by 1·5 to 2·5 μ, which latter are provided with flagella measuring about 3 μ in length.'

Basile concludes that there is a cycle of development with preflagellate, flagellate, and post-flagellate forms. But a number of fleas have been found to possess natural parasites belonging to the genera *Herpetomonas* and *Crithidia*, and Miss Porter has definitely proved that *Crithidia pulicis* is a true parasite of *P. irritans*. The list of known flea parasites is:—

Crithidia pulicis Wenyon, 1908, in *Xenopsylla cleopatræ*.
Crithidia ctenophthalmi Patton and Strickland, 1908, in *Ptenophthalmus ægyrtes*.
Crithidia hystrichopsyllæ Mackinnon, 1909, in *Hystrichopsylla talpæ*.
Crithidia pulicis Porter, 1911, in *Pulex irritans*.
Herpetomonas ctenophthalmi Mackinnon, 1909, in *Ptenophthalmus ægyrtes*.

There are also a number of unnamed flagellates recorded—*e.g.*, a species of *Herpetomonas* by Balfour in 1906 in *Læmopsylla cleopatræ*, which may be the same as Wenyon's *Crithidia*. It does not appear certain that Miss Porter's *Crithidia* and Wenyon's *Crithidia* are the same, and if they are not, then Miss Porter's *Crithidia* must be given a different name.

The identity of infantile kala-azar and canine kala-azar is supported also by Bandi's experiments on agglutination. Animals inoculated by him with cultures of *L. infantum* developed agglutinins for this species, and nearly in the same amount also for the Leishmania isolated from dogs, and *vice versâ*.

Franchini states that *Anopheles maculipennis* can be infected with cultural forms of Leishmania. Gabbi inculpated at one time *Musca domestica* as a carrier.

Morphology.—*L. infantum* so closely resembles *L. donovani* as to be indistinguishable morphologically.

Life-History.—It exists in the peripheral blood, bone-marrow, spleen, and liver in children, and suspicion is aroused that it may be spread by fleas, and that aflagellate and flagellate organisms seen in these parasites may be stages in the life-cycle.

Culture.—It is easily cultivated upon the Nicolle, Novy, MacNeal (or N.N.N.) medium, as was first shown by Nicolle. The organisms develop in the condensation liquid and on the moist surface of the agar. It can be subcultured indefinitely. No distinct differences can be discerned between the three species of Leishmania in culture. *L. infantum* can to a certain extent be distinguished from *L. donovani* by the fact that the latter is less easily inoculable with success into dogs.

Pathogenicity.—It is the cause of infantile kala-azar, and at one time was considered to be the cause of canine kala-azar, which we will now describe.

Canine Kala-Azar.—There are two types of canine kala-azar—an acute and a chronic.

Acute canine kala-azar, usually appears in young dogs, when it is associated with fever (39° to 40° C.) of a remittent type, followed by loss of appetite, wasting, tremors, motor disturbance in the hind-limbs, and rarely diarrhœa. The animal finally dies in a comatose condition at the end of three to five months.

Chronic canine kala-azar begins without any apparent symptoms, except, perhaps, loss in weight, but as it progresses anæmia sets in, and tremors, together with motor disturbances of the hind-limbs, may be noticed. It is therefore milder than the preceding, is very chronic, and associated with considerable enlargement of the spleen. The inoculated dogs have several times been reported to exhibit symptoms resembling dumb rabies. Post mortem examination exhibits that the spleen has a thickened capsule, with hypertrophy of the lymphoid elements; the epithelium of the blood-lacunæ are much hypertrophied, and full of parasites. The liver cells show fatty degeneration; parasites are found in the liver cells and in the endothelium of the lymphatics. The interstitial tissue of the kidney is increased, and parasites occur in the endothelial cells. Parasites may be found in the round-celled infiltration under the capsule of the kidney. The suprarenal bodies show cloudy swelling of the cortical cells, infarcts in the medulla, and vacuolation of the cells, which may be invaded in patches by the parasites. The pancreas showed a hypertrophy of the connective tissue, with the presence of the parasites in the endothelium of the lymphatics. The bone-marrow showed large numbers of mononuclear cells with parasites. The heart muscle showed cloudy swelling. No parasites are found in the lungs.

There is a growing suspicion that this is quite distinct from any human disease, because-

1. Canine Leishmaniasis exists in places like Marseilles, where there is no Mediterranean kala azar, and this disease exists in Palermo, where Canine Leishmaniasis, according to Caronia and di Giorgio, is absent.
2. Spagnolio says that in Bordonaro, in 1910, Basile found Canine Leishmaniasis in 70 per cent. of dogs examined. From 1910 onwards a number of dogs were destroyed, and in 1914 a very large number were killed because of threatened rabies. In 1915 some seventeen dogs were examined for Leishmania and found negative, and yet the human endemic disease had not diminished.

It is known to occur in Africa, Europe, and Asia, but not in America or Oceania.

The formation of a local sore on the cornea of a rabbit must be remembered as indicating the possibility of a local disease like that caused by *L. tropica*.

Leishmania tropica Wright, 1903.

Synonyms.- -*Helcosoma tropicum* Wright, 1903; *Crithidia cunninghami* Carter, 1909; *Sporozoön furunculosum* Firth, 1891.

History.- This parasite was described by Wright in a case of Oriental sore, and later Martinowski and Bognoff found the same parasites in Bouton d'Alep. It is believed by some that this parasite was first described by Cunningham in 1885, and more completely studied by Firth, who called it *Sporozoön furunculosum* Firth, 1891; if this is so, the correct name of the parasite should be *L. furunculosa* Firth, 1891.

It was specially investigated in 1905 by James in Delhi sore, Lahore sore, and Frontier sore. Nicolle has obtained cultures of the parasite on the McNeal Novy medium, and Carter describes sexual forms. Carter, Balfour, and Nattan-Larrier believe, in our opinion correctly, that there are several varieties or species included under the term *L. tropica*; thus Carter maintains that the Cambay sore is different from the 'clou de Gafsa' of Africa. Werner, Carini, and Splendore have shown that the sore may spread to or begin on mucous membranes.

Distribution.- It is found principally in Asia, in India, China, Asia Minor, Persia, etc., but also occurs in Africa, Algeria, Tunisia, on the Niger and in the Egyptian Sudan, in Mexico, Panama, and South America.

Morphology.- It differs in no morphological respect from *Leishmania donovani* in the human body, though certain minor differences have been described in the flagellate forms in cultures.

Cultivation.- In 1908 Nicolle first cultivated the parasite on blood-agar and on the modified Nicolle, Novy, McNeal medium often called 'N.N.N.' It grew slowly both in the liquor of condensation and on the agar at 20° to 22° C., producing flagellate and division forms on the fourth day, which increased in numbers by the eighth to tenth day, when rosettes appeared and increased in such numbers that the masses were visible to the naked eye. After this a tendency to agglutination develops and increases until after one or two months the parasites die. The typical flagellate of these cultures is herpetomad-like, measuring with the flagellum 40 to 45 μ with a breadth of 2 to 4 μ, but the flagellum alone measures 16 to 20 μ. There is no undulating membrane, but a trophonucleus and kinetonucleus can be seen. Three types of flagellates can be seen in cultures—viz., one almost spherical, a second short and stumpy, and a third long and narrow. Subcultures are best made from the tenth to the fifteenth day, and these can be repeated apparently indefinitely. Forty-five generations have been recorded during a period of eighteen months.

It is usual to state that there are no differences between the cultural forms of *L. tropica* and *L. donovani*, but Row considers that there are several points of difference—viz., that the flagellate forms of *L. tropica* are longer and larger, that the flagellum is longer, while the growth is quicker and may take place at higher temperatures than in *L. donovani*.

Inoculation.—Martzinowsky, Wenyon, and Patton have successfully inoculated themselves, and other people have also been successfully inoculated from cases of Oriental sore. The incubation period varies from sixteen days to six and a half months, and the papule is generally ushered in with febrile symptoms lasting several days. The inoculated sore begins as a papule, and becomes a nodule; when excised and examined it presents the typical appearances of Oriental sore, and contains *L. tropica*.

Successful inoculations are recorded from man to monkeys and dogs, from monkeys to man, other monkeys and dogs, from dogs to dogs, and from cultures to man, monkeys, and dogs.

Immunity.—Infection confers immunity if the cure is complete, and if a sufficient interval has elapsed between the cure and the reinfection; if not, a condition of hypersensibility is produced, as demonstrated by a shortened incubation period. Kala-azar infection in dogs affords immunity against *L. tropica* during and after the attack; Oriental sore protects monkeys partially or completely against *L. donovani*.

Insect Carriers.—No insect at present has been demonstrated to be the true host of *L. tropica*. *Musca domestica* may possibly be a carrier because the parasites can retain their vitality therein, and may be transferred to any raw surface, and thus induce infection, but it is not a true host, though Row has found the contents of the gut to be infective, and believes that infection can be spread by its fæces. There can be no doubt that a natural culture producing flagellates and, according to Patton, even post-flagellate forms, can take place in the bed-bug *Clinocoris rotundatus*, but all attempts at transmission have failed, and the same condition of affairs holds good for *Stegomyia fasciata*. Phlebotomus is suspected, but there is no experimental evidence. Flu suspects ticks as being the possible carriers in Dutch Guiana. Pediculi have no supporters, and *Stomoxys* is not regarded as a likely carrier. As Patton has recorded the presence of *L. tropica* in the peripheral blood, it might not be necessary for a blood-sucker to ingest juices from the local sore.

Pathogenicity.—It is the cause of specific sores found in the skin and on mucous membranes in Asia, Africa, and America, and which are commonly known as Oriental sore, but which also have a large number of local names, such as pian-bois, espundia, Delhi sore, Bagdad button, clou de Gafsa, ulcer of Bauru, etc.

Laveran and Nattan-Larrier have created the variety *americana* (*L. tropica* Wright var. *americana* Laveran and Nattan-Larrier) for the Leishmania found in *Espundia*, characterized by a flattened nucleus. Vianna has created a new species, *L. braziliensis*, for a Leishmania observed by him in cases of ulcer, but Marchoux doubts whether this new species is justifiable, as it has no distinctive characters.

SUBFAMILY TRYPANOSOMINÆ CASTELLANI AND CHALMERS, 1919.

Definition.—Trypanosomidæ in which the kinetonucleus is situate in certain stages of the life-cycle between the trophonucleus and the aflagellar extremity of the body. A well-developed undulating membrane is present.

Type Genus.—*Trypanosoma* Gruby, 1843, *emendavit* Laveran and Mesnil, 1901.

Classification.—A brief history of the discovery of the more important species of this family has been given in Chapter I. The genera which have been described are:

Trypanosoma Gruby, 1843, *emendavit* Laveran and Mesnil, 1901.
Trypanoplasma Laveran and Mesnil, 1901, *emendavit* 1904.
Trypanophis Keysselitz, 1904.
Endotrypanum Mesnil and Brimont, 1908.
Schizotrypanum Chagas, 1909.
Rhynchoidomonas Patton, 1912.

But Trypanoplasma and Trypanophis belong to the Bodonidæ, and not to the Trypanosomidæ (*vide* p. 337).

Endotrypanum would appear to be an immature trypanosome, without an undulating membrane, and parasitic in red corpuscles. In 1905 Nissle drew attention to the occasional invasion of red cells by trypanosomes, and in 1904 Moore found peg-shaped bodies in the red blood-corpuscles of cattle suffering from trypanosomiasis in Southern Nigeria.

With regard to Schizotrypanum, it was at first classified as a trypanosome, but when its peculiar schizogony became known, it was thought necessary to separate it therefrom under a separate generic name, and to this we now adhere.

The subfamily therefore contains the genus Trypanosoma, of which we shall presently suggest a classification (*vide* p. 395), and the genera Endotrypanum, Schizotrypanum, and Rhynchoidomonas.

Trypanosoma Gruby, 1843.

Synonyms.—*Amœba* Mayer, 1843; *Paramœcium* Mayer, 1843; *Globularia* Wedl, 1850; *Undulina* Lankester, 1871; *Herpetomonas* Kent, 1878; *Hæmatomonas* Mitrophan, 1883; *Trypanosomonas* Danilewsky, 1885; *Trypanozoön* Luehe, 1906.

Definition.—Trypanosominæ, with the periplast raised into a longitudinal undulating membrane, along which the single flagellum runs.

Historical. The history of the genus has been largely detailed in Chapter I., and we need only remind the reader it commenced by Valentin, in 1841, reporting minute bodies in the blood of *Salmofario* Linnæus, the brown trout, which induced Gluge to bring forward his discovery of *Trypanosoma sanguinis* in frog's blood, while Gros, in 1845, found them in mice and moles. Later, in 1850, Wedl found the same parasites in the blood of birds and mammals, while Chaussat in the same year and Lewis in 1879 found them in rats, and Danilewsky studied their structure and started interest in them.

Morphology.—The usual form in which trypanosomes are found in vertebrate blood is that of an elongated, spindle-shaped mass of cytoplasm composed of an inner granular endoplasm, and surrounded by ectoplasm (periplast). The shape of the parasite is, however, by no means always a spindle, but, on the contrary, varies considerably in different species, and may even be rounded.

In the endoplasm is situated a trophonucleus, often called the 'nucleus,' concerning the structure of which there is considerable difference of opinion. Some authorities—*e.g.*, Prowazek, etc.—with regard to the nucleus of *T. lewisi* and *T. brucei*, and Miss Robertson, with regard to *T. raiæ*, say that the nucleus is complex and resembles the description already given for that of *Hæmoproteus noctuæ*, that of *T. lewisi* having eight chromosomes and a centrosome connected by a strand.

Other authorities, like Ross and Moore, Breinl and Hindle, consider that observers have been led astray by using dried films; for, according to them, though pretty pictures of the parasite are produced by this method, still, such delicate structures as the details of the nucleus are ruined; and therefore, in order to study these bodies accurately, the films must be fixed while wet in such a reagent as Fleming's fluid, and suitably stained. If this is done properly, according to them, it is seen that the nucleus is a vesicle bounded by a nuclear membrane, and having in its centre one small chromatin sphere, called by some the intranuclear centrosome.

Situated somewhere in the cytoplasm, and generally near the aflagellar extremity, is another mass of chromatin, the kinetonucleus. From this kinetonucleus a faint strand—the rhizoplast—proceeds, which ends in a little bead—the blepharoplast—from which the flagellum, which is also composed of chromatin, arises. A more primitive arrangement is for the kinetonucleus to contain the blepharoplast, which is really only a centrosome. Under these circumstances the flagellum will arise from the kinetonucleus. When the blepharoplast is separate from the kinetonucleus it is a moot point as to whether there is or there is not another centrosome in that nucleus.

The flagellum runs outwards through the endoplasm to the ectoplasm, which it raises into a membrane, the undulating membrane, and turns, and runs along the remaining length of the cytoplasm, in which it may end, or it may project as a free lash beyond the cytoplasm. In this course it presents three portions: (1) The root in the endoplasm; (2) the undulating portion in the ectoplasm, and (3) the free portion. In some stages of the life-history the flagellum, instead of turning along the undulating membrane, projects from its blepharoplast through the endo and ecto-plasm to the outside of the parasite.

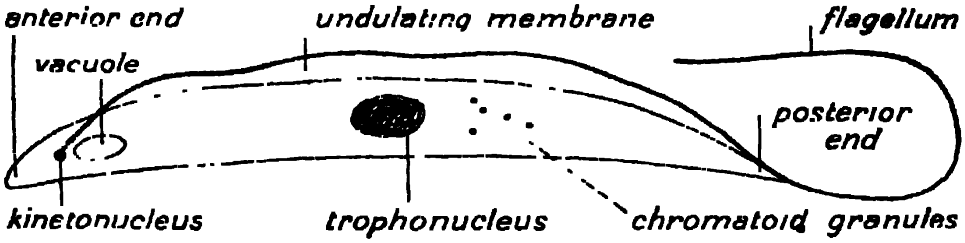


FIG. 88. - DIAGRAM SHOWING THE STRUCTURE AND POLARITY OF A TRYPANOSOME.

The undulating membrane, therefore, is the layer of ectoplasm (periplast) raised from the surface of the parasite by the second portion of the flagellum along a line sometimes called dorsal, and may be prolonged a certain distance along what is generally considered to be its free portion. The membrane is variously described as being homogeneous or strengthened by myonemes as in *Hæmoproteus noctuæ*.

Besides these structures the endoplasm often contains a vacuole, looked upon by some observers as a contractile vacuole, while others deny its existence. There is no doubt about its existence in *Trypanosoma castellanii*. Chromatoid granules can also be seen in the cytoplasm.

Before leaving this part of the subject it must be noted that many authors have given various names to the trophonucleus, kinetonucleus, centrosome, and blepharoplast. We use the terms in the same sense in which they have been used by Minchin and Woodcock—viz., the principal nucleus is a trophonucleus, because it is believed to be largely concerned in nutrition; it contains an achromatic body, which is the centrosome. The smaller nucleus is a kinetonucleus, because it is mainly concerned in motion; while the little bead connected with the flagellum is looked upon as a blepharoplast, because it is an achromatic body connected with a cilium or a flagellum.

We now come to a point on which there is a great difference of opinion—viz., the polarity of the parasite. There can be no doubt, in our opinion, that, as a rule, the anterior end of a parasite should be the non-flagellate end, as first suggested by Sambon, because, in wending its way through the blood, that end goes first, and the undulating membrane and flagellum follow, and blood being the natural habitat of the parasite, this method of propulsion must be considered to be normal. Moreover, morphologists (Woodcock) support this view. There is, however, no doubt that, at times, the flagellate end can be in front.

Movement is largely caused by the undulating membrane, while the flagellum assists; but creeping or gregarinoid movements have been noted by Léger, and zigzag movements by Gray and Tulloch, and in both of these the non-flagellate ends go first. In this work anterior, therefore, means the non-flagellate end of the trypanosome and posterior the flagellate end.

The anterior end is very variable, and may be even amœboid, while the posterior end is generally tapering, because the cytoplasm extends some way along the flagellum.

It has already been noted that the body of the parasite is slightly compressed laterally, and the edge with the undulating membrane is considered to be dorsal. In some species a supporting structure somewhat of the nature of an axostyle has been described.

The measurements of the parasite are from the non-flagellate extremity to the kinetonucleus, from that to the anterior end of the trophonucleus, from that to the posterior end of the trophonucleus, from that to the tip of the flagellum, the sum of these giving the length; while the width is taken in the region of the trophonucleus.

Stephens' method of measurement is, after outlining the parasite, to draw a straight line on a piece of transparent paper, and to mark one end, which is made to coincide with one extremity of the outlined trypanosome and then transfixed by a vertical needle. The transparent paper is now rotated so that the line runs in the long axis of the parasite. Where it deviates another pin is inserted and the first removed. The transparent paper is again rotated to take in another portion of the axis of the parasite, and this is repeated until all the deviations of the parasite have been followed and the distal extremity reached.

The results of careful measurements have been to show that some trypanosomes are polymorphic and others are not.

Food is absorbed by osmosis from the liquid in which the parasite is living.

Life-History.—The life-history of a trypanosome is not as yet fully known, but it is recognized that it has an alternation of generations associated with an alteration of hosts, one generation being usually completed in the blood of a vertebrate, and the other in the alimentary canal and its appendages of some blood-sucking invertebrate.

In the Vertebrate.—If an uninfected or clean non-immune is infected by the bites of infective invertebrates, at first no parasites are to be found in the peripheral blood, and some days must elapse before they appear. This interval is *the incubation period.* What takes place during this period is but little known, the only observations being those by Fantham, who saw a few rounded forms fifteen to eighteen hours after inoculating *T. castellanii* and *T. rhodesiense* into rats; and those by França, who reports the presence of similar forms at a later stage of incubation. These are probably multiplication forms, which are the parent forms of the trypanosomes presently to be seen in increasing numbers in the blood.

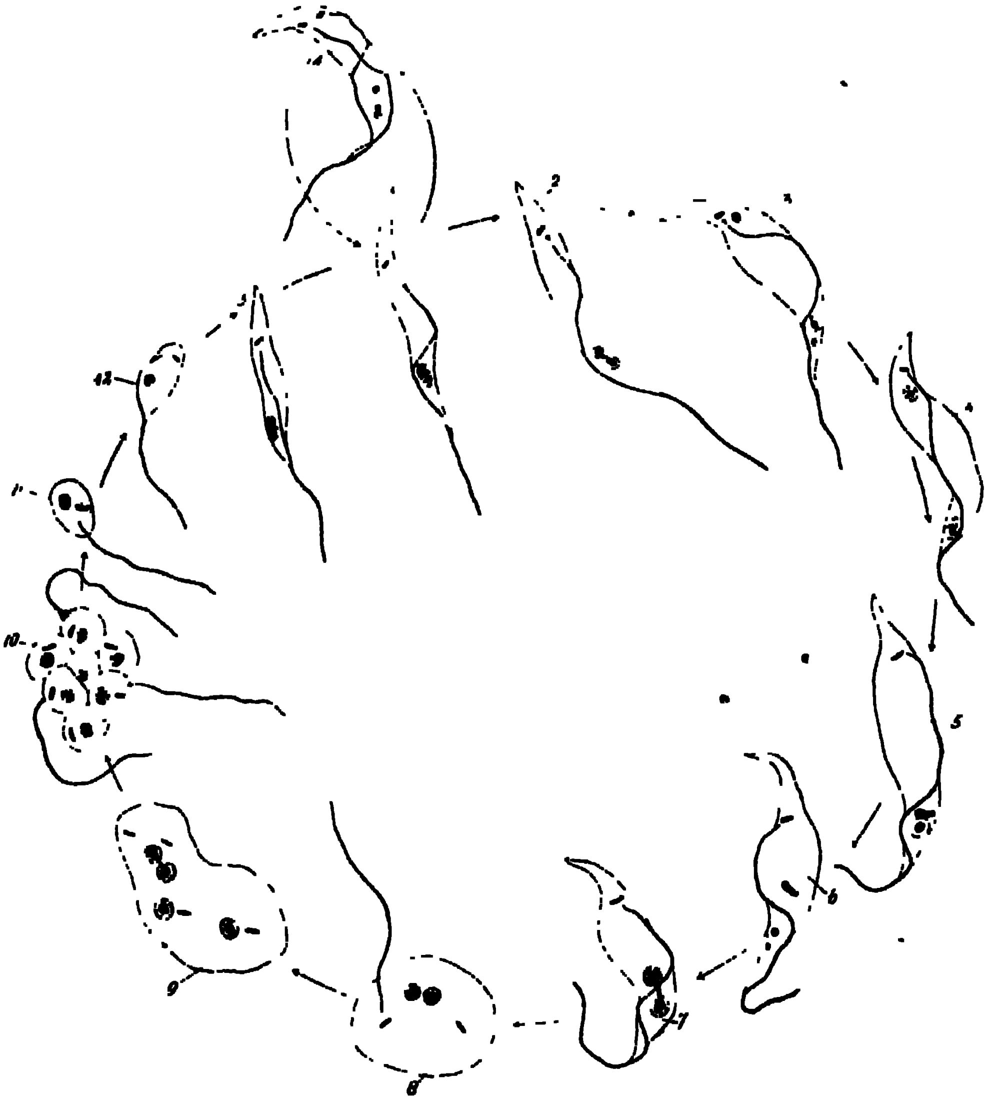


FIG. 69.—DIAGRAM OF THE LIFE-CYCLE OF *Trypanosoma lewisi* SAVILLE KENT, 1880, IN THE BODY OF THE RAT.

1, Trypanosoma lewisi; 2-10, stages in rosette formation; 11-13, development of a small flagellate form into a trypanosome; 14, binary fission.

(Constructed from drawings by Moore, Breinl, and Hindle in the *Annals of Tropical Medicine and Parasitology*.)

When the parasites are present in the peripheral blood, they usually show a marked pleomorphism. Thus, in *T. castellanii* Miss Robertson finds short forms 14 to 20 μ in length, medium forms 20 to 24 μ in length, and long forms 23 to 33 μ in length. Until recently it was usual to consider these variations as being probably indicative of sexual differentiation, but she concludes that this is not so, but that they are variations due to different stages of growth and subsequent division. The multiplication of the trypanosome in the blood is usually by longitudinal fission, but it may also take place by schizogony, with or without entering an endothelial or other cell. The number of trypanosomes in the blood varies considerably from time to time, apparently in more or less regular cycles, and their disappearance appears to be associated with the encystment in the lungs, spleen, bone-marrow, etc., in the form of the latent bodies described by Breinl, Fantham, and others. During their life in the vertebrate it was, at one time, thought that they could propagate their species—in part, at all events—by granules, which are comparable to the 'infective granule' described by Balfour for spirochaetes, because Fry demonstrated that *T. brucei* could throw off granules, and his observations had been confirmed by Ranken. This granule-shedding was described as taking place in the liver, spleen, lungs, and lymphatic glands. At first the granule was simply a free pyriform body, but later it developed a flagellum and became actively motile. Its further history was, however, untraced in trypanosomes

There can be no doubt that there is a reaction on the part of the cells of the vertebrate against the trypanosomes with the formation of antibodies in the form of trypanolysins, etc., but more will be said on this subject later.

Binary Fission. A binary fission takes place with or without growth. This is brought about by amitotic division of the kinetonucleus and trophonucleus, followed by the formation of a new flagellum in the daughter parasite and the division of the cytoplasm.

The details of the division are as follows:—

1. The kinetonucleus swells up and forms a vesicle through which the chromatin is evenly distributed.
2. The chromatin forms a band across the middle of the vesicle.
3. The band elongates and divides into two portions.
4. The two portions move apart, all trace of the vesicle disappears, and the two new kinetonuclei are formed.
5. The blepharoplast divides at the same time as the kinetonucleus.
6. Either the old flagellum divides or a new flagellum develops from one of the new blepharoplasts. The process varies in different species.
7. The central karyosome of the trophonucleus either divides and the two portions move to opposite poles of the nucleus, but are connected by a fine line, or the chromatin forms an equatorial plate,

which divides transversely, and each half goes to an opposite pole, or the chromatin gathers around opposite poles.

8. The connecting line disappears and two new trophonuclei are formed.

Rosette Formation.—The medium-sized parasite, according to Moore, Breinl, and Hindle, grows into large forms, which pass through the following development:—

1. The trophonucleus undergoes reduction by amitosis, the reduction body disappearing.

2. The kinetonucleus gives off a body, which travels—increasing in size as it proceeds—to the trophonucleus, with which it perhaps fuses, but this is not definitely known.

In *T. castellanii* a strand forms between the kineto- and trophonuclei, instead of this travelling body, which is seen in *T. lewisi* and *T. equiperdum*.

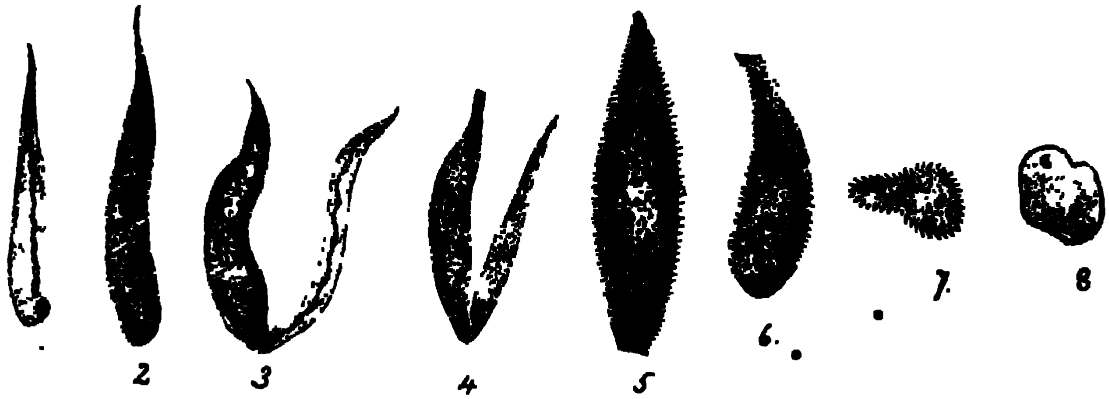


FIG. 90.—*Crithidia melophagia* FLU.

(After Flu.)

1, Microgamete; 2, macrogamete; 3, zygosis; 4, oökinete and degenerating microgamete; 5-8, oökinete in the alimentary canal and ovary.

3. The tropho- and kineto-nuclei divide to form fusion masses consisting of two, four, seven, or more small parasites, which at first possess only the old flagellum, but in which later new flagella form (the rosette formation). This stage is not definitely known in *T. castellanii*.

4. The small parasites, which must be looked upon as representing latent phases, separate from the fusion mass. These small parasites grow into medium-sized parasites, thus completing the cycle.

All observers are agreed as to the rosette formation, and with regard to the process from the kinetonucleus, this was first pointed out by Miss Robertson, whose work is therefore confirmed. The band is said to be composed of volutine. As to the latent phases, we believe that they are the same as the peculiar aflagellate round and oval forms described several years ago by Castellani, in the cerebro-spinal fluid of sleeping-sickness patients, and which he compared to the amœboid forms found by Plimmer in the brains of animals infected with nagana.

The development of Schizotrypanum differs in many points from this description, for the trypanosome enters an endothelial cell in the lung, or a cardiac muscle fibre, or a neuroglia cell of the central nervous system, or a striped muscular fibre. In these situations it becomes simply a rounded body, which possesses trophonucleus and kinetonucleus, but has lost its flagellum and undulating membrane. This body undergoes repeated divisions, and each division eventuaally becomes a trypanosome.

In the Invertebrate Host.—Theoretically, it would be expected that sexual forms, male and female, would be found in the blood of the vertebrate, and that these, taken into the alimentary canal of the blood-sucker, would conjugate and produce oökinetes, and perhaps oöcysts, from which forms would be produced which might infect the proboscis of the same individual, or, by entering into the eggs, infect a new generation, which alone might be the means of dissemination of the parasite. But these theoretical views have so far not been confirmed by actual observations, which must now be discussed seriatim.

So-called Sexual Forms.—According to Prowazek, *T. lewisi* can be differentiated into three forms—(1) male, (2) female, (3) indifferent; and, according to Prowazek, Lühe, Nocht, and Mayer, the same can be seen in *T. castellanii*; but according to Holmes, only males, females, and young females can be seen in *T. evansi*.

Male Forms.—These are defined to be very slender trypanosomes, actively motile, with an elongated nucleus, which stains well.

Female Forms.—Broad, sluggish trypanosomes, with reticulated protoplasm and a round nucleus, both of which stain poorly. They possess a slender, undulating membrane and a short flagellum.

Indifferent Forms.—These are the forms most commonly met with, possessing granular cytoplasm and a not very well-defined nucleus.

It must be admitted that between these there are all stages of intermediary forms, so that they are not sharply defined; and some of these may be simply the ordinary trypanosome in various stages of growth and division, as described above.

Miss Robertson has probably arrived at the truth when she says that the short forms (13-20 microns) of *T. castellanii*, the so-called female forms, are really the adults, which by growth become the indifferent forms which are merely steps in the formation of the slender forms, so-called male forms, which are the dividing stage of this trypanosome.

Chagas has shown that *Schizotrypanum cruzi* in the lungs may lose its flagellum and become curved into an arc, the extremities of which fuse, forming at first a ring, which subsequently becomes a sphere, with a trophonucleus and a kinetonucleus, the latter of which is expelled in female forms, while it is retained in male forms. In this manner the macrogametocytes and the microgametocytes arise. Each of these divides into eight macrogametes, which are uninuclear, and eight microgametes, which have a trophonucleus and kinetonucleus united by a filament. These gametes escape from the cyst which is formed by the periplast of the original trypanosome, and enter red blood-cells, in which they develop into sexually differentiated trypanosomes—*i.e.*, females with one and males with two nuclei. These are the forms which infect the *Lamus*, or invertebrate host, and do not multiply in the vertebrate host.

Method of Transmission.—The blood of the infected vertebrate is not always infective for the invertebrate host. Thus Miss Robertson has shown, with regard to *T. castellanii*, that the tsetse-fly cannot be infected by feeding just before an outburst of multiplication in the vertebrate host, or during the period of destruction which precedes a paucity period or at the summit of an exalted period, or during certain periods of rapid multiplication, when the absolute and relative numbers of the short forms mentioned above are diminished.

Immediately after infection the invertebrate host can *mechanically* convey the infection to a *clean* host, and this power persists for about twenty-four hours, after which the invertebrate host becomes non-infective and remains so for a varying period, which was found by Kleine not to be less than eighteen days as regards *Glossina palpalis* and *T. castellanii*, and by Kinghorn and Yorke to be about fourteen days in *G. morsitans* infected with *T. rhodesiense*, after which the flies become again infective, and apparently remain so for a very long period, probably for the rest of their lives. These facts prove definitely that the parasites undergo some changes of an important nature in the flies in question, and that the second infective period cannot possibly be classed as mechanical. The fact that *Lamus megistus* remains infective ten to twenty-five days after feeding on a host infected with *S. cruzi* also proves that the infection is not mechanical. We therefore draw the conclusion that the trypanosome undergoes part of its life-cycle in the invertebrate host, and the first question which naturally arises is the fate of the so-called 'male' and 'female' forms found in the blood of the vertebrate. Are they true male and female forms, and do they conjugate and form an oökinete or zygote, or do they not?

Conjugation. It is difficult to be certain that conjugation has been seen, and not division. It has been described by Keysselitz as occurring in leeches fed on a carp infected with *Trypanoplasma borreli*, by Prowazek in lice fed on rats infected with *T. lewisi*, and by Flu in *Crithidia melophagia*, to which reference will be made under the heading of Crithidia.

On the other hand, careful observers like Miss Robertson and Captain Patton have quite failed to see this process in their studies of trypanosomes and herpetomonads. The conclusion is that conjugation has not been proved to be present in trypanosomes so far.

Development without Conjugation. According to most observers, there is no conjugation, but development takes place asexually in the invertebrate host. This development varies in different species, and may be classified as follows:

A. Development in the proboscis.
B. Development in the anterior portions of the alimentary canal.
C. Development in the whole alimentary canal.
D. Development associated with infection of the salivary glands.
E. Rectal encystment—fæcal infection.
F. Ovum infection.

A. *Proboscian Development.* Roubaud has described a form of asexual development of *T. castellanii* and *T. brucei* in the proboscis of *Glossina palpalis* in which the undulating membrane disappears; the flagellum is shortened, and the kinetonucleus approaches the trophonucleus, while the parasite becomes attached to the wall of the proboscis, and multiplies, forming masses of parasites, the whole process occupying only a few minutes.

Though he thinks that this method of development explains the infection of man and animals by tsetse-flies in Africa, he was unable to produce infection of susceptible animals by inoculation of these forms.

This form of development occurs in *T. vivax* and in *T. cazalboui.*

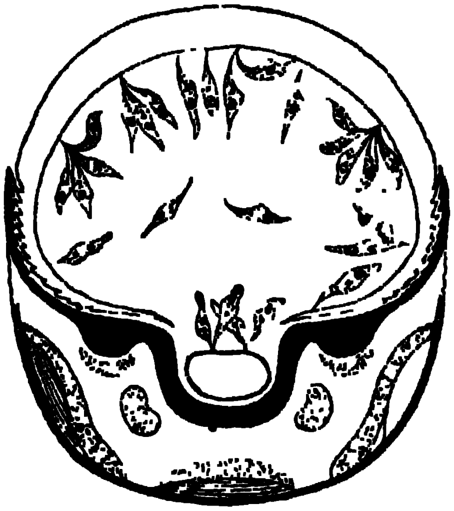


FIG. 91. PROBOSCIAN DEVELOPMENT. (After Roubaud.)

B. *Anterior Development.* Miss Robertson has shown that the trypanosomes of fresh water fish, when ingested by the leech *Hemiclepsis marginata,* first of all undergo rapid multiplication by unequal binary fission, giving rise to small crithidial like individuals, which also multiply in the crop, and then towards the end of digestion pass forward as long, slender trypanosomes into the proboscis sheath, and are capable of infecting a new host; while the crithidial forms which remain in the crop become Leishmania like bodies which multiply again when fresh blood is ingested. The development of *T. vittata* of the milk tortoise *Emyda vittata,* takes place in a somewhat similar manner in the leech *Glossiphonia* sp. (?).

C. *Entire Canal Development.* This form of development is exemplified by *T. rajæ* in the leech *Pontobdella muricata,* but in this case the trypanosomes in the crop give rise to binucleate, rounded, Leishmania-like forms without locomotor apparatus, which pass into the intestine, where they become flagellate, and appear as crithidial forms and multiply rapidly. During hunger periods they become Leishmania-like bodies, only to revert to the crithidial form when food is ingested. These crithidial-like forms become long, slender trypanosomes, which pass forward into the proboscis and are the infective agents.

D. *Salivary Gland Infection.*—According to Bruce and his collaborators, if *G. palpalis* is fed with *T. castellanii*, the proboscis is not involved in the further development. The fly now becomes non-infective for some twenty-eight days on an average. The trypanosomes in five to seven days disappear (possibly become intracellular), but later return in a small percentage of flies, and multiply in the fore, mid, and hind guts, generally as long, moderately broad forms, with protoplasm which stains well, and contains an oval central nucleus, a small micronucleus, undulating membrane, and a flagellum with a blepharoplast. After twenty-eight days it is found that the salivary glands become infected with the short, stumpy forms already mentioned above, and now the fly is found to be infective and to remain so for long periods. These short stumpy forms have been noted by Kleine in the intestine. Miss Robertson finds that the trypanosomes infect the salivary glands from the gut via the proboscis and the salivary ducts.

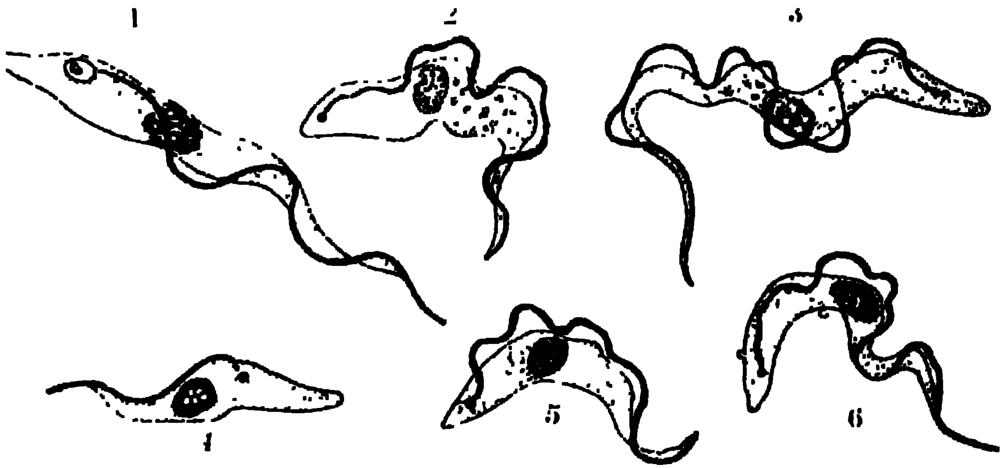


FIG. 92.—DEVELOPMENT OF *T. castellanii* KRUSE, 1903.

1, In the vertebrate blood; 2 and 3, in the mid gut; 4 and 5, in the hind-gut; 6, in the salivary glands of the tsetse-fly.

(After Bruce, Hamerton, Bateman, and Mackie.)

Kinghorn and Yorke have shown that the salivary glands of *Glossina morsitans* become infected in somewhat similar manner with *T. rhodesiense*.

Chagas has seen trypanosomes in the body cavity and salivary glands of *Lamus megistus*, which are without doubt the forms which are inoculated in infections.

E. *Rectal Encystment.* Minchin finds that the crithidial forms of *T. grayi* become encysted in the rectum of *G. palpalis*.

F. *Ovum Infection.*—This has not been proved to take place.

Conditions Influencing Development.—Kinghorn and Yorke have shown that the development of *T. rhodesiense* in *G. morsitans* is markedly influenced by the temperature of the air, 75° to 85° F. being more favourable than 60° to 70° F., and, under favourable conditions, the first stage of development can take place, but not the later stages, and flies may remain with the parasites incompletely developed for eighty days. Humidity is without effect. Another important matter, as we shall see later, is the effect of the next following clean feed after an infected feed.

Methods of Infection.—In nature there can be no doubt that infection can take place in more than one way, and Minchin has pointed out that the different methods may be :—

1. CONTAMINATIVE.—This is the infection of the host by swallowing encysted parasites. At present there is no proof that this exists in trypanosomes. But Minchin has shown that *T. grayi* becomes encysted while lying in the proctodæum of *Glossina palpalis*, by a shortening of the flagellum and an excretion of a cyst-wall, which, beginning at the anterior extremity, gradually spreads round the shortening parasite while the flagellum is being absorbed. The cysts which lie quite free from the proctodæum are first pear-shaped and then oval, and the trophonuclei and kinetonuclei break up into chromidia. Minchin believes that these cysts will be found to infect some vertebrate, but there is no proof of this at present.

2. INOCULATIVE.—The spread of a trypanosome from one vertebrate host to another was demonstrated by Bruce while studying *T. brucei*, and also by the same observer, Nabarro, and Kleine, for *T. castellanii*, both diseases being spread by tsetse-flies, though with regard to the former it had long been known that the tsetse-fly was the carrier of the disease.

There are, however, two ways in which a blood-sucker can spread an infection: (*a*) the direct; (*b*) the indirect.

(*a*) *The Direct.*—In this the blood-sucker simply transmits the parasite unchanged.

(*b*) *The Indirect.*—In this method the parasite undergoes a cycle of development in the blood-sucker, the nature of which has been fully discussed already.

It would appear probable that it is only in the natural hosts that forms develop which are infective for the invertebrate.

Effects upon the Vertebrate Host.—Trypanosomes may produce pathological effects on their vertebrate host, or may apparently be harmless, and certain harmless trypanosomes will only live in some particular vertebrate and die when injected into others, but no pathogenic trypanosome is restricted to one host.

The best known of the former are *T. gambiense*, *T. castellanii* and *T. rhodesiense*, the causes of sleeping sickness; *S. cruzi*, of American trypanosomiasis; *T. evansi*, of surra in horses, etc., in India and elsewhere; *T. brucei*, of nagana in cattle and horses, etc.; *T. vivax*, of disease in cattle, sheep, and goats, in the Cameroons; *T. nanum*, of cattle sickness in the Anglo-Egyptian Sudan; *T. dimorphon*, of the Gambia horse sickness; *T. cazalboui*, of souma, a disease of cattle in the French Sudan, and *T. pecaudi*, of sheep in the same place; *T. equinum* of mal de caderas in South America; *T. equiperdum*, of dourine in horses in Europe and Africa.

SYMPTOMS.—The pathogenic effects of the parasites show themselves in the production of fever, skin eruptions, emaciation, local or general œdema, and disease of the nervous system. Secondary bacterial affections are also common. The mortality is often high.

MORBID ANATOMY.—The lesions are often insignificant, but inflammation and enlargement of the lymphatic glands is characteristic, and dropsy and inflammation of the meninges are also found, which in human trypanosomiasis takes the form of meningo-encephalitis, as will be described later.

INOCULATIONS.—The parasites can be spread from one animal and from one species to another by inoculation of infected blood.

AGGLUTININS.—While in the body of the host agglutinins are formed, for if blood containing trypanosomes is treated with the serum of an animal which has had one or more injections of blood containing the same parasite, a rapid massing of the parasites into rosettes, with the anterior ends pointing inwards and the flagella outwards, takes place.

This is called agglomeration, and may last a few minutes, the parasites being unaffected, or may persist till they die.

REDUCING POWER. Trypanosomes have been shown by Nauss and Yorke to have a marked reducing power on hæmoglobin.

PRECIPITINS.—Mayer has shown that the serum of a dog infected by *T. brucei* is precipitated by a salt extract of the same parasite, but not by that of *T. equinum*, thus proving the presence of specific precipitins.

IMMUNITY. Active immunity, due to the action of the leucocytes (Laveran and Mesnil) or to cytolysins (McNeal), can be produced in certain cases, but it is not carried from mother to young. Léger and Ringenbach have shown that the serum of animals affected with nagana and surra, also *T. equinum*, *T. castellanii*, and *T. congolense*, is trypanolytic for homologous and allied trypanosomes, but not for others.

Chalmers and O'Farrell have shown that *T. castellanii* can be separated from *T. rhodesiense* by immune serum reactions *in vitro* and *in vivo*.

INVOLUTION FORMS.—Degenerated, vacuolated involution forms may be seen as a result of immunity coming on or of treatment by drugs. Advanced forms after treatment with immune serum have been noted by Chalmers and O'Farrell.

TOXINS.—Uhlenhuth, Hübener, and Worthe have demonstrated the presence of endotoxins in *T. equiperdum*, which observation supports McNeal's suggestion as to their presence, and also the work of Martin, Darre, and Leber. Free toxins do not exist, but endotoxins can be set free by trypanolysis.

Local Reservoirs.—The long-continued infectivity of *Glossina palpalis* after the removal of man from a district points to either long duration of infectivity in the fly or to a local reservoir, which may perhaps be found in antelopes, and perhaps other animals in the case of *T. castellani*.

Cultivation.—McNeal and Novy cultivated *T. lewisi* in the water of condensation of blood-agar tubes in 1903, and obtained, at 37° C., and also at the room temperature, good cultures, in which *T. lewisi* varied in size from minute forms 1 to 2 microns in length up to 50 to 60 microns, and colonies of rosettes were seen with all the flagella turned inwards. The flagellum in cultivated forms projects directly from the kinetonuclear end of the parasite.

The following have been cultivated: *S. cruzi*, by Chagas; *T. brucei*, by McNeal and Novy, and by Laveran and Mesnil; *T. equinum*, by R. Thomas and Breinl, *T. equiperdum*, by Thomas and Breinl, with slight success; *T. castellanii*, by Thomas, Breinl, Gray, and Tulloch, with partial success; *T. evansi*, by Novy, McNeal, and Hare, and by Thomas and Breinl, but were found to be non-virulent, and subcultures could not be obtained.

Effects upon the Invertebrate Host.—The effects of trypanosome infection upon the invertebrate host has been but little studied, except with reference to *T. castellanii* and *Glossina palpalis*, and the result may be tabulated as follows:

A. NON-INFECTION OF THE FLY.—1. The trypanosomes introduced by the infective feed may entirely disappear, being digested in some fifty to seventy hours.

2. The trypanosomes may multiply in the crop, but disappear after the next feed if non-infective.

3. The trypanosomes may grow and multiply in the gut, and yet be all swept out by the next feed if clean.

4. The trypanosomes may survive and develop in the crop for twelve days, providing that blood is always present, but no trypanosomes appear in the gut, and the infection dies out.

B. INFECTION OF THE FLY DOUBTFUL.—In the third instance quoted above infection may take place; everything depends upon the effects of the second feed.

C. INFECTION OF THE FLY.—The trypanosomes persist after the clean feed has displaced the blood from the gut, but the infection also depends upon the strain of trypanosome, as there is undoubtedly a struggle for existence between the trypanosome and the chemical defences of the fly against *T. castellanii*.

Type Species.—*Trypanosoma rotatorium* Mayer, 1843.

It is necessary, for purposes of classification, that the reader should clearly understand the nature of the type species.

Trypanosoma rotatorium Mayer, 1843.

Synonyms.—*Paramœcium loricatum*, seu *costatum* Mayer, 1843, *Amœba rotatoria* Mayer, 1843, *Trypanosoma sanguinis* Gruby, 1843, *Monas rotatorium* Lieberkühn, 1870, *Undulina ranarum* Ray Lankester 1871, *Paramœcioides costatus* Grassi, 1872.

History.—Gluge in 1842 discovered in the blood of frogs an organism resembling that which had been discovered by Valentin in the previous year in *Salmo fario*, the brown trout, and which was thought to be related to the genus *Amœba* of Ehrenberg, but which from his description and from his figures is more probably a trypanosome. Gluge's description is also very short, and he is followed by Mayer, in 1843, who describes two forms—an *Amœba rotatoria* and a *Paramœcium loricatum*, or *costatum*—but in November of the same year Gruby gave a clear description of the organism, and applied the generic term 'Trypanosoma' to it, so that it becomes the type species of the genus, from which any variation in the classification of the species must be made.

Ogawa has studied this parasite in the frog in 1913, as well as Doflein and Mendeleeft-Goldberg.

Gruby's Original Description.—'Its elongated body is flattened, transparent, curved like a centre-bit; the cephalic end is terminated in a thin, elongated filament; the caudal end is terminated also in a pointed filament. The length of the animal is 40 to 80 *μ*, its breadth is 5 to 10 *μ*, the filamentous pointed cephalic end has the greatest mobility, the length of the cephalic filament is 10 to 12 *μ*; its body is elongated, flat, and toothed like the blade of a saw all along the length of one of its margins; it is, as I have above mentioned, supple and twisted two or three times around its axis, like an auger or a corkscrew, which is the reason why I propose to name this hæmatozoön "*Trypanosoma*."'

Zoological Distribution.—It has been found in *Rana esculenta* Linnæus, in *R. temporaria* Linnæus in Europe; in *R. speciosa* in the Congo; in *R. trinodis* in the Gambia. Whether the species found in *Hyla arborea* are truly *T. rotatorium* or not is uncertain.

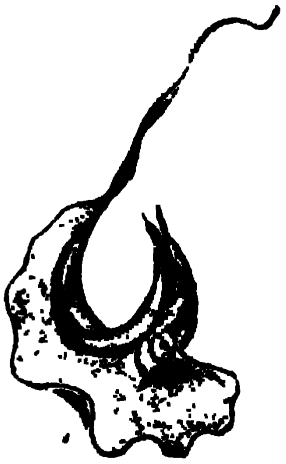


FIG. 93.—*Trypanosoma rotatorium* MAYER (After Dutton and Todd.)

Morphology.—The pleomorphism exhibited by this form is so varied that it requires classification, for, as Chalachnikov has shown, the following varieties exist:

1. *Flattened Forms.*—(*a*) Simple plain forms; (*b*) plain forms rolled on themselves; (*c*) spiral forms.

2. *Pectinated Forms.*—(*a*) Pectinated spiral forms; (*b*) cornucopial forms. In all these forms the undulating membrane is much folded, and has a thickened edge. The flagellum, which is short, starts from the kinetonucleus, which is situate at a variable distance from the aflagellar extremity. The trophonucleus is round or oval. The usual length varies from 40 to 80 *μ*, the breadth from 5 to 40 *μ*, and the flagellum is about 10 to 12 *μ* long.

Doflein finds that in the blood and internal organs forms intermediate between the flagellate and the non-flagellate organisms are found. The latter cannot divide.

Life-History.—The life-history is but little known. Asexual multiplication takes place by the trypanosome becoming round and losing its locomotor apparatus, and dividing by mitosis. It is but rarely inoculable into other frogs, but it grows in cultures, especially upon Novy-McNeal's medium, but the cultures are not inoculable. In the cultures leptomonas and rosette forms are seen. The researches of França show that it is capable of developing in the leech (*Helobdella algira*), in which it gives rise to leptomonas-like forms, which are to be seen located against the walls of the gastric intestinal pouches. Frogs can be infected by the bites of infected leeches or by the inoculation of the intestinal contents.

Cultivation.—It has been cultivated in acid bouillon-blood media by Ponselle in 1917.

Classification.—The question is unsettled as to whether there are more than one species included under the term *T. rotatorium*.

Pathogenicity.—It is believed to be non-pathogenic. This immunity of the frog has been studied by Doflein and others.

Classification.—If the section on evolution contained in Chapter V. be read, it will be seen that we believe that new diseases can arise at the present time; that organisms usually harmless in a given environment may become so altered under certain circumstances that they may become pathogenic; and that this change, though merely at first chemical, may subsequently become structural.

The researches of O'Farrell, Fantham, and Porter, already referred to under the Herpetomoninæ, seem to indicate that the original trypanosomes were parasites of such invertebrates as Annulates, Arachnids, and Hexapoda, from which they spread to vertebrates.

With regard to man, it would appear as though his infection was of comparatively recent date, and that in him and in the tsetse-flies which infect him the adaptation of the trypanosomes to the new environments is not yet complete, and therefore the differential characters of the various species infecting him have not yet become completely crystallized.

It therefore appears to us that a natural division of the numerous species of trypanosomes would be into -

A. Trypanosomes infecting invertebrata:—
  I. Trypanosomes of Hirudinea.
  II. Trypanosomes of Arachnida.
  III. Trypanosomes of Hexapoda.

B. Trypanosomes infectin[illegible]ld-blooded vertebrates:-
  I. Trypanosomes of Pisces.
  II. Trypanosomes of Amphibia.
  III. Trypanosomes of Reptilia.

C. Trypanosomes infecting warm-blooded vertebrates:—
  I. Trypanosomes of Aves.
  II. Trypanosomes of Mammalia.

It is not our purpose to write accounts of all known trypanosomes, but merely those which infect man, and to sketchily describe some of those which produce disease in the mammalia, and to draw attention to others which can be classified in the series of divisions given above.

With regard to the trypanosomes of mammals, it appears to us, from an evolutionary point of view, to be correct to divide them into two sections --viz.:- –

A. Non-pathogenic mammalian trypanosomes.
B. Pathogenic mammalian trypanosomes.

As it is the last section only with which tropical medicine is concerned, we shall restrict our further remarks on classification until we come to these organisms.

A New Classification.--Although, for purposes of general information, we have given the usual classification, still, it must be obvious even to the casual reader that the genus Trypanosoma comprises an enormous number of species, some of which are of very diverse form.

We feel that the time has arrived in which to bring forward a fuller and more useful classification, based upon morphological and physiological characters, especially as classifications have been outlined by Nöller, while Minchin, had he lived, would probably have brought forward one.

In the Trypanosominæ the definitive, and hence primitive, host is the invertebrate, and we should expect to find some trypanosomes which were solely denizens of these animals, and apparently this is so. Unfortunately, their full life history still requires much elucidation, but such forms as *Cystotrypanosoma intestinale* Roubaud, 1911, are worthy of more consideration; and it is obvious that such forms deserve separate classifications, and should form part of a tribe *Cystotrypaneæ*, with *Cystotrypanosoma* as type genus and *C. intestinale* as type species.

As evolution proceeds so life-histories tend to become complicated. In this case the complication is the introduction of a vertebrate intermediary host, and with the change in environment one meets with the large, relatively slow-moving, trypanosome of the cold-blooded vertebrate and the smaller, quicker-moving, trypanosome of the warm blooded vertebrate. They appear to us to deserve to be ranked into tribes and to merit more study. The type of the first is obviously Glugea's parasite, and of the second the organism found, by one of us, to be the cause of sleeping sickness.

These various ideas may be crystallized as follows:—

A. Live *only* in a definitive invertebrate host:—
  Type genus: *Cystotrypanosoma* Roubaud, 1911– Tribe 1, *Cystotrypaneæ* Chalmers, 1918.
  Type species: *C. intestinale* Roubaud, 1911.

B. Live in a definitive invertebrate host and in a cold-blooded intermediate vertebrate host:—
  Type genus: *Trypanosoma* Gruby, 1843—Tribe 2. *Trypanosomeæ* Chalmers, 1918.
  Type species: *T. rotatorium* Gruby, 1843.

C. Live in a definitive invertebrate host and in a warm blooded intermediate vertebrate host:—
  Type genus: *Castellanella* Chalmers, 1918– Tribe 3, *Trypocastellanelleæ* Chalmers, 1918.
  Co-type species: *C. gambiensis* (Dutton, 1902).
  C. castellanii (Kruse, 1903).

In the present work we are chiefly concerned with the third tribe, '*Trypocastellanelleæ*.'

SERIES A: TRYPANOSOMES INFECTING INVERTEBRATA.

TRIBE 1: CYSTOTRYPANEÆ.

This tribe has not yet been fully studied, but provisionally it can be classified as follows:—

A. *Forms carefully studied*:—

Snout long, no free flagellum forms like *T. dimorphon*:—

1. Trophonucleus round—*Rhynchoidomonas* Patton, 1910.
2. Trophonucleus elongate—*Cystotrypanosoma* Roubaud, 1911.

B. *Forms not yet fully studied*:—

We still retain the old term *Trypanosoma sensû lato* for these forms, pending further investigation, and divide them into:—

I. Trypanosomes of Hirudinea.
II. Trypanosomes of Arachnida.
III. Trypanosomes of Hexapoda.

Forms Carefully Studied.

Genus Rhynchoidomonas Patton, 1910.

Definition. *Cystotrypaneæ* with large kinetonucleus situated on the aflagellar side of the rounded trophonucleus, with distinct undulating membrane and with the aflagellar end drawn out considerably.

Rhynchoidomonas luciliæ Patton, 1910.

This parasite is found in the Malpighian tubes of *Lucilia serenissima* Walker, and *Musca nebula* Fabricius, in India. It moves by sharp jerking movements, and has no free flagellum, but a pointed flagellar extremity and a pointed aflagellar extremity. The kinetonucleus is large and circular, while the trophonucleus is also large. The cytoplasm contains many chromatoid granules.

Genus Cystotrypanosoma Roubaud, 1911.

Definition.—*Cystotrypaneæ* with small terminal kinetonucleus situate on the aflagellar side of an elongated trophonucleus. There is no free flagellum. It gives rise to pyriform cysts.

Cystotrypanosoma intestinale Roubaud, 1911.

This parasite is found in the intestine of a species of *Lucilia* at Bamako in French West Africa.

Forms not yet Fully Studied.

Trypanosomes belonging to the invertebrate and not due to the sucking of contaminated blood have been found in the tsetse-fly, in mosquitoes, in ticks, and perhaps in leeches, but it is doubtful about the last named.

The presence of the Herpetomonas, Crithidia, and Trypanosoma in blood-sucking Arthropods may, therefore, be peculiar to those animals, or only acquired from their hosts. Hence it is quite possible for serious errors to arise in working out the life history of these parasites, especially as infection of the blood-sucker may come from the eggs.

SECTION I.: TRYPANOSOMES OF *Hirudinea*.

Trypanosoma inopinatum is believed to be a true parasite of the leech *Helobdella agira*, though, according to some observers, it is the same as the parasite of the frog.

SECTION II.: TRYPANOSOMES OF *Arachnida*.

T. christophersi Novy, 1907, found in *Rhipicephalus sanguineus*, fed on dogs.

SECTION III.: TRYPANOSOMES OF *Hexapoda*.

Trypanosoma boylei Lafont, 1902, has been found in *Conorhinus rubrofasciatus*, an insect which attacks man in Mauritius and Réunion.

Trypanosoma tullochi Minchin, 1907.—This parasite closely resembles *C. castellanii* from which it can be differentiated by the central round nucleus and the small centrosome. It is found in *G. palpalis*.

T. culicis Novy, 1907, is found in various Culicinæ. Novy strongly advocated the view that the trypanosomes found in mosquitoes which Schaudinn had fed on *Athene noctuæ* infected with halteridium should be defined as *T. noctuæ* Schaudinn, 1904, a parasite of *Culex pipiens*, and the same for *T. ziemanni* Schaudinn, 1904, also in *Culex pipiens*; and, further, that the trypanosome found by Durham in *Stegomyia fasciata*, which had been fed on bats, should be looked upon as belonging to the mosquito

T. triatomæ Kofoid and McCulloch, 1916, is a parasite of *Triatoma protracta*, found in nests of the wood-rat *Neotoma fuscipes*.

SERIES B: TRYPANOSOMES INFECTING COLD-BLOODED VERTEBRATES.

TRIBE 2: TRYPANOSOMEÆ.

At present this tribe contains one genus—viz., *Trypanosoma sensû stricto*, as defined above, and with *T. rotatorium* Mayer, 1843, as the type.

It is probable that, as constituted, the genus still contains a number of non-defined genera, but these require further investigation, and we therefore divide the species into:—

Section I.: Trypanosomes of Fish.
Section II.: Trypanosomes of Amphibia.
Section III.: Trypanosomes of Reptilia.

SECTION I.: TRYPANOSOMES OF FISH.

In 1841 the first known trypanosome was found by Valentin in the blood of *Salmo fario*, the brown trout.

Since that time a considerable number have been found in fresh- and salt-water fish all over the world. As examples may be mentioned *T. remaki* Laveran and Mesnil, 1901, which exists in two varieties—*parva* and *magna*—and is found in pike; *T. rajæ* Laveran and Mesnil, 1902, in *Raja punctata*,

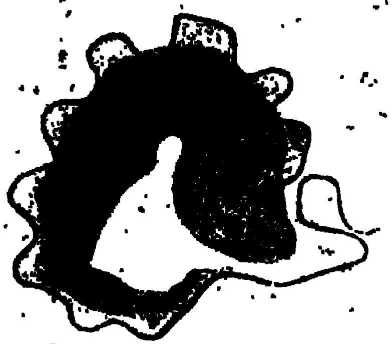


FIG. 94.—*Trypanosoma leschenaultii* ROBERTSON.

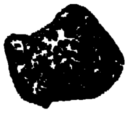


FIG. 95.—*Trypanosoma rajæ*. ROUND FORM, IN THE LEECH.

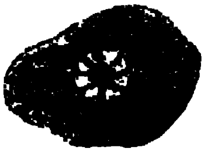


FIG. 96.—*Trypanosoma rajæ*: ROUND FORM, OLDER STAGE.

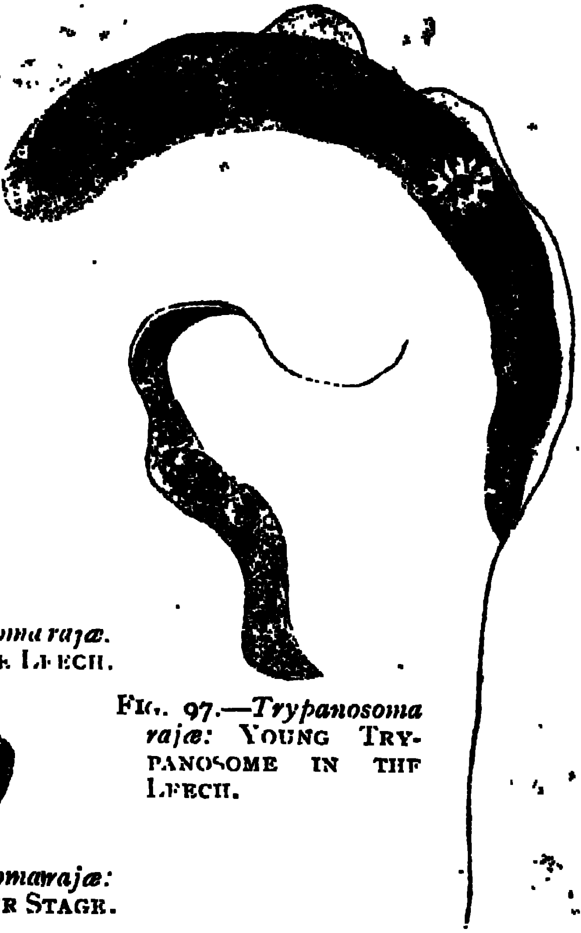


FIG. 97.—*Trypanosoma rajæ*: YOUNG TRYPANOSOME IN THE LEECH.

FIG. 98.—*Trypanosoma rajæ*: POSSIBLY FEMALE FORM, IN THE LEECH.

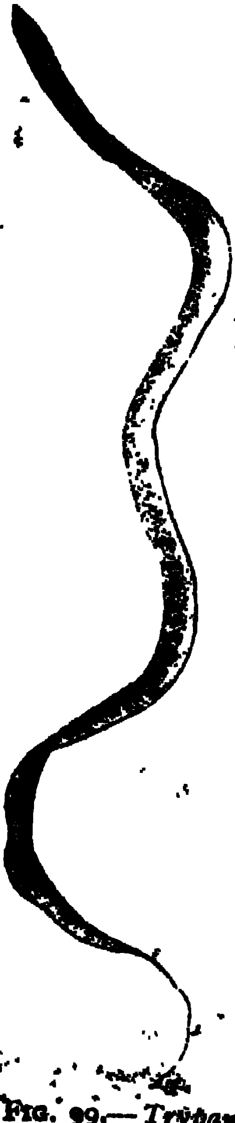


FIG. 99.—*Trypanosoma rajæ*: POSSIBLY A MALE FORM IN THE LEECH.

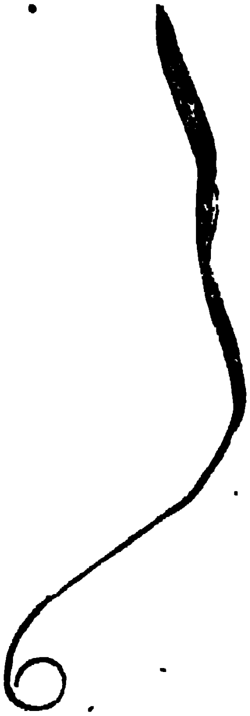


FIG. 100.—*Trypanosoma rajæ*: SLENDER FORM, FROM THE PROBOSCIS OF THE LEECH.

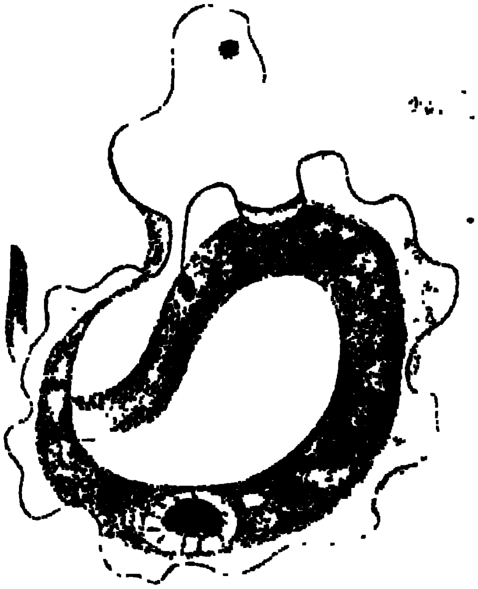


FIG. 101.—*Trypanosoma rajæ*: FULLY DEVELOPED TRYPANOSOME IN THE SKATE.

(All after Miss Robertson.)

and is thought to be spread by a leech—*Pontobdella muricata*; *T. saccobranchi* Castellani and Willey, 1905, in *Saccobranchus fossilis* in the Lake of Colombo, Ceylon.

Trypanosomes have been found in eels. Brumpt in 1906 described a number of new species in different kinds of fish, and Zupitza, in 1909, made a valuable addition to the knowledge of this subject.

Some trypanosomes found in fish are *T. danilewskyi* Laveran and Mesnil, 1904, in *Cyprinus carpis*; *T. carassii* Mitrophanov, 1883, in *Zagassius vulgaris*; *T. tincæ* Laveran and Mesnil, 1904, in *Tinca tinca*; *T. barbæ* Brumpt, 1906, in *Barbus fluviatilis*; *T. elegans* Brumpt, 1906, in *Gobio fluviatalis*; *T. phoxini* Brumpt, 1906, in *Phoxinus lævis*; *T. abramidis* Laveran and Mesnil, 1904, in *Abramis brama*; *T. leucisci* Brumpt, 1906, in *Leuciscus* sp. (?); *T. scardini* Brumpt, 1906, in *Scardinius erythrophthalmus*; *T. squalii* Brumpt, 1906, in *Squalius cephalus*; *T. cobitis* Mitrophanov, 1883, in *Cobitis fossilis*. There are, however, many others described. *T. roulei* Mathis et Léger, 1911, in *Monopteres javanensis*; *T. pellegrini* Mathis et Léger, 1911, in *Macropodus viridi auratus*; *T. chagasi* Horta and Machado, 1911, *T. dorhni* Yakimoff, 1912, in Solea; *T. yakimoffi* in Syngnatis

SECTION II.: TRYPANOSOMES OF AMPHIBIA.

The trypanosomes of frogs were discovered by Gluge as far back as 1842 in the form of the largest trypanosome known—*i.e.*, *T. rotatorium*.

It seems probable that leeches are the carriers of these parasites.

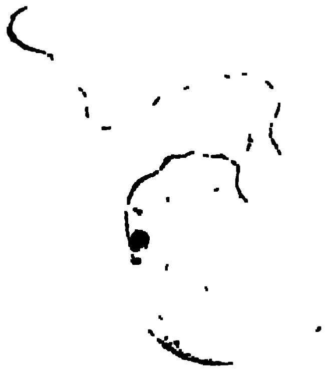


FIG. 102.—*Trypanosoma pertenue* ROBERTSON.

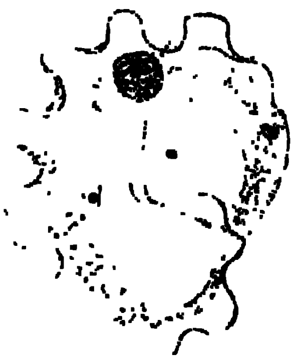


FIG. 103.—*Trypanosoma vittatæ* ROBERTSON SHOWS THE TRYPANOSOME ROLLING UP PRIOR TO DIVISION

(From drawing by Miss Robertson)

Trypanosoma inopinatum Ed. and Et. Sergent, 1904.

Synonyms.—*T. elegans* França and Athias; *T. undulans* França; *T. hendersoni* Patton.

Found in *R. esculenta* L. in Algeria, in *R. hexodactyla* and *R. tigrana* in India. It is very like *T. lewisi*, but is more stumpy. It is spread by the leech, *Helobdella algira*. It gives rise to herpetomonas and crithidial forms and Brumpt has been able to infect frogs by the bite of the infected leeches, and has shown that the infection can be spread by the second generation also—*i.e.*, that it is hereditary. It is also inoculable. The crithidial forms are said to be the infective agent by França.

Trypanosoma nelspruitense Laveran, 1904.

Discovered by Theiler in *R. angolensis* Bocage and in *R. theileri* Macquart.

Trypanosoma somalense Brumpt, 1906.

In *Bufo reticulatus* from Somaliland.

Trypanosoma sp. (?).

Found by Tobey in the American newt, *Diemyctylus viridescens*.

SECTION III.: TRYPANOSOMES OF REPTILIA.

Tortoises.—*Trypanosoma damoniæ* Laveran and Mesnil, 1902, in *Damonia reevesi*, an Asiatic tortoise; *T. vittatæ* Robertson, 1907, in *Emyda vittata* in Ceylon, the intermediate host being a leech.

Crocodilia.—*Trypanosoma grayi* Novy.—This parasite, which was thought to be part of the life-cycle of the *Trypanosoma* of the crocodile, is now known to be a Crithidia.

Lizards.—*T. boueti* Martin, 1907, in *Mabuia raddoni*; *T. leschenaultii* Robertson, 1907, in *Hemidactylus leschenaultii*, in Ceylon; *T. pertenue* Robertson, 1907, in *Hemidactylus triedri leschenaulti*, in Ceylon.

Ophidia.—*T. pythonis* Robertson; Mesnil is doubtful whether this is not a hæmoproteus, while Sambon considers that it is a hæmogregarine, (*H. robertsoni*). *T. erythrolampri* Wenyon, 1909, in *Erythrolampus æsculapii*, *T. primeti* Mathis et Léger in *H. piscator*, *T. najæ* Wenyon, 1909, in *Naja nigricollis*.

SERIES C: TRYPANOSOMES INFECTING WARM-BLOODED ANIMALS.

TRIBE 3: TRYPOCASTELLANELLEÆ.

This tribe may be divided into:—

SECTION I.: TRYPANOSOMES OF AVES. These are but little known, and, pending further study, we must retain the old genus *Trypanosoma sensû lato*.

SECTION II.: TRYPANOSOMES OF MAMMALIA.—They may be classified as follows:—

Series (*a*).—Non-Pathogenic.

1. *Classifiable*:—
   Genus Lewisonella.
   Genus Endotrypanum.
2. *Unclassifiable*:—
   Old genus *Trypanosoma sensû lato* pending further work.

Series (*b*).—Pathogenic.

1. *Classifiable*:—
   Genus Schizotrypanum.
   Genus Castellanella.
   Genus Duttonella.
2. *Unclassifiable*:—
   Old genus *Trypanosoma sensù lato* pending more research.
3. *Little known.*

The classifiable mammalian trypanosomes may be recognized by the characters given in the following table:—

A. With schizogony in the vertebrate host—*Schizotrypanum* Chagas, 1909.

B. Without schizogony in the vertebrate host:—

- I. Enters red blood-corpuscles—*Endotrypanum* Mesnil and Brimont, 1908.
- II. Does not enter red blood-corpuscles.
  - (*a*) Final stage of development in the definitive host is in the hind gut. Infection is contaminative. Aflagellar extremity long drawn out and pointed. Cytoplasm free from granules—*Lewisonella* Chalmers, 1918.
  - (*b*) Final stage of development in the definitive host is in the salivary glands, proboscis, or hypopharynx. Infection inoculative.
    - 1. Polymorphic, with granular cytoplasm, small kinetonucleus, and well-developed undulating membrane. Final stage in the definitive host takes place in the salivary glands—*Castellanella* Chalmers, 1918.
    - 2. Monomorphic, with non-granular cytoplasm, large kinetonucleus, and with or without well-developed undulating membrane. Final stage of development anterior, but not in the salivary glands *Duttonella* Chalmers, 1918.

The type species of these genera are as follows:—

Schizotrypanum cruzi, synonym *Trypanosoma cruzi* Chagas, 1909.

Endotrypanum schaudinni Mesnil and Brimont, 1908.

Lewisonella lewisi, synonym *Trypanosoma lewisi* Kent, 1879.

Castellanella gambiensis Dutton, 1902 (co-type species: *Castellanella castellanii* Kruse, 1903, synonym *Trypanosoma castellanii* Kruse, 1903).

Duttonella vivax, synonym *Trypanosoma vivax* Ziemann, 1905.

SECTION I.: TRYPANOSOMES OF AVES.

In 1845 Gros found trypanosomes in the blood of goat-suckers and cranes which are now known to be very common in birds, but the detection in blood-films is not easy, as the parasites are few and far between. According to Novy and McNeal, the cultivation method is much better.

Laveran and Mesnil summarize them into three types:—(1) Trypanosomes of type of *T. lewisi* in rats (*T. avium minus*), (2) trypanosomes of type of *T. rotatorium* of the frog, (3) long thin trypanosomes without free flagellum—distinct type.

A few examples may be mentioned:—*T. avium* Laveran, 1903, in *Syrnium aluco* L., the wood-owl; *T. confusum* Lühe, 1906, in *Agelaius phœniceus* L., and other North American birds; *T. laverani* Novy and McNeal, 1905, in *Astragalinus tristis* L., North America; *T. paddæ* L. and Mesnil, 1904, in *Padda oryzivora*, the Java sparrow.

Also *T. lagonostictæ* Marullaz, 1914, from *Lagonostictæ senegala*; and *T. Leothricis*, from the Japanese nightingale, *Leothrix luteus*.

SECTION II.: THE TRYPANOSOMES OF THE MAMMALIA

Mammalian trypanosomes may be classified according to Laveran and Mesnil, into:—

Series (*a*).—The non-pathogenic mammalian trypanosomes.

Series (*b*).—The pathogenic mammalian trypanosomes.

This classification is, in our opinion, in accord with evolutionary knowledge.

SERIES A: THE NON-PATHOGENIC MAMMALIAN TRYPANOSOMES.

It is quite beyond the limits of this book to give detailed accounts of these trypanosomes, and all that we can do is to attach a list of the more common with an account of a few.

Classifiable.

Two genera are known—viz.:—

A. Endoglobular forms known—*Endotrypanum*.
B. Endoglobular forms unknown—*Lewisonella*.

Unclassifiable.

C. Little known forms *Trypanosoma sensû lato*.

Genus Lewisonella Chalmers, 1918.

Definition.—Trypocastellanelleæ, found in mammals, non-pathogenic, without endoglobular forms.

Type Species:—*Lewisonella lewisi* Saville Kent, 1880.

We will describe the type species *L. lewisi* Saville Kent, 1880, in greater detail.

Lewisonella lewisi (Saville Kent, 1880).

Synonyms.—*Herpetomonas lewisi* Kent, 1880; *Trichomonas lewisi* Crookshank, 1886; *Trypanomonas lewisi* Labbé, 1891; *Trypanosoma sanguinis* Kanthack, Durham, and Blandford, 1898; *T. rattorum* Borner, 1901; *Trypanomonas murium* Danil, 1899; *Trypanozoon lewisi* Lühe, 1906; *Trypanosoma lewisi* Kent, 1880.

Remarks.—*L. lewisi* was the first mammalian trypanosome to be discovered, for it was seen by Chussat in 1850 in *Epimys rattus* (probably not by Gros in 1845), who thought it was a young nematode, while Lewis, in Calcutta, in 1877, rediscovered it, and recognized that it was a protozoon. It is a typical Lewisonella, and is found in *Epimys rattus* L., *E. norvegicus* Pall, and *E. rufescens* Gray all over the world—in Asia (India, Ceylon, Java, Philippines, Japan), in Europe (England, Ireland, France, Holland, Germany, Russia), in Africa (Uganda, Abyssinia, Gambia, and Cameroons), and in America (United States and Brazil). It is non-pathogenic and restricted to rats, among which it is spread by *Ceratophyllus fasciatus*, the rat-flea.

Morphology.—It is a very active, worm-like little parasite darting about among the corpuscles. It is 24 to 25 μ in length and 1·5 μ in breadth. The anterior end is very pointed, and the whole parasite is thin. The trophonucleus is situated near the junction of the middle and posterior thirds of the body, and the kinetonucleus, which is rod-shaped, is situated anteriorly. There are eight myonemes in the ectoplasm (periplast). Prowazek distinguishes small male forms with a nucleus rich in chromatin, large female forms with clear cytoplasm, and indifferent forms with many granules and poorly defined nucleus.

Life-History—*In the Vertebrate.*—The life-history in the rat has been worked out by Breinl and Hindle (Fig. 89, p. 384). The filament they mention as occurring between the kinetonucleus and the trophonucleus appears to have been also seen by Prowazek. Asexual reproduction may be summarized into reproduction with longitudinal division and reproduction with rosette formation and encystment after some interchange between the kineto- and tropho-nuclei, followed in due course by increased power for longitudinal division. Battaglia describes a process of sporogony with the formation of macro- and micro-gametocytes, and of macrogametes and microgametes, and a similar reproduction has been described by Pricolo. Carini's cyst-like bodies in the lungs are considered by Delinois to be a coccidium, *Pneumocystis carinii*.

In the Invertebrate.—The rat flea, *Ceratophyllus fasciatus*, is the true carrier of *T. lewisi*, as was first demonstrated by Nuttall, and the rare development which may take place in louse *Polyplax spinulosa* is more of the nature of a natural culture than a proper development. The development in the flea has been studied by Swellengrebel and Strickland, and more recently by Minchin and Thompson.

When the flea ingests blood containing the flagellates, they pass directly to the mid-gut, where they enter the epithelial cells, inside which they attain a large size and undergo multiplication in a peculiar manner by forming a large spherical body containing a number of tropho- and kineto-nuclei, and developing flagella, while the original flagellum still remains attached, but is subsequently lost; and then the cytoplasm divides into the daughter trypanosomes, which are now set free, and, passing into the rectum, become crithidial forms by the kinetonucleus travelling past the trophonucleus towards the flagellum. These crithidial forms attach themselves to the wall of the rectum, and shorten into Leishmania-like forms without flagella or without free flagella. These in their turn develop into trypanosome forms, which pass forwards into the mid-gut.

The intracellular stage is at its height about the end of the first day after infection, the rectal stage begins during the second day, the trypaniform types pass into the mid-gut towards the end of the fifth day; and the flea is infective in about six days after its own infective meal.

The 1915 work of Minchin and Thompson may be summarized as follows:—

T. lewisi is transmitted from rat to rat by the rat-flea *Ceratophyllus fasciatus*, but infection does not occur by the flea-bites, but is contaminative by the rat licking from its fur or skin the moist fæces of infective fleas containing the final propagative form, or by eating the fleas.

The cycle of development is as follows —The flea sucks the blood of an infected rat, and so acquires the trypanosomes, which require a minimum of five days to attain the infective stage, which is a small trypanosome which does not penetrate the salivary glands, but remains in the digestive tract, from which it escapes in the fæces, which are taken into the mouth of the rat while licking the fur. The flea remains infective for a long time, but does not pass the germ on to the next generation. After infection some five to seven days elapse before the trypanosome appears in the rat's blood, in which it multiplies till the eleventh to thirteenth day after infection.

In the louse, *Polyplax spinulosa*, the life-cycle has been studied by Prowazek, who finds that the micro- and macro-gametocytes undergo first a reduction of the trophonucleus from sixteen chromosomes to four, and that then the microgametocyte gives rise to only one microgamete, which fuses with the macrogamete, forming an ookinete. This becomes a trypanosome by the separation of the kinetonucleus from the synkaryon. The flagellum projects from the posterior end, which the kinetonucleus now leaves, and, taking the flagellum with it, proceeds towards the anterior end, thus forming the undulating membrane. Gregariniform non-flagellate forms also appear, which penetrate between the epithelial cells. Prowazek failed to infect rats by the bite of the louse, but this has been done successfully since. Swellengrebel and Strickland find that the development in the louse is very irregular and not to be compared with that in the flea.

Cultivation.—Cultural experiments have been carried out successfully by Novy and McNeal on a medium prepared by mixing agar and defibrinated rabbit's blood in equal parts, when forms from 1½ to 60 μ in length may be found, and also rosettes, but the forms are herpetomoniform, with the kinetonucleus at the flagellar end.

Pathogenicity.—Inoculation can only be carried out successfully in rats, in which it is generally non-pathogenic, though some observers have described the rare occurrence of dyspnœa, œdema, and subcutaneous hæmorrhages in intense infections. Some strains may become very pathogenic for rats. These strains show morphological and developmental anomalies—*e.g.*, forms without a blepharoplast—and there is a correlation between virulence and these changes.

Immunity.—Immunity is gained when a rat becomes free from the parasites, and hyperimmunity can be obtained by inoculations. It is thought that the immunity is largely due to phagocytosis, but this is being questioned in many species of trypanosomes. A protective serum is obtainable from hyperimmune rats. Immune serum will agglomerate the trypanosomes.

Hereditary Infection.—The parasites cannot be transmitted from the mother to young, as it appears that they cannot traverse the placenta.

Genus Endotrypanum Mesnil and Brimont, 1908.

Definition.—Trypocastellanelleæ, found in mammals, non-pathogenic, and with endoglobular forms.

Type Species.—*Endotrypanum schaudinni* Mesnil and Brimont, 1908.

Endotrypanum schaudinni Mesnil and Brimont, 1908.

This trypanosome, 13·4 × 3·5 microns, is only known in the endoglobular form in the red blood cells of the sloth, in which it appears as a peg-top-shaped trypanosome with a short flagellum possessing trophonucleus and kinetonucleus. This must be only one stage in its life-history, and as yet the other stages are unknown; and though a free trypanosome was seen in the same animal as the encysted forms, it was considered to be different from the endoglobular forms. In 1914 Darling confirmed these researches, finding the organism in *Cholœpus didactylus* in Panama. No free trypanosomes were seen in the sloth. Free forms only occur after fresh preparations have stood some time.

Unclassifiable.

The following is a list of the unclassifi species, divided according to the classification of the host and nged according to known importance:—

Trypanosomes found in Monkeys.—America: *T. minasense* Chagas, 1909; *T. prowazeki* Gossler, 1908. Asia: *T. rhesii* Terry, 1911; *T. vickersæ* Brumpt, 1909. Africa: A number of unnamed trypanosomes are reported in chimpanzees and species of Cercopithecus.

Trypanosomes of Ungulata.—*Trypanosoma theileri* Bruce, 1902.

Trypanosomes of Rodents.—*T. duttoni* Thiroux, 1905; *T. musculi* Kendall, 1906; *T. grosi* Laveran and Pettit, 1909; *T. microti* Laveran and Pettit, 1909; *T. blanchardi* Brumpt, 1905 (= *T. myoxi* Blanchard); *T. evotomys* Hadwen; *T. peromysci* Watson; *T. criceti* Lühe, 1906; *T. cuniculi* R. Blanchard, 1906; *T. bandicotti* Lingard, 1904; *T. nabiasi* Railliet; *T. leporis sylvatici* Watson; *T. acouchii* Brimont; *T. indicum* Lühe; *T. citelli* Watson; *T. spermophili* Laveran; *T. otospermophili* Wellman and Wherry; *T. petrodromi* Bruce, 1915.

Trypanosomes of Bats.—*T. vespertilionis* Battaglia, 1904; *T. megaderma* Wenyon, 1908; *T. nicolleorum* Ed. and Et. Sergent, 1905; *T. lineatus* Iturbe and Gonzalez, 1916.

Trypanosomes of Insectivora.—*T. talpæ* Nabarro; *T soricis* Hadwen.

Trypanosomes of Edentata.—*T. légeri* Mesnil and Brimont, 1910.

Trypanosomes of Carnivora.—*T. pestanai* Bettencourt and França, 1905.

Trypanosoma duttoni Thiroux, 1905.

Dutton and Todd in 1903 saw a flagellate organism in the blood of mice obtained in a house in McCarthy Island on the Gambia River, but they considered it to be of the type of a *Herpetomonas*; but in 1905 Thiroux described a definite trypanosome in *Mus musculus* L. in Senegal which will only infect mice of all kinds—*e.g.*, *M. minutus* L. (the harvest-mouse)—and it is possible that Dutton and Todd saw one stage of its development.

A number of interesting researches have taken place with this trypanosome. Pricolo found that it could pass through the placenta and multiply in the fœtus, in which he describes latent forms very like those already mentioned in *T. lewisi*—*i.e.*, which resembled Leishmania—having only a rod-shaped kinetonucleus and trophonucleus.

Trypanosomes were found in fleas caught on infected animals, but they did not show any development.

Trypanosoma musculi Kendall, 1906.

This parasite was found in 8 per cent. of the mice examined by Kendall in Panama. It was non-pathogenic, and resembled *T. duttoni*.

Trypanosoma microti Laveran and Pettit, 1909.

Found in *Microtus arvalis* Pallas. It is 25 to 30 μ by 1·5 μ.

Trypanosoma blanchardi Brumpt, 1905.

In *Myoxis glis*, the common dormouse. Like *T. lewisi*, but not inoculable into rats.

Trypanosoma myoxi R. Blanchard, 1906.

Found by Galli-Valerio in *Muscardium* (*Myoxis*) *avellanarius* L., but nothing much is known about the parasite.

Trypanosoma arvicanthidis Delanoe, 1915, from species of Arvicanthus and *T. eburnense* Delanoe, 1915, from Mus concha are varieties of *T. lewisi*.

Trypanosoma criceti Lühe, 1906.

Synonyms. *T. rabinowitschi* Brumpt, 1906.

This trypanosome, which is very like *T. lewisi*, but distinguished by not being transferable to the rat, was found in the hamster (*Cricetus cricetus* L.) by Koch in 1881. A blood-sucking louse has not been found on the hamster, but *Ceratophyllus fasciatus* Bosc is common.

Trypanosoma cuniculi R. Blanchard, 1906.

This trypanosome was found by Jobjet and Nabois in 1891 in the rabbit (*Lepus cuniculus* L.), in which it causes emaciation and perhaps diarrhœa. It is very similar to *T. lewisi*, but smaller. It will not infect white rats and guinea-pigs, but it can be cultivated. It is suspected that *Hæmatopinus ventricosus* Denny and *Pulex goniocephalus* Taschenberg may perhaps have something to do with its life-history.

Trypanosoma bandicotti Lingard, 1904.

This trypanosome is probably not the same as *T. lewisi*, which it resembles in being pathogenic to guinea-pigs. It is found in *Nesokia bandicotti* Bechst in Bombay and the Deccan.

Trypanosoma indicum Lühe, 1906.

T. indicum is found in the Indian squirrel (*Funambulus palmarum* L.) in Madras. It is very like *T. lewisi*, and only slight morphological differences can be found.

Trypanosoma vespertilionis Battaglia, 1905.

Synonym.- *Trypanosoma dionisii* Bettencourt and França, 1908.

Dionisi found a trypanosome in the Italian bat (*Miniopterus schreibersii*) in 1899, and since then numerous bats have been found to carry trypanosomes, and also they can be inoculated with the parasites of surra and mbori, which produce pathogenic effects.

T. vespertilionis has been found in bats from South Italy (Battaglia), Roman Campagna (Sambon), Brazil (Durham), India (Donovan), North Africa (Sergents), and from Portugal (Bettencourt and França). This parasite has been investigated by Battaglia, who has described a process of sporogony, and has shown that the blood filtered through a Kitasato filter is still infectious.

According to Pringault, *T. vespertilionis* is spread by *Cimex pipistrelli*.

Trypanosoma nicolleorum Ed. and Et. Sergent, 1905.

In the blood of *Vespertilio kuhli* Natt and *V. myotis* Bechst in Algeria; not transmissible to mice, rats, or rabbits.

The carrier of the infection is not known. Durham saw trypanosomes in *Stegomyia fasciata* which had fed on a bat, but they might have belonged to the mosquito. Fleas have been examined without success.

Trypanosoma theileri Bruce, 1902.

Synonym. *T. transvaaliense* Laveran, 1902

T. theileri is found in the Transvaal, in Togoland, East Africa, Transcaucasia, and in India. It is of large size, 60 to 70 μ in length and 4 to 5 μ in breadth. A small form is known, 25 to 53 μ in length and 2 to 3 μ in breadth. It moves very rapidly, and has a long flagellum, while the anterior end is pointed and the kinetonucleus is oval. Multiplication is by simple longitudinal fission. A female form has been described by Lühe. It is believed to be spread by species of Hippobosca, and is specific for bovines, not being inoculable into other animals. According to Nocht and Mayer, it is not the cause of gall-sickness or galziekté in cattle in Africa.

Carrier: *Hippobosca rufipes* (Fig. 117, p. 851). An allied species is *T. wrublewskii* Wladimiroff and Yakimoff, 1909.

Similar species are *T. himalayanum*, *T. indicum*, *T. muktesari* Langeard, 1904; *T. franki* Frosch, 1909, *T. americanum* Crawley, 1909; *T. rutherfordi* Hadwen, 1912.

SERIES B: THE PATHOGENIC MAMMALIAN TRYPANOSOMES.

Bruce has classified pathogenic mammalian trypanosomes into groups as follows:—

A. *Polymorphic trypanosomes* with granular cytoplasm, active movements, well-developed undulating membrane, small kinetonucleus. Spread by tsetse-flies, which are the definitive hosts in which development is completed in the salivary glands—*T. gambiense*, *T. brucei*, *T. rhodesiense*, *T. evansi*, *T. equiperdum*. (This group corresponds with the genus *Castellanella*.)

B. *Monomorphic trypanosomes* with non-granular cytoplasm. Spread by tsetse-flies, in which development is confined to the proboscis and hypopharynx. (This group agrees with the genus *Duttonella.*)

  I. Kinetonucleus large and terminal. Undulating membrane poorly developed and simple. Movements very rapid—*T. vivax, T. capræ, T. uniforme.* (Vivax sub-group.)

  II. Kinetonucleus prominent and subterminal. Undulating membrane well developed. Movements active—*T. pecorum* and *T. simiæ.* (Pecorum sub-group.)

Taking into consideration the above, we may arrange the pathogenic mammalian trypanosomes as follows:—

A. Classifiable:—

  I. Genus *Castellanella.*

Genus Castellanella Chalmers, 1918.

Definition.—Trypocastellanelleæ with the definitive host a fly and the intermediate host in a warm-blooded vertebrate. Without reproduction by schizogony in the vertebrate host, in which it is polymorphic, with granular cytoplasm, small kinetonucleus, and well-developed undulating membrane. Final stage in the definitive host is in the salivary glands. Infection is inoculative and transmission is ingestive (see Chapter XXXV., p. 878).

Co-Type Species.—*Castellanella gambiensis* (Dutton, 1902) and *Castellanella castellanii* (Kruse, 1903).

Other Species.—The species of the genus may be differentiated as follows:—

A. *Posteriorly nucleate in rats*:—
  I. Will not infect man. Kills an animal immunized against *C. rhodesiensis*—*C. brucei.*
  II. Infects man. Kills an animal immunized against *C. brucei*—*C. rhodesiensis.*
B. *Not posteriorly nucleate in rats*:—
  I. Infection direct from vertebrate host to vertebrate host during coitus—*C. equiperdum.*
  II. Infection by means of a definitive host:—
    (*a*) Definitive host not a tsetse-fly—*C. evansi.*
    (*b*) Definitive host a tsetse-fly:
      1. Causes chronic and often mild infections in man—*C. gambiensis.*
      2. Causes acute and severe infections in man—*C. castellanii.*

  II. Genus *Duttonella.*

Genus Duttonella Chalmers, 1918.

Definition.—Trypocastellanelleæ with definitive host in a fly and intermediate host in a warm-blooded vertebrate. Without reproduction by schizogony in the vertebrate host, in which it is monomorphic, with non-granular cytoplasm, a large kinetonucleus, which may be terminal or subterminal, with or without a well-developed undulating membrane. Movements active. Final stage in the definitive host is confined to the proboscis and hypopharynx.

Type Species.—Bruce's Uganda strain of *vivax*, which is probably the same as *cazalboui*.

Other Species.—The other species may be recognized as follows:—

(*a*) Kinetonucleus large and terminal. Undulating membrane well developed and simple. Invertebrate host a glossina:—
  1. Rats refractory—*Uniformis*.
  2. Rats susceptible—*Vivax*.
  3. Only equidæ and ruminants susceptible—*Capræ*.

(*b*) Kinetonucleus prominent and subterminal. Undulating membrane poorly developed:—
  1. Small, 8-18 microns; found in cattle—*Pecorum*.
  2. Larger, 14-24 microns; found in monkeys—*Simiæ*.

B. Unclassifiable:—

Genus *Trypanosoma sensû lato*:—

Group 1: Part of the flagellum always free.
Group 2: No part of the flagellum free.
Group 3: Part of the flagellum may or may not be free.
Group 4: Little-known forms.

TRYPANOSOMES OF ANIMALS.

FORMS CLASSIFIABLE.

Genus Castellanella Chalmers, 1918.

Castellanella evansi Steel, 1885.

Synonyms.—*Spirochæta evansi* Steel, 1885; *Hæmatomonas evansi* Crookshank, 1886; and *Trichomonas evansi* Crookshank, 1886. According to Yorke and Blacklock, *T. soudanense* and *T. venezuelense*, according to Bruce, *T. soudanense* Laveran.

Castellanella evansi, discovered by Evans in India in 1880, is the cause of a disease called surra, which occurs in horses, mules, camels, and cattle in India, Burma, Indo-China, Java, Philippines, Mauritius, and North Africa. With regard to cattle, they were supposed to be immune until the outbreak in Mauritius in 1902, which killed from 25 to 100 per cent. of the infected cattle.

Morphology.—This trypanosome, 25 μ in length and 1·5 μ in breadth, has a pointed anterior extremity, a long flagellum, and is actively motile. It reproduces asexually by simple division.

Walker finds that a schizogony takes place in the spleen of the vertebrate host. The trypanosome in the capillary bends round until its two ends meet and fuse, forming a ring, which may become a disc with the flagellum at first attached, but subsequently lost. These bodies measure 2·5 μ in diameter, and possess a kinetonucleus and a trophonucleus. They grow, and their nuclei divide until they reach a size of 10 to 15 μ in diameter, and divide into four to sixteen kineto- and tropho-nuclei, and eventually form mesozoites inside a thin cyst wall. Each mesozoite is 6 to 10 μ in length and 1 to 1·5 μ in width, with two nuclei, but no flagellum or undulating membrane. These mesozoites are believed to develop into trypanosomes. No dimorphism in these bodies has been seen.

Life-History.—Holmes recognizes male and female forms, which he considers conjugate by the anterior extremities only, after which the female divides, forming four amœboid bodies, which, in the liver, spleen, and bone-marrow, develop into trypanosomes. This appears to somewhat resemble the descriptions of Breinl and Hindle of latent forms in *C. castellanii*. *C. evansi* can be cultivated, and appears to develop in certain flies—for example, *Tabanus tropicus*, *T. lineola*, *Stomoxys calcitrans*, *S. geniculatus*, in the stomach of the last of which it has been found. Certainly it can be transmitted to healthy animals by the bites of flies and fleas. It is said that it can also be contracted by eating infected meat.

T. striatus Fabricius, according to Mitzmain, can mechanically transmit surra.

Pathogenicity. The symptoms are fever, remittent or intermittent, emaciation, œdema of the limbs and ventral surfaces, frequently lesions of the eyes and eyelids, great muscular weakness, paralysis, and death. The treatment is by arsenic. A variety, *C. evansi* var. *mborii* Laveran, 1905, is the cause of the disease mborri in dromedaries in Africa.

Castellanella brucei Plimmer and Bradford, 1899.

Synonyms.—Perhaps *T. cani* Blacklock and Yorke, 1913. According to Bruce, *T. rhodesiense* and *T. ugandæ*.

This parasite was discovered by Sir David and Lady Bruce in 1895 in animals suffering from the tsetse-fly disease or nagana (which means 'weakness') in Zululand. At the same time they showed that the tsetse-fly (*Glossina morsitans*) disseminated the disease.

The parasite is widespread throughout Africa, especially in Zululand, Northern Transvaal, and its surrounding countries; also from Pretoria to Lake Nyassa in the basin of the Limpopo, in the basin of the Zambesi, in East Africa, where it causes nagana or the fly disease, and in Uganda, where it is called 'jinja'.

Morphology. The appearance of the parasite is worm like, being 28 to 33 μ in length in horses and donkeys. The length is constant for the given animal, but varies in different hosts, being 26 to 27 μ in rats, mice, guinea pigs, rabbits, and dogs. The anterior end (non-flagellate) is a truncated cone, behind which lies the kinetonucleus as a well-marked rounded mass, posterior to which the flagellum arises. The trophonucleus lies in the middle of the body, and many chromatoid granules may be seen posterior to it, while still further posterior the free whip of the flagellum may be noted. Koch considers *C. brucei* to be identical with *C. evansi*, but the animal reactions clearly show them to be different species.

Life-History.—The life-cycle in the vertebrate host has not been very fully worked out, but the longitudinal division is well known. The kinetonucleus divides first, then the flagellum, then the trophonucleus, and finally the cytoplasm, but, according to Prowazek, division is really a very complicated process. First the blepharoplast becomes thickened, elongated, and dumb-bell-shaped, and then divides. In the trophonucleus the chromosomes behave like the kinetonucleus and the centrosome, and, having divided, the whole nucleus divides. The chromatin granules in the cytoplasm are also said to undergo fission, while a new flagellum develops from the new kinetonucleus. Parasites resembling the latent forms of Breinl and Hindle are known, and are called involution forms.

It is believed by some authorities that the parasite lives in nature in the wildebeeste (*Catoblepas gnu*), the koodoo (*Strepsiceros capensis*), the bush-buck (*Tragelaphus scriptus sylvaticus*), and the hyena, without causing disease. These may form a reserve from which the tsetse-flies *G. morsitans*, *G. pallidipes*, and *G. fusca* can obtain parasites which undergo development in their alimentary canal, during which time they are non-pathogenic, and when fully developed are found in the proboscis, and are again capable of being inoculated into animals, in some of which they are pathogenic. Kleine has proved that the transmission of the trypanosome is not merely mechanical, as suggested by Bruce and others, but also takes place after the trypanosome has undergone development in the fly, which is its true host. Thus, freshly caught *G. morsitans* for the first three days infected cattle, and then, from the fourth to the tenth day the flies were non-infective, but from the eleventh to the forty-fourth day they were very infective. This shows that the parasite must undergo a development in the fly.

Cultivation.—Novy and McNeal have cultivated *C. brucei* in the same manner as *Lewisonella lewisi*, and found some evidence of a toxin, but it only grows exceptionally in the water of condensation from the agar medium which contains half or less than half its volume of blood. Agglomeration takes place under various circumstances—*e.g.*, mixture with immune blood or a few drops of dilute acetic acid, etc.

Pathogenicity.—The disease can therefore be spread by the bites of certain tsetse-flies, particularly *G. morsitans* and perhaps the others mentioned above.

It can, however, be also spread by inoculation and by eating the blood of animals recently dead from the disease. The incubation period is about ten days, and the effects produced in animals vary considerably in the following manner:—

1. It is an acute disease in mice, rats, dogs, monkeys, cats, etc., dogs dying in two to six days, rats in three to six days.

2. It is a subacute disease in rabbits, guinea-pigs, equines, and pigs, a horse dying in fifteen to nineteen days.

3. It is a chronic disease in cattle, goats, geese, and fowls. In cattle it lasts from one week to six months.

Battaglia has succeeded in inoculating bitches by injecting some infected blood *in vaginam*. He has also infected rabbits by inoculating blood on the penis, when a hard, granulomatous nodule, very similar to a human syphilitic primary sore, developed.

Nagana is invariably fatal to the horse, the ass, and the dog, but a small percentage of bovines recover. In these animals it is characterized by fever, by an infiltration of coagulable lymph in the subcutaneous tissue of the neck, of the abdomen, or of the extremities, giving a swollen appearance to those parts; by a destruction more or less rapid of the red corpuscles of the blood, with an extreme emaciation, often blindness; and by the presence constantly in the blood of *C. brucei*.

Very few lesions are found at the autopsy, the most characteristic being:—

1. Enlargement of the spleen.

2. Trypanosomes in the blood.

3. Hypertrophy of the lymphatic glands, but apparently not associated with a development of the parasites in these organs.

4. In horses, the liver and spleen are hypertrophied, and there is yellow serous infiltration under the skin and mucosa and between the muscles, as well as some pleural and pericardial exudations and subpericardial ecchymoses. A gelatinous substance is found at times around the spinal cord.

According to Bradford, Plimmer, Yakimoff, Lanfranchi, Rondoni, Goretti and others, the spleen has a trypanolytic action, but this is denied by Laveran, Thiroux, Massaglia, and others.

The best treatment is arsenic in some form. Trypanroth, a benzine colour, and serum treatment have not proved of great service.

Castellanella equiperdum Doflein, 1901.

Synonym.—*T. rougeti* Laveran and Mesnil.

C. equiperdum is the cause of the disease called dourine or mal du coït in horses in Europe, India, North Africa (Algeria), and North America.

Morphology.—It is about 25 to 28 μ in length, and has no chromatic granules in the cytoplasm. It is difficult to find in naturally infected animals, being best obtained from the plaques of the eruption. Salvin-Moore and Breinl reported the presence of latent bodies in inoculated rats.

Life-History.—It does not appear to be spread by a fly, but by coitus between stallion and mare. Hence the disease resembles syphilis, and proves that a trypanosome is capable of penetrating a mucous membrane. The incubation is from eleven to twenty days.

Stage 1, *or the Period of Œdema.*—The genital organs begin to show signs of œdema, generally painless and not inflammatory, though there is some fever. In about a month the œdema disappears, and weakness and emaciation begin.

Stage 2, *or the Period of Eruption*, is characterized by the appearance in about forty to forty-five days (or two months) after infection of an eruption,

characterized by circular œdematous areas about the size of a two-shilling piece, generally under the skin of the sides and hind-quarters, but sometimes also under that of the neck, shoulders, and thighs. This eruption is very variable, and may appear in the morning and disappear at night, but generally it lasts a week, and leaves the animal in a feeble condition. There is also synovial engorgement of the joints and tendon-sheaths, and enlargement of the lymphatic glands, particularly the inguinal. The temperature is often raised to 39° C. (102·2° F.) in the evening, and falls to 38·5° C. (101·4° F.) in the morning.

Stage 3, or the Period of Anæmia and Paralysis.—The animal now becomes very anæmic, with pale mucosæ, and emaciation is marked. There are often superficial abscesses which do not heal, and some conjunctivitis and ulcerative keratitis. Micturition is difficult, and the urine is thick. Sensibility is diminished, and paralysis comes on, due to softening of the cord, and in from two to eighteen months the animal dies. The disease is said to be always fatal.

The above is the usual type of the disease, and may be called chronic dourine, but in addition there is an acute type, in which the animal dies after the first stage from acute paralysis, which comes on suddenly a few days after the appearance of the eruption.

The post-mortem lesions are in the spinal cord and the lymphatic glands. In the cord there is gelatinous exudation around the lumbar area, and cervical enlargement with intense chronic inflammation of the posterior spinal ganglia, with degeneration of the perikarya and their associated neurones, causing degeneration of the posterior roots and columns, as in tabes dorsalis.

The grey matter of the cord also shows chromolytic changes, with capillary hæmorrhages due to chronic inflammation. Mott says that the infiltration and thickening of the septa of the cord, the infiltration of the nerve roots and the vessel walls with lymphocytes, is like a syphilitic meningitis. The membranes at the base of the brain may also be affected. The lymphatic glands are enlarged, congested, and softened. The disease appears to begin by inoculation, and then to spread to the inguinal glands, and then to the pelvic lymphatics, and from them to the posterior lumbo-sacral roots, and thus the cord becomes affected. Other lesions are gelatinous exudation under the skin, serous effusions into the pleural and peritoneal cavities, wasting and pallor of muscles, with fatty degeneration and an interstitial keratitis.

Genus Duttonella Chalmers, 1918.

Duttonella vivax Ziemann, 1905.

Synonym. *Trypanosoma vivax* Ziemann, 1905.

This trypanosome was found by Ziemann in 1905 in the blood of cattle, sheep, and goats, suffering from 'souma' in the Cameroons. Morphologically it closely resembles *T. cazalboui*, but it differs in the following:—

1. Rats are susceptible to *T. vivax*, but not to *T. cazalboui*.
2. Cross immunity experiments indicate distinct differences.

Bruce's *T. vivax* is *T. cazalboui*, because rats are not susceptible to Bruce's Uganda strain. It is possible that a strain allied to *D. vivax* has been found by Macfie in human blood (*vide* p. 430).

The flagellate is very rapid in its movements. A large kinetonucleus and clear cytoplasm are present. It measures 16-31 × 2-3 microns, and has its flagellum always free. It is pathogenic for equidæ and ruminants. The development is anterior in the tsetse-fly, being confined to the proboscis.

Duttonella capræ Kleine, 1910.

Synonym. *Trypanosoma capræ* Kleine, 1910.

Found in sick goats near Tanganyika, it is capable of passing through its cycle of development in *G. morsitans* in some nineteen days after infection. Development only takes place in the proboscis. The final stage is in the hypopharynx, where the trypanosomes revert to the blood form and become infective.

It is a heavily built trypanosome, with very rapid movements, measuring

18-32 × 1·75-4·25 microns, and having the flagellum always free. It is pathogenic for equidæ and ruminants only.

Duttonella uniformis Bruce, Hamerton, Bateman, and Mackay, 1911.

Synonym.—*Trypanosoma uniforme* Bruce, Hamerton, Bateman, Mackie.

It is very like *T. cazalboui*, but smaller, and causes a very fatal disease in cattle. It is a small active trypanosome 16 × 1·5-2·5 microns, with the free part of the flagellum some 1-5 microns in length. There is no narrowing opposite the trophonucleus. It is spread by *Glossina palpalis*, which becomes infective in twenty-seven to thirty-seven days. The development is anterior, being confined to the proboscis.

Duttonella pecorum Bruce, Hamerton, Bateman, Mackie, 1910.

Synonym.—*Trypanosoma pecorum.*

This term probably includes *Trypanosoma dimorphon*, *T. congolense*, and *T. confusum*, Dr. Edington's Zanzibar trypanosome, the trypanosomes from Chai-Chai and from Southern Rhodesia.

It is found in cattle. It measures 8·0-18·0 microns, and is capable of passing through a cycle of development in *G. morsitans*, which becomes infective after twenty days. Development takes place like *T. simiæ* first in the gut, then in the labial cavity, and finally in the hypopharynx, where it becomes infective.

Duttonella simiæ Bruce, Harvey, Hamerton, Davey, and Lady Bruce, 1912.

Synonym.—*Trypanosoma ignotum* Kinghorn and Yorke, 1902.

It causes a rapidly fatal disease in monkeys and a chronic disease in goats. It is abundantly present in *Glossina morsitans* in Nyassaland and North-Eastern Rhodesia. It measures 14-24 × 1-2·75 microns, and is monomorphic. Its natural host appears to be *G. morsitans*, and the monkey seems to be a new host. The development is completed in the proboscis and hypopharynx.

FORMS UNCLASSIFIABLE.

Genus Trypanosoma *sensû lato.*

GROUP I: PART OF THE FLAGELLUM ALWAYS FREE.

They may be separated from one another according to the following scheme, based upon the invertebrate host, the pathogenicity, and the serum reactions:—

- A. *No invertebrate host*, spread directly from male to female by coitus:—
  - Kinetonucleus near aflagellar end and easily seen. Habitat America—*Hippicum*.
- B. *Invertebrate host not a Glossina*:—
  - I. Kinetonucleus very insignificant. Habitat, South America—*Equinum*.
  - II. Kinetonucleus ordinary. Parasite monomorphic. Habitat, various. Animal immune to *C. evansi* becomes infected with *T. togolense* and *T. soudanense*.
    - (*a*) Animal immune to *T. togolense*, infective by *C. evansi* and *T. soudanense*—*Togolense*.
    - (*b*) Animal immune to *T. soudanense* becomes infective by *C. evansi* and *T. togolense*—*Soudanense*.

C. *Invertebrate host a Glossina* :—
  Rats refractory. Large forms, 24 microns—*Cazalboui*.
D. *Invertebrate host unknown* :—
  I. Attacks horses :—
    (*a*) In Venezuela—*Venezuelense*.
    (*b*) In Morocco, separated by cross immunity—*Marocanum*.
    (*c*) In Algeria, separated by cross immunity—*Berberum*.
  II. Attacks horses and cattle :—
    In Annam—*Annamense*.
  III. Attacks cattle :—
    In Italian Somaliland—*Cellii*.

Trypanosoma equinum Vosges, 1901.

Synonym.—*T. elmassiani* Lignières.

T. equinum, discovered by Elmassian, is the cause of mal de caderas in horses and dogs in South America.

Morphology.—This parasite closely resembles *T. brucei* and *T. evansi*. In length it is 22 to 24 μ, and in breadth 1·5 μ, and it has the same measurements in different species of animals. It is very active, but its principal characteristic is that the kinetonucleus is very insignificant.

Life-History.—Multiplication is by equal binary division. It agglomerates, and has been cultivated by Thomas and Breinl on a rabbit's blood and chicken-broth agar medium.

It can be inoculated into the ordinary laboratory animals. Its mode of propagation is not well known, but Migone has shown that it is the cause of a disease which kills the capybara (*Hydrochœrus capybara*), which appears to be the reservoir for the parasite, as monkeys inoculated from a sick *Hydrochærus* died in seventeen days. How the disease spreads from the Carpinchós (*Hydrochærus*) to the horses is not clear. Dogs may be infected by eating diseased animals, and then from the dog the infection may be spread to the horse by fleas, because they have been found to infect rats. Some authorities consider that it may be spread by members of the Tabanidæ (Chrysops ?) and by *Stomoxys*, but Neiva has infected *Triatoma infestans* Klug, and its fæces produced the disease in guinea-pigs when placed on the conjunctiva.

Pathogenicity.—Mal de caderas is a very fatal disease among the horses of South America. The first sign of the disease is weakness, which makes rapid progress, though the appetite remains good. The temperature is febrile, and after a variable period the hind-quarters become paralyzed and the horse drags its limbs, the hoofs scraping the ground. As it walks it staggers, the hind-quarters oscillating from right to left, which characteristic gives the disease its name of mal de caderas, the disease of the hind-quarters. In the stable it can support itself against the walls, but in the open air it staggers and falls. There may be albuminuria and hæmaturia, and an eruption on the neck, shoulders, and hind-quarters. The eyelids show conjunctivitis and chemosis. The horse lives about two months after the paralysis sets in.

Congestion and enlargement of the spleen and mesenteric glands are seen in post mortems. The kidneys are affected, nephritis and interstitial hæmorrhages being noted. There are also serous exudations into the peritoneum, the pleura, the pericardium, and the spinal canal.

Trypanosoma soudanense Laveran, 1907.

Type of *Trypanosoma evansi* causing tahaga in dromedaries in the Upper Niger, el debab in Southern Algeria, and the zousfana in horses in Southern Algeria. Carriers Tabanidæ. Yorke and Blacklock consider this to be the same as *Castellanella evansi*.

Trypanosoma togolense Mesnil and Brimont, 1909.

Type of *Castellanella evansi*, parasitic in horses and cattle, and the cause of nagana in Togoland.

Trypanosoma (Duttonella) cazalboui Laveran, 1906.

This organism, which should be placed in the genus Duttonella, was found by Cazalbou in 1904 in 'souma,' a form of cattle trypanosomiasis in Upper Nigeria. The disease is known in West Africa, in Uganda, the French Congo, the Congo, and Rhodesia. It affects cattle, horses, mules, and donkeys, the incubation being seven days and the disease acute, subacute, or chronic. Cattle may die in eight days, two months, or more than twelve months. It is monomorphic, 24 × 1·5-2 microns, with an oval trophonucleus situate about the middle of the body, and a spherical kinetonucleus lying near the aflagellar extremity. The undulating membrane is not markedly folded, and the flagellum always becomes free. In the vertebrate there is the usual longitudinal division. Trautmann records the successful inoculation of *Cercopithecus patas*. It may develop in *G. palpalis*, *G. tachinoides*, *G. longipalpis*, or *G. morsitans*, and may be directly conveyed by stomoxys. *G. palpalis* is the usual carrier. The development is anterior, being restricted to the proboscis. The first three carriers become infective in six to seven days, and *G. morsitans* in eight to ten days, but in Uganda it may require eleven to thirty-five days to become infective in a fly, which difference may be due to climate. In the proboscis the trypanosome passes through leptomonas or crithidial forms, and becomes attached to the walls of the labrum and multiplies. Under the influence of the salivary secretion these forms become small, actively motile trypanosomes, which are the infective agent, and apparently remain in the fly for the remainder of its life.

Trypanosoma hippicum Darling, 1910.

This trypanosome causes a disease called murrina among mules, and was first described in some animals imported from the United States via New Orleans to Panama. The trypanosome resembles *Castellanella evansi*, being 18 to 28 μ in length, with a width of 1·5 to 3 μ. The trophonucleus is oval and median. The kinetonucleus, which is near the aflagellar end, is very easily seen, which is a characteristic feature of the parasite. The undulating membrane is not much folded. It divides longitudinally in the blood. It is spread by coitus, and can also be spread mechanically by species of *Musca*, *Compsomyia*, and *Sarcophaga* sucking wounds in the diseased and the healthy. The essential pathology of murrina is an intoxication resulting in cellular degeneration and necrosis. These toxins produce endotheliolysis, lymphocytosis, auto hæmagglutination, phagocytosis of erythrocytes and trypanosomes, hyperplasia of the spleen, bone marrow, and lymph glands, and cellular exudations into the kidney, liver, etc. Owing to the destruction of the endothelium there is considerable amount of ecchymosis in various regions.

Trypanosoma venezuelense Mesnil, 1910.

Type of *Castellanella evansi*, and considered by Yorke and Blacklock to be identical. Attacks horses in Venezuela; carrier unknown.

Trypanosoma annamense Laveran, 1911.

Type of *Castellanella evansi*; causes disease in horses and cattle in Annam. Carriers: Tabanidæ and Hippoboscidæ.

Trypanosoma cellii Martoglio, 1911

This trypanosome is pathogenic for cattle in Italian Somaliland, causing a disease called 'gobiat.' Pathogenic for dogs, rabbits, rats, and mice.

In bovines there are the following types: (1) Irregularly rounded, with short flagella inside some; (2) Leishmania-like forms; (3) Trypanosomes.

Trypanosoma marocanum Sergent, Lhéritier, and Belleval, 1915 (16-21 × 1·5-2·5 microns), is the cause of a disease of horses at Casablanca in Morocco. Morphologically it is identical with *T. berberum*, the cause of debab, but crossed immunity experiments separate it from this organism and from *T. equiperdum* and *T. soudanense*. Laveran says that there are two trypanosomes at work on Moroccan horses, one monomorphic and one polymorphic.

Trypanosoma berberum Edmond and Et. Sergent, and Lheritier, 1912, is the cause of debab in Algerian horses.

Group 2: No Part of the Flagellum Free.

Trypanosoma congolense Broden, 1904.

Synonyms.—According to Blacklock and Yorke, *T. dimorphon* (*sensû* Laveran and Mesnil); *T. confusum* (Montgomery and Kinghorn); *T. pecorum* (Bruce); *T. nanum* (Laveran).

This trypanosome causes disease among horses, cattle, sheep, and dromedaries in the French and Belgian Congos and in North-East Rhodesia. It is 10 to 17 μ long and 1 to 2 μ broad. Carrier, *Glossina morsitans*, which is infective twenty-three days after a feed thereon. The alimentary canal is full of parasites, and the labrum contains the Leptomonas type, while the small infective trypanosomes are in the hypopharynx.

Trypanosoma dimorphon Laveran and Mesnil, 1904.

This trypanosome was discovered by Dutton and Todd in 1904 in horses on the Gambia, and is now known to exist in several parts of Africa, where perhaps a wide equatorial belt across the continent is affected. It is also found in cattle, dogs, pigs, sheep, and goats.

Morphology.—It exists in three forms:

1. *Tadpole Form.*—Found in the early stage of the disease, 11 to 13 μ long and 0·18 μ broad.

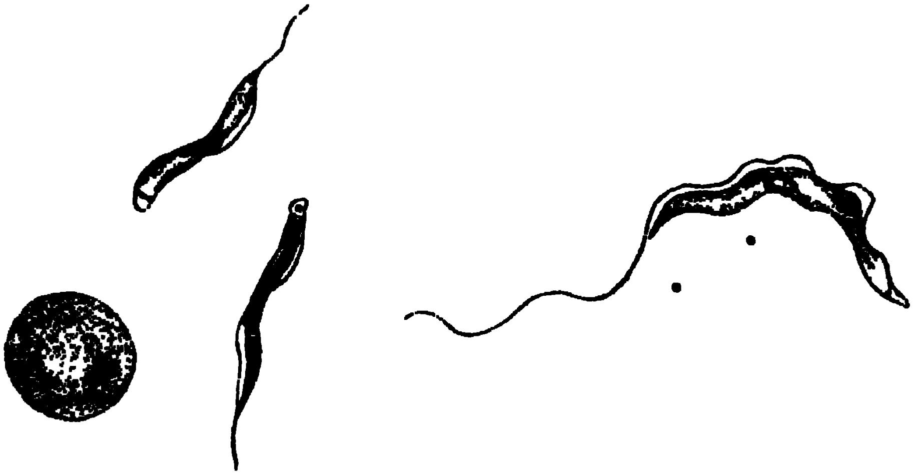


FIG. 104.—*Trypanosoma dimorphon* LAVERAN AND MESNIL.
(After Dutton and Todd.)

2. *Stumpy Form.*—Seen when the disease is not too far advanced, and characterized by a short thick body and a short flagellum. Length 16 to 19 μ, breadth 3·4 to 3·5 μ.

3. *Long Form.*—With long thin body and long flagellum, found a few days before death. Length, 26 to 30 μ; breadth, 1·6 to 2 μ.

These may be respectively indifferent, female, and male forms of the parasite, a view supported by Hindle.

It has been cultivated, and it can be inoculated into rats, mice, guinea-pigs, and rabbits, as well as horses.

Life-History.—Hindle's observations show that the indifferent forms give rise to latent bodies or cysts which gather in the spleen, where they lie dormant for a time, and finally develop again in trypanosomes. It apparently can undergo development in *Glossina palpalis*, as Bruce and Hamerton have shown that it is a carrier, while Bouet and Roubaud have shown that *G. tachinoides* and *G. longipalpis* can also transmit the parasite as in *G. morsitans*. The development is by multiplication in the intestine, and then in the form of Leptomonas or Crithidia in the proboscis, after which the fly becomes infective in about eighteen days from the date of the infective feed.

Pathogenicity.—The symptoms in the horse begin with loss of vigour, followed in two to three weeks by fever. During the next month the weakness is more marked and the abdomen swells, the testicles hang down and are œdematous, the coat becomes staring, the animal looks apathetic, and death ensues in about a year.

The post mortem shows œdema of the abdominal wall and a coloured fluid in the pleura and pericardium, with hypertrophy of the lymphatic glands, fatty liver, and congestion of the lungs. The spleen is normal.

Trypanosoma frobeniusi Weissenborn, 1911.

Allied to *T. dimorphon* and *T. congolense*, and found in horses in Togoland.

Trypanosoma nanum Laveran 1905.

Balfour in 1904 discovered this parasite in cattle, which appeared to be ill, on the White Nile. The parasites are small (10 to 14 μ by 1·5 to 2 μ), with no free flagellum, and are non-pathogenic for dogs, rabbits, and monkeys. Amœboid forms were found in the cerebro-spinal fluid. Duke in 1912 showed that it was transmitted by *Glossina palpalis*, in which it developed in the hind gut, and from thence forwards to the œsophagus, but did not infect the salivary glands. Development according to Miss Robertson, takes place in *G. palpalis*, and is like *Castellanella castellanii*, but with crithidial phase in proboscis, not in salivary glands. The parasite develops in the hind intestine and reaches the proventriculus on the twentieth day, and the proboscis on the twenty fifth, where they become crithidial forms, and finally trypanosomes which, however, may only be developed in the hypopharynx.

GROUP 3: PART OF THE FLAGELLUM MAY OR MAY NOT BE FREE.

Trypanosoma pecaudi Laveran, 1907.

In the French Sudan, in addition to m'bori and souma, there is a third disease, baleri, in Equidae caused by *T. pecaudi*, with two forms like *T. dimorphon*: (1) long and slender (25 to 35 μ by 1·5 μ), (2) short and broad (14 to 20 μ by 3 to 4 μ). Carriers: *Glossina longipalpis*, rarely *G. palpalis* and *G. tachinoides*.

The incubation in *G. longipalpis* is about twenty three days. The trypanosomes multiply in the intestine, and in seven to nine days invade the whole intestine and pharynx. The parasites now enter the proboscis and pass through crithidial and leptomonas stages. Finally, some reach the hypopharynx, where they assume the '*salivary trypanosome form*' and become infective.

LITTLE KNOWN TRYPANOSOMES

Trypanosoma elephantis Bruce, Hamerton, and Mackie, 1909, has been found in the elephant in Uganda; it resembles *T. soudanense*.

Trypanosoma ingens Bruce, Hamerton, and Mackie, 1909, has been found in the reed buck and ox in Uganda, it is of large size (72 to 122 μ by 7 to 10 μ).

Trypanosoma giganteum Lingard was found twice in cattle suffering from symptoms similar to those found in surra.

Trypanosoma bovis Kleine was found in sick cattle near Tanganyika

THE TRYPANOSOMES OF MAN.

There is evidence that man is infected with a variety of trypanosomes, the number of which is likely to be increased in the near future. Those described in man are:

1. *Trypanosoma gambiense* Dutton, 1902.
2. *Trypanosoma castellanii* Kruse, 1903.
3. *Trypanosoma vivax* Ziemann, 1905, varietas *macfiense.*
4. *Trypanosoma cruzi* Chagas, 1909.
5. *Trypanosoma rhodesiense* Stephens and Fantham, 1910.
6. *Trypanosoma nigeriense* Macfie, 1913.
7. *Trypanosoma gambiense* varietas *longum* Da Costa, St. Anna, Dos Santos, and Alvares, 1915.

When a classification is desired it is always necessary to attempt to discover the characters of the original species, which in this case is *T. gambiense* Dutton, 1902. Sixteen years have passed since the slides containing the original specimens of Dutton and Todd were made, and, therefore, as the original strain has long been lost, the only method of comparing other organisms with the original specimens is morphological. Chalmers and O'Farrell have made this comparison by measuring one thousand non-dividing forms in the original slides. As far as measurements go, these strains are very similar, but, as we have repeatedly insisted, morphology often may not help in separating closely related but perhaps quite distinct species, which require to be studied serologically and with regard to animal pathogenicity, and, in cases of human infection, with regard to the nature of the disease in man. Thus Stephens has pointed out that *T. lewisi* and *T. rabinowitschi*, *T. brucei* and *T. evansi*, *T. pecaudi* and *T. ugandæ*, *T. rhodesiense* and *T. pecaudi* are indistinguishable morphologically, but are distinct biologically.

We mention these points in order to make clear to the reader the necessity of comparing human trypanosomes by means of the clinical features of the disease in man, the serum reactions and animal experiments, as well as by morphological characters, and we have suggested for years that the name *T. gambiense* covered a number of different forms, which at the present time is generally admitted with regard to *T. rhodesiense*. And why not? Are there not a number of different trypanosomes in wild animals in Africa, and is it impossible that man should from time to time become infected by one of these, even if it does not appear in epidemic form in the human race? To exemplify we draw attention to an organism resembling *T. vivax* found by Macfie in man.

Sir David Bruce believes that *T. rhodesiense* Stephens and Fantham, 1910, is the same as *T. brucei* Plimmer and Bradford, 1899, but this can hardly be so, because Laveran and Nattan-Larrier have immunized a ram against *T. brucei*, and then infected it with *T. rhodesiense*, an acutely lethal infection ensuing. The serological experiments of Chalmers and O'Farrell *in vitro* and *in vivo* also show the same marked differences between *T. rhodesiense* and another posterior nucleate trypanosome. These experiments, to our mind, are more important than measurements, and more important than finding that the development in *Glossina morsitans* is very similar in both variants. *T. rhodesiense* may have been derived in recent times from *T. brucei*, but its altered environment in man has changed its physiological characters. As the fly remains the same, one would expect this portion of the life-cycle to be similar in the two trypanosomes.

We look upon *T. nigeriense* and *T. gambiense* var. *longum* as belonging to *T. gambiense*, because, apart from the morphological similarity, to which we do not assign importance, their pathological action in man and the lower animals appears to be identical.

As a result of these considerations, and changing the names so as to agree with the new nomenclature, we recognize the following parasites of man:—

A. *Belonging to the genus Castellanella*:—
  1. *Castellanella gambiensis* (Dutton, 1902).
  2. *Castellanella castellanii* (Kruse, 1903).
  3. *Castellanella rhodesiensis* (Stephens and Fantham, 1910).
B. *Belonging to the genus Duttonella*:
  4. *Duttonella vivax* (Ziemann, 1905), var. *Macfiensis* (Castellani and Chalmers, 1918)
C. *Belonging to the genus Schizotrypanum*:—
  5. *Schizotrypanum cruzi* Chagas 1909.

These five species may be differentiated as follows:—

A. With schizogony—*S. cruzi*.
B. Without schizogony:—
  I. Monomorphic—*D. vivax*.
  II. Polymorphic:
    (*a*) Posteriorly nucleate *C. rhodesiensis*.
    (*b*) Not posteriorly nucleate.—
      1. Animal infections chronic and comparatively mild. Common North-West Africa—*C. gambiensis*.
      2. Animal infections severe. Common Equatorial Africa—*C. castellanii*.

Castellanella gambiensis (Dutton, 1902).

Usual old name *Trypanosoma gambiense* Dutton, 1902.

Synonyms.—*T. nepveui* Sambon, 1903; *T. hominis* Manson, 1903; *T. fordii* Maxwell, 1903; *T. nigeriense* Macfie, 1913; *T. gambiense* var. *longum* Da Costa, St. Anna, Dos Santos, and Alvares, 1915.

Definition.—Castellanella without schizogony, polymorphic, trophonucleus not situate close to aflagellar end. Infections chronic.

History.—This trypanosome was first noticed by Ford in a case of peculiar fever on the Gambia. He showed the parasite to Dutton, who, recognizing it to be a trypanosome, described and named it; and they considered it to be the cause of Gambia fever, which was never thought by them to be connected with sleeping sickness. The organism had, however, been previously seen in the blood of man and imperfectly described by Nepveu. We consider it to be the same organism as that described by Scott Macfie in 1913 as *T. nigeriense*. Yorke and Blacklock in 1915 consider that man is the chief reservoir of this parasite in Sierra Leone, where sleeping sickness is very chronic and difficult to recognize. A secondary reservoir is in cattle. They record two cases with very mild symptoms. Sartory, Lasseur, and Brissaud record *C. gambiensis* trypanosomiasis in a French soldier who had left Africa for eight years, and had never been in a tsetse-fly area. In Africa he lived in Algiers, at El Golea, and went to Timimoun. Bagshawe draws attention to Nepveu's 1888 and 1890 observations, which have never been explained.

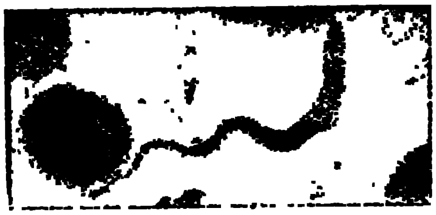


Fig. 105.—*Castellanella gambiensis* (Dutton, 1902). (× 1,200 Diameters.) Long form from the original Gambia fever case (Mr. K.) discovered by Dutton. (Photomicrograph.)

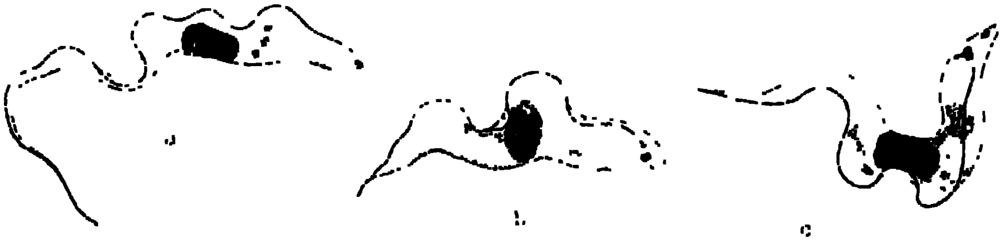


Fig. 106.—*Castellanella gambiensis* (Dutton, 1902). (× 1,200 Diameters.) Original Gambia specimens from a rat inoculated from the second case of Gambia fever, showing polymorphism [illegible], long, intermediate, and short forms.

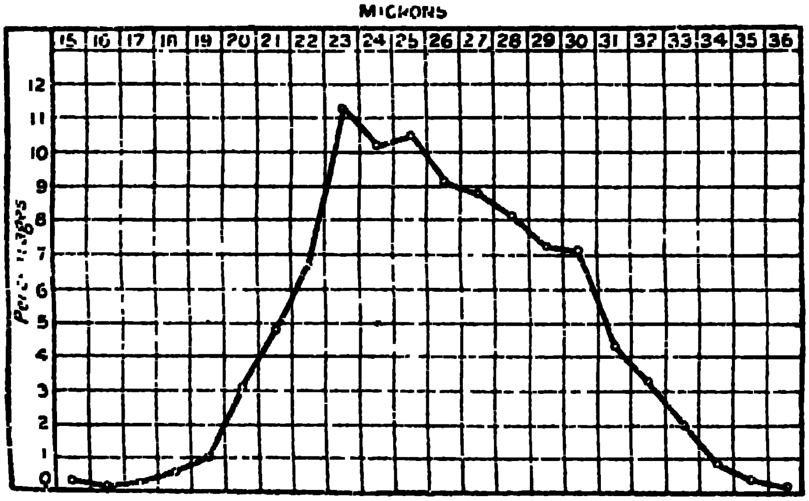


Fig. 107.—*Castellanella gambiensis* (Dutton). Chart of Lengths.

Morphology.—It is a polymorphic trypanosome, and morphologically does not differ essentially from *C. castellanii*, of which a detailed description is given below.

Life-History. This has not been fully studied, and it is not definitely known whether it takes place in *Glossina palpalis* or in some allied tsetse-fly.

Serum Reactions.—These reactions require to be studied in detail.

Pathogenicity. It causes a form of sleeping sickness, which apparently is more chronic than that produced by *C. castellanii*, while the symptoms are often less severe, though the termination is fatal without treatment, to which it appears to be more amenable.

Castellanella castellanii (Kruse, 1903).

Usual old name *Trypanosoma castellanii* Kruse, 1903.

Synonym.—*T. ugandense* Castellani, 1903.

C. castellanii was first seen in the cerebro-spinal fluid of cases of sleeping sickness by Castellani in 1902, and reported by him as the cause of the disease in 1903; he asserted also the probable plurality of species of the trypanosomes affecting man, in analogy to what takes place in the lower animals, such as horses and cattle. Bruce and Nabarro demonstrated the fact first suggested by Sambon and Brumpt that it could be spread by a tsetse-fly, *Glossina palpalis*; and Kleine has demonstrated that the transmission is not merely mechanical, but also takes place after a period during which the fly is non-infective, the deduction being that the trypanosome must undergo a development in the fly which acts as a true host. Finally Miss Robertson worked out the life cycle in the tsetse-fly.

FIG. 108.—*Castellanella castellanii* (KRUSE, 1903).

The original trypanosome found by Castellani in cerebro-spinal fluid of a case of sleeping sickness in Uganda. (Photomicrograph.)

Morphology.—*C. castellanii* measures from 14 to 33 μ in length and from 2 to 2·5 μ in breadth (Laveran and Mesnil give 17 to 28 μ in length and 1·4 to 2 μ in breadth); but, as already stated, it is very polymorphic, having short forms 14 to 20 μ, medium forms 20 to 24 μ, and long forms 23 to 33 μ. The anterior end is variable and sometimes rounded; the kinetonucleus is an oval body, behind which is often seen a vacuole. The trophonucleus is oval in shape, and situated about the middle of the body, behind which there may be some chromatic granules in the cytoplasm, which at the posterior end runs along the flagellum for a considerable distance.

Asexual Reproduction.—The life-history of the parasite in the human body is not accurately known. It can often be obtained from the peripheral blood, but sometimes the most prolonged search fails to demonstrate it. It can then be found by puncturing the enlarged lymphatic glands, by scarification of the eruption, or by puncture of the spinal canal, if the case is one of sleeping sickness.

Salvin, Moore, and Breinl have, however, investigated the life-cycle in the rat, in which, after inoculation, the parasites increase to a maximum in the peripheral blood, and then decline gradually to nil, at which they remain for a period—the latent period—and then increase again in numbers and reappear in the peripheral blood.

Their investigations give the following results: The parasite may grow to a fair size, and then divide into two by simple fission, and this may be repeated till the blood is swarming with them. When this is the case, a relatively thick band, said by Swellengrebel to be composed of metachromatic or volutine granules (axial filament), such as that described by Miss Robertson in *T. rajæ* and by Prowazek in *T. lewisi*, grows from the kinetonucleus down the endoplasm till it reaches or even passes the nucleus, or it may coil on itself, but eventually is connected with the trophonucleus.

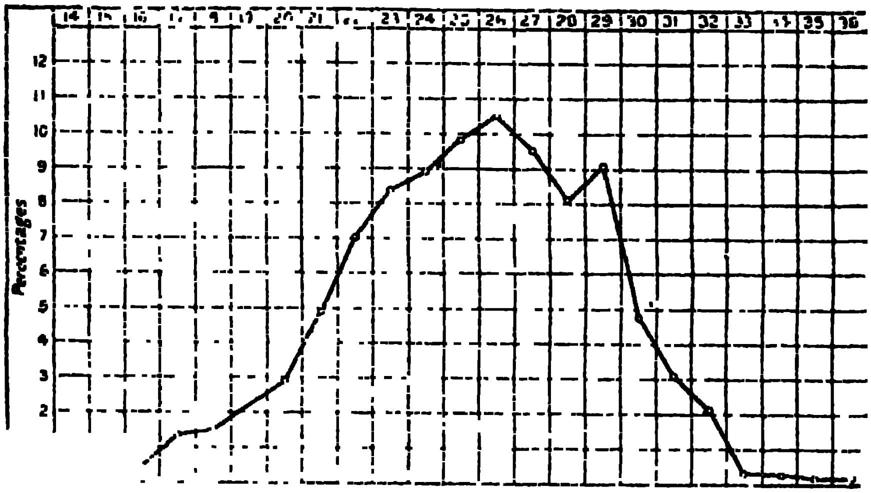


FIG. 109.—*Castellanella castellanii.* CHART OF LENGTHS.

The trypanosomes now decrease in numbers in the peripheral blood, and are found in the lungs, spleen, and bone-marrow. In these organs the protoplasm becomes detached from the periphery of the nucleus, which lies in a clear space. The nucleus contracts, and a large clear vesicle forms in connection with it, and around both a cytoplasmic sheath is formed. The rest of the cell body now disintegrates, and the flagellum with the kinetonucleus may be seen lying detached. These bodies now become lodged in the spleen and bone-marrow, where they remain intact for a period of ten days or more—through the whole of the negative or latent period when the trypanosomes are missing from the blood of the infected rat. Moore and Breinl, therefore, call them latent bodies. They consist of a flattened nucleus, containing a centrosome, and attached to a vesicle, the whole being surrounded by a ring of cytoplasm. This latent phase has been confirmed by Fantham.

Just before the reappearance of the trypanosomes in the peri-

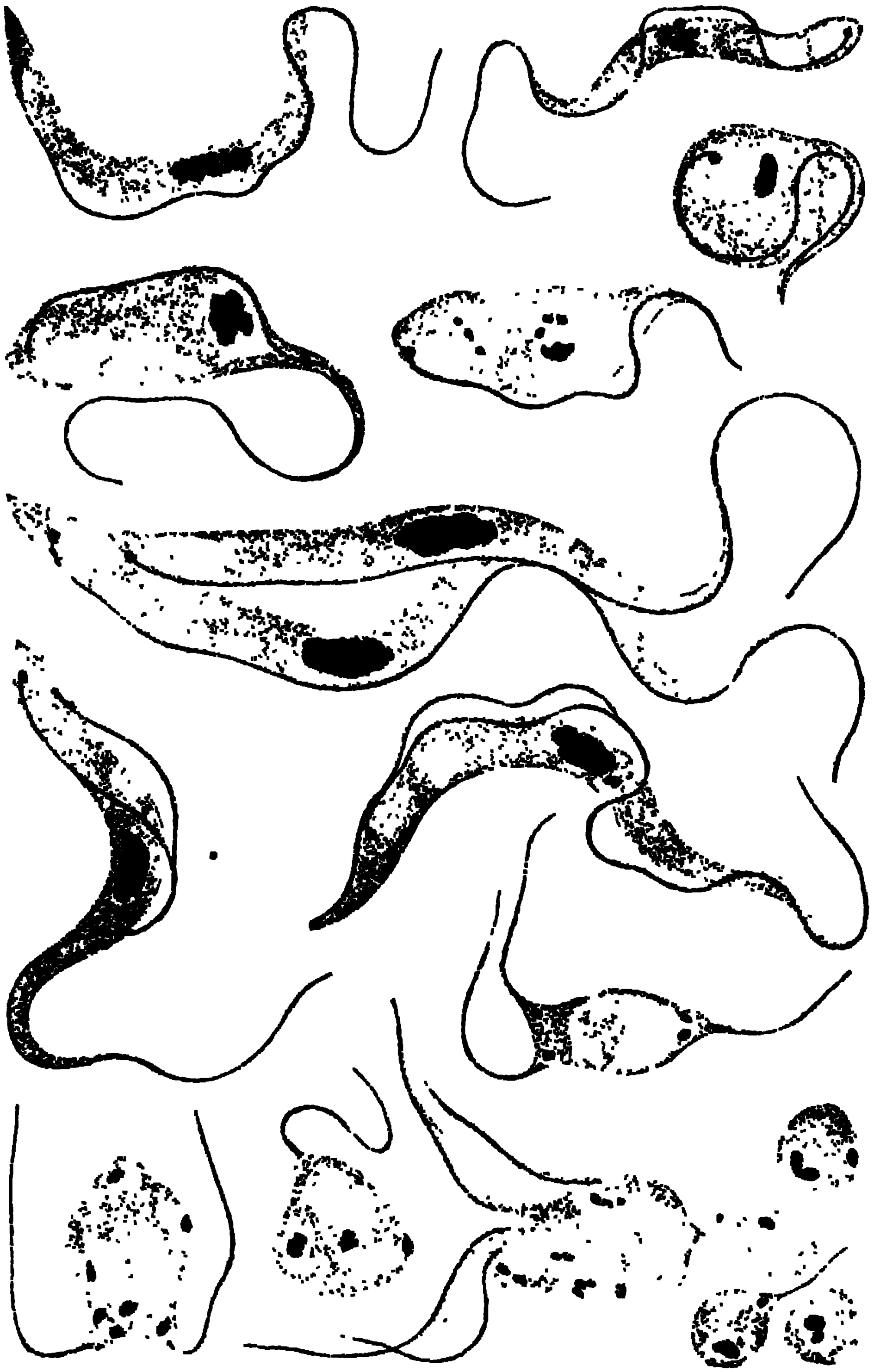


FIG. 110 *Castellanella castellanii* (KRUSE, 1903).

(Forms found in the cerebro-spinal fluid.)

The figures in the top row show the ordinary forms; in the second row the stumpy forms; in the third and fourth rows longitudinal division. The lowest row shows multinucleate and polyflagellate forms (Rabinowitsch-Kempner forms), and small round flagellate and non-flagellate forms (Plimmer-Bradford and Castellani's forms). (From Castellani's report in Reports of the Royal Society on Sleeping Sickness.)

pheral blood the centrosome inside the nucleus divides, and the new centrosome, escaping from the nucleus, becomes the kinetonucleus, and lies in the cytoplasm, which has now increased in amount. The vesicle has gradually disappeared. A new flagellum now appears, and gradually the latent body becomes a trypanosome. The rounded bodies with one or two nuclei, with or without the small flagella, are probably identical with the forms found by Castellani several years ago in the cerebro-spinal fluid of cases of sleeping sickness, and described by him under the term 'amœboid forms.'

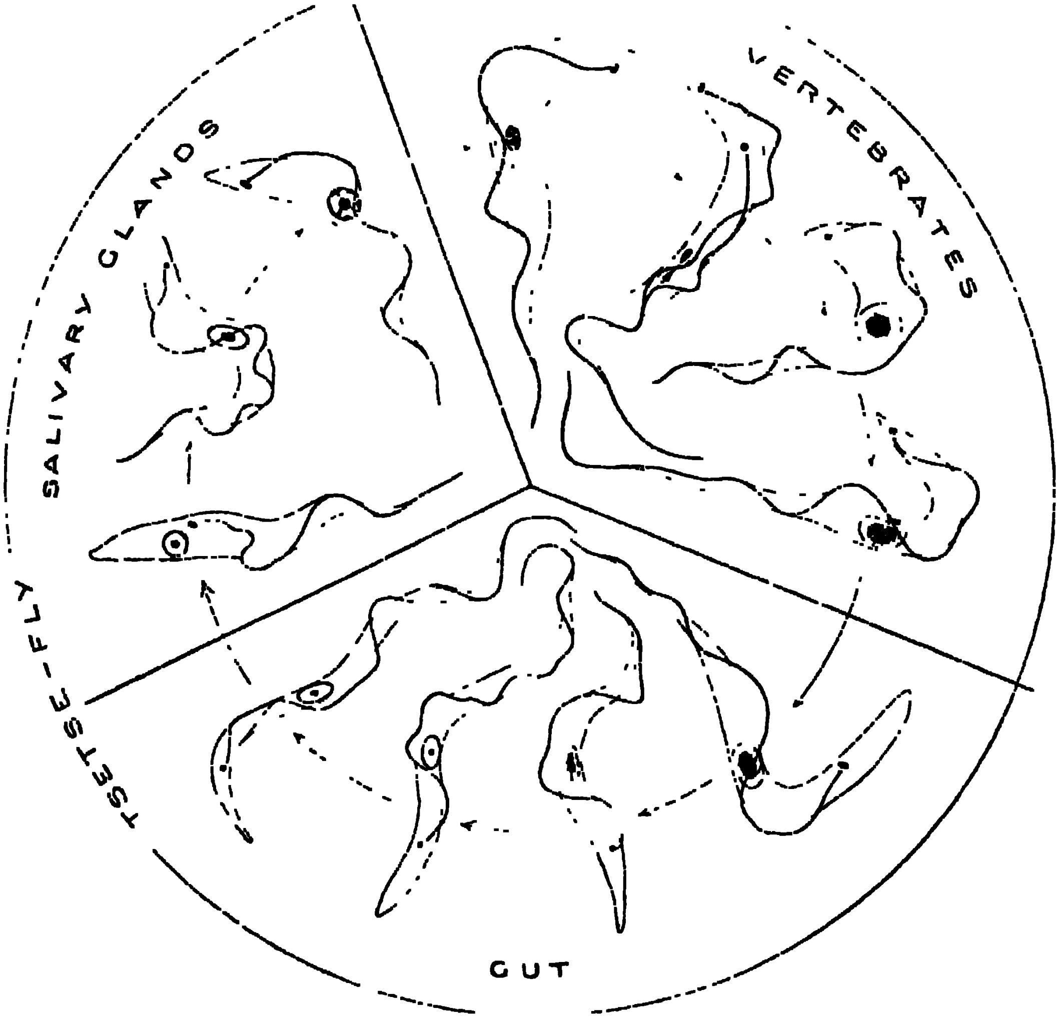


FIG. 111.—*Castellanella castellanii.* Life-Cycle.

Reproduction in the Fly. The researches of Kleine, Taute, Bruce, Hamerton, Bateman, and Mackie have shown that, after ingestion at a correct period (as demonstrated by Miss Robertson), the trypanosomes enter the stomach of the fly, and in twenty-four hours lose their infectivity, as demonstrated by inoculation. According to Miss Robertson, the trypanosomes multiply in the posterior part of the mid-gut, and after the tenth or twelfth day give rise to long forms which move forwards into the proventriculus between the twelfth and twentieth day, after which they pass along the hypopharynx into the salivary glands. Here they become attached to the walls and are converted into crithidial forms, which divide, forming small trypanosomes similar to those found in the blood of the vertebrate. The salivary gland development requires two to five days before the fly becomes infective, which only happens in about 8 per cent. of flies. The duration of the life cycle in the fly depends upon the air temperature.

Vertebrate Reservoir.—Duke considers that he has proved that the Sitatunga antelope is a reservoir for this trypanosome, and considers that the infection of two boys working on the uninhabited islands of Victoria Nyanza and constantly exposed to bites of *G. palpalis* is confirmatory.

Pathogenicity.—It is the cause of one form of sleeping sickness.

Castellanella rhodesiensis (Stephens and Fantham, 1910).

Synonym. *Trypanosoma rhodesiense* Stephens and Fantham, 1910.

History.—In 1910 Stephens and Fantham advanced the view that the trypanosomes found in cases of sleeping sickness in the Luangwa Valley in Rhodesia belonged to a new species, because the trophonucleus of a certain percentage of short forms was situate either close to or even on the aflagellar side of the kinetonucleus. This view is at the present time accepted by the majority of authorities, although there are some who maintain that it is a variety of *C. brucei*, in which similar forms have also been seen. The animal reactions of the new trypanosome were studied by Yorke in 1910, Bevan in 1911, and more recently by other observers. In 1912 Kinghorn and Yorke showed that this trypanosome was transmissible by *Glossina morsitans*, in which it underwent development. They demonstrated that it occurred in waterbuck, hartebeest, impala, and wart-hogs, as well as in native dogs, and they further showed the importance of atmospheric temperature on the length of time required for the cycle of development in the fly.

Morphology.—*C. rhodesiensis* closely resembles *C. castellanii* in general appearance. It has a length varying from 12 to 31 μ, with an average of 21·5 μ, and shows the usual pleomorphic forms—*e.g.*, short stumpy forms varying from 13 to 21 μ in length; intermediate forms, 22 to 24 μ in length; and long, slender forms 25 μ or more in length. The most common are the long, slender forms. The position of the trophonucleus is variable, but it is usually situate towards the aflagellar end of the parasite, and in the short stumpy forms is often close to the kinetonucleus, or even on its aflagellar side.

Life-History.—(*a*) *In the Vertebrate* longitudinal division can take place as in *C. castellanii*. About the time that trypanosomes are most numerous in the blood the researches of Fantham show that some forms in the lungs become converted into latent bodies by disintegration and loss of the flagellar end, followed by a migration of the kinetonucleus towards the trophonucleus, and a subsequent casting off of the aflagellar end with the remains of the flagellum. The result of this posterior and anterior reduction in length is to produce a rounded body, with a trophonucleus and a kinetonucleus, which surrounds itself with a capsule and forms the latent body or *the post-flagellate stage* of the life-cycle. These cysts are about 2 to 4 μ in diameter.

After a time these bodies become the *preflagellate stage*, increase in size and length, and eventually a flagellum grows out from the kinetonucleus and gives rise to the undulating membrane, and thus again forms the usual *flagellate stage*.

(*b*) *In the Invertebrate.* *Glossina morsitans*, when fed upon infected animals, is capable of spreading the infection mechanically for about twenty-four hours, after which period it ceases to be infective, and remains non-infective for at least fourteen days, after which about 5 per cent. of flies become again infective, when trypanosomes can be demonstrated in its alimentary canal and in its salivary glands.

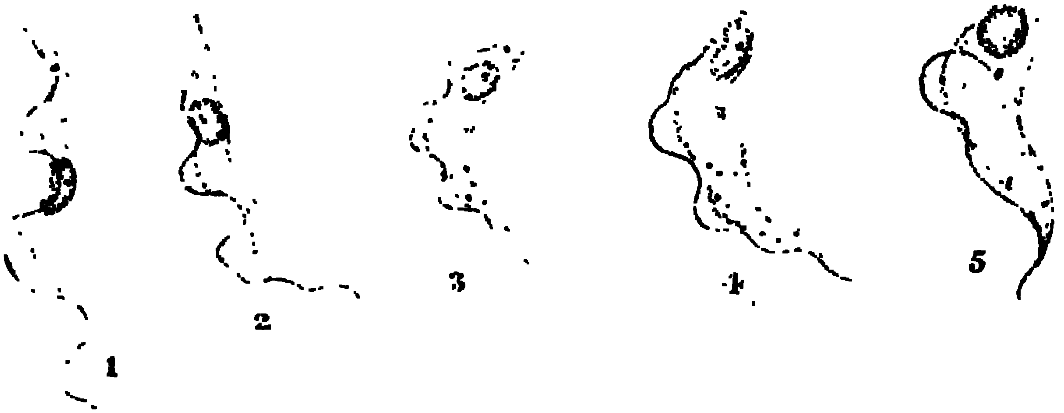


FIG. 112.—*Castellanella rhodesiensis* (STEPHENS AND FANTHAM).
(After Stephens and Fantham.)
1, Long narrow form; 2-4, nucleus passing to aflagellar end; 5, nucleus at the aflagellar end.

Zoological Distribution.—As mentioned above, this parasite occurs not merely in man and domestic animals, but also in big game.

Specificity.—The question now arises, Is it a good species or not? First of all, is it *T. castellanii*?

(*a*) *Sero Diagnosis.*—(1) Attachment experiments are very inconstant, and do not distinguish between the two.

(2) Trypanolysis does not help, being also inconstant.

(3) *C. castellanii* is resistant to human serum. *C. rhodesiensis* is less resistant.

(*b*) *Crossed Immunity.*—An animal having an immunity against *C. castellanii* can be infected by *C. rhodesiensis*. The reverse experiment has not yet been conducted.

We may therefore conclude that *C. castellanii* and *C. rhodesiensis* are different species.

Is *C. rhodesiensis* a variety of *C. brucei*? The answer is No, because Laveran has shown that animals immunized against

C. brucei are susceptible to *C. rhodesiensis*. Is *C. rhodesiensis* a variety of *T. pecaudi ?* No, because the former is more virulent than the latter to animals, and because sleeping sickness is unknown in the region where 'baleri' is intense, and, finally, because an animal immunized against *C. rhodesiensis* is not immune against *T. pecaudi*.

We may therefore conclude that *C. rhodesiensis* Stephens and Fantham, 1910, is a good species.

Cultures.—Thomson has cultured it with partial success on a modification of the Novy-McNeal-Nicolle medium.

Vertebrate Reservoir.—It is claimed that the larger game animals are the reservoir of this trypanosome.

Pathogenicity.—*C. rhodesiensis* is the cause of one form of sleeping sickness.

Schizotrypanum cruzi Chagas, 1909.

Synonym.—*Trypanosoma cruzi* Chagas, 1909.

History.—This trypanosome was discovered by Chagas in the intestine of *Lamus megistus* Burmeister in Brazil, and later it was found in the blood of a child suffering from irregular fever, progressive anaemia, and enlargement of various groups of lymphatic glands. The trypanosome was characterized by the presence of a large kinetonucleus, and by the facility with which it could be cultivated on blood agar. In 1910-11 Chagas published a series of papers upon the life-history of the parasite and the symptomatology of the disease which it produces. In 1911 Vianna studied the pathological anatomy, while further studies on the parasite were made by Brumpt, Martin Mayer, Rocha-Lima, and others.

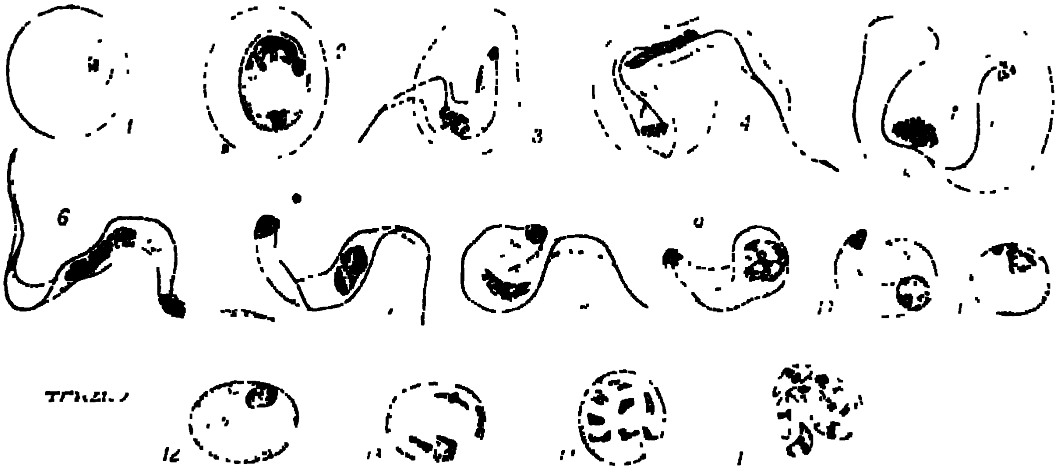


FIG. 113.—SCHIZOGONY OF *Schizotrypanum cruzi* CHAGAS. (After Chagas.)

1, Merozoite in red blood cell; 2, parasite totally enclosed in red cell, no flagellum or undulating membrane; 3-5, parasites partially enclosed in red cell; 6, 7, parasites in human blood; 8-11, parasites in the lungs of Callithrix; 12, 13, initial forms of schizogony; 14, 15, schizogony in the lungs of Callithrix.

Morphology.—In the peripheral blood of man *S. cruzi* appears in two forms—either free or in the red blood-corpuscles.

The free forms are also differentiated into two forms—viz., one with a large egg-shaped kinetonucleus, with a chromatic appendage, and with an oval or band-like trophonucleus with a centrosome. The flagellum starts from the kinetonucleus or from its chromatic appendage.

In the second free form the kinetonucleus is round and smaller than the first, and has, as a rule, no chromatic appendage. This form is broader than the one previously described. Whether this is a sexual differentiation or not is unknown.

The intraglobular forms may be completely or partially enclosed in the red cell, or merely attached by the aflagellar end.

Measurements of these forms were not originally given by Chagas, but it would appear as though the average length was 20 μ, with a certain amount of variation.

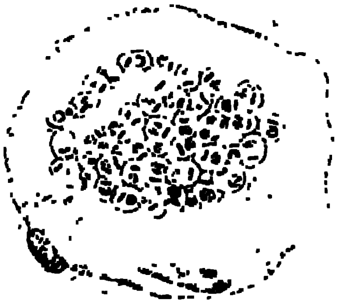


FIG. 114. TRANSVERSE SECTION OF A STRIATED MUSCLE CONTAINING *S. cruzi* CHAGAS IN THE CENTRAL PORTION (× 1,300.)

(After Vianna.)

Life-History.—*Schizogony.*—*S. cruzi* is remarkable in that it is not known to undergo longitudinal division either in the peripheral blood or the internal organs of its host. According to Chagas, there is a regular cyclic development, the parasite entering the capillaries of the lungs, where it loses its flagellum and undulating membrane, while the trophonucleus moves nearer the flagellar end, and the whole parasite becomes curved, first into a half-moon, and finally so much that the two ends fuse, forming a ring and finally a disc. In some instances the kinetonucleus disappears, while in others it fuses with the trophonucleus, after which the nucleus divides into eight, and eventually gives rise to eight merozoites lying inside the periplast, which acts like a cyst wall. The merozoites with kinetonuclei are considered to be microgametes, and those without kinetonuclei to be macrogametes. The merozoites escape from the periplast wall singly, and, entering the red blood cells, become flagellates, and, finally leaving the red cell, become free in the liquor sanguinis, thus completing the cycle of gametogony, or differentiation and multiplication of gametes.

Agamogony, or asexual reproduction, takes place in the cells of various organs—*i.e.*, in hypertrophied endothelial cells in the lungs, in the cardiac muscle, in the neuroglia of the central nervous system, and in striped muscle. In these situations the parasite appears as a rounded body with trophonucleus and kinetonucleus, but without flagellum or undulating membrane. Agamogony increases the number of parasites in the host, and is responsible for the production of the symptoms, while gametogony differentiates the sexual forms, and presumably lays the basis for the infection of the invertebrate host. This form of development is confirmed by Brumpt.

In the Invertebrate.—The further development takes place in the bug *Lamus megistus* (*Triatoma megista*) and allied forms, in which Chagas notes two forms of development: the first is considered to be sexual, and the second to be asexual.

The sexual method is as follows: In about six hours after the ingestion of blood the kinetonucleus moves close to the trophonucleus, with which it possibly blends; the flagellum and undulating membrane are now usually lost, but some forms retain the flagellum. The parasite now becomes rounded, and multiplies rapidly by division, but after this has ceased it becomes pear-shaped, develops a flagellum, and becomes a crithidial form, and then passes into the cylindrical portion of the intestine in which it can be seen in about twenty-five hours after the ingestion of blood. These crithidial forms can also be found in the rectum and in the fæces. The final stage is a small trypaniform type—*i.e.*, long, slim forms, with band-like trophonucleus and large kinetonucleus. These are found in the hind-gut in the body cavity, and in the salivary glands, and are the forms by which the parasite is transmitted to a new vertebrate host. The development in the bug requires at least eight days for its completion.

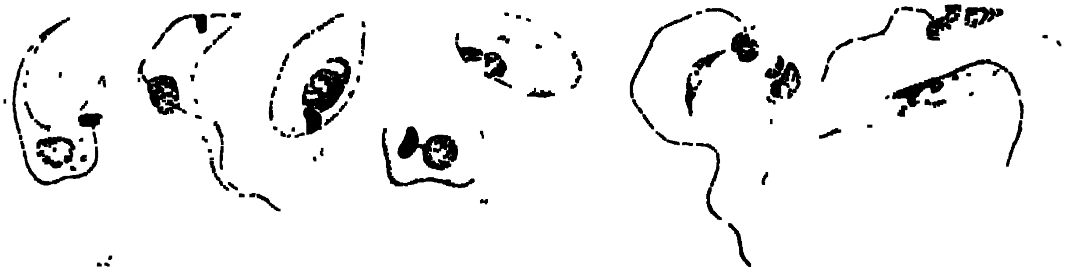


FIG. 115. *Schizotrypanum cruzi* CHAGAS: DEVELOPMENT IN *Lamus megistus* (*Triatoma megista*).

(After Chagas.)

1-6, Forms found in the mid-gut of *Lamus megistus*; 7, flagellate forms found in the posterior segment of *L. megistus*.

FIG. 116. *Schizotrypanum cruzi* CHAGAS.

(After Chagas.)

Forms found in the salivary glands of *Lamus megistus* (*Triatoma megista*)

The asexual method is a constant process, and resembles the growth seen in artificial cultures, and is a simple multiplication, giving rise to crithidial forms which are found principally in the hind-gut.

Brumpt finds that the parasite lives well in *Clinocoris lectularius*, *C. rotundatus*, *Clinocoris boueti*, and *Ornithodorus moubata*. His account of the cycle of development is as follows:—Starting with the trypanosome in the posterior part of the intestine, when this is inoculated into the vertebrate, it enters the cells of the body, and becomes Leishmania-like bodies, which eventually develop into free-swimming trypanosomes, from which the form capable of continuing the infection in the vertebrate or invertebrate is produced. In the invertebrate these become crithidia-like forms, and eventually trypanosomes capable of infecting vertebrates, and thus completing the cycle of life history.

Brumpt and Gonzalez-Lugo have found the parasite in the fæces of *Rhodnius prolixus* two months after infection. *Triatoma vitticeps* and *T. dimidiata* are also carriers, as is *T. sordida* Stal and *Rhipicephalus sanguineus*.

Culture.—*S. cruzi* is easily cultivated upon the Novy-McNeal medium, when the first changes begin in about six hours, and closely resemble those already described in the bug.

Pathogenicity.—Two to three days after an infective feed the larvæ of *Lamus* cease to be infective to vertebrates, and first become so on the eighth to the tenth day, after which they remain infective for a long period. The parasites so introduced into man give rise to American trypanosomiasis.

Reduction in Virulence.—*S. cruzi*, when repeatedly passed through animals of the same species, become weakened in virulence, but regain this when transmitted to a fresh species.

Infectivity.—The infected monkey is infective for the bug, while the infected guinea-pig is not.

Duttonella vivax Ziemann, 1905, var. macfiensis.

Synonym.—*Trypanosoma vivax* (Ziemann, 1905) *pro parte*.

In 1917 Macfie described a monomorphic trypanosome very closely resembling *T. vivax*, but slightly smaller, with the crest in curves of measurements at 21 instead of at 23 microns. It is said to be intermediate between *T. uniforme* and *T. vivax*.

It was found in the blood of a man suffering from trypanosomiasis on the Gold Coast, where *T. vivax* is common in the humpbacked cattle at Accra. The maximum length was 24 microns, the minimum 18 microns, and the average 20·7 microns.

It is monomorphic, with abrupt narrowing of the body immediately anterior to the trophonucleus. The posterior (aflagellar) end is blunt, and the large rounded kinetonucleus is terminal or nearly so. The undulating membrane is narrow, and there is always a long free flagellum.

Castellanella nigeriensis Macfie, 1913.

This trypanosome was found in cases of human trypanosomiasis from the Eket district of Southern Nigeria, by Macfie, where it was common in young people. It appears to give rise to a not very virulent, non epidemic form of trypanosomiasis. It is polymorphic, and in our opinion is the same parasite as the original *C. gambiensis*, of which it appears to be merely a variant. We have placed it as a synonym of *C. gambiensis*.

Castellanella lanfranchii Lanfranchi, 1915.

It approximates to *C. evansi*, and is the organism with which Lanfranchi accidentally inoculated himself. As regards precipitating and complement fixation power is very similar to *C. evansi*, but as regards trypanolytic action of the serum it approximates more *C. castellanii*.

APPENDIX: INCERTÆ SEDIS.

In this addendum to the Trypanosomidæ we include the genus Leucocytozoön and the Spirochætacea. With regard to the former—*Leucocytozoön* Danilewsky, 1889—a number of species have been described of which the life-history is but imperfectly known, except in the case of *L. ziemanni*, which has been studied by Schaudinn, and partly in *L. lovati*, which has been carefully studied by Fantham. They are only definitely known to occur in birds, and must be distinguished from the Hæmogregarines of mammals.

Leucocytozoön Danilewsky, 1889.

Synonyms.—*Hæmamœba* Laveran, 1903; *Spirochæta* Schaudinn, 1904; *Trypanomorpha* Woodcock, 1906.

The leucocytozoa were first described by Danilewsky between 1884 and 1886 in the blood of the wood-owl (*Syrnium aluco*) and other Strigidæ.

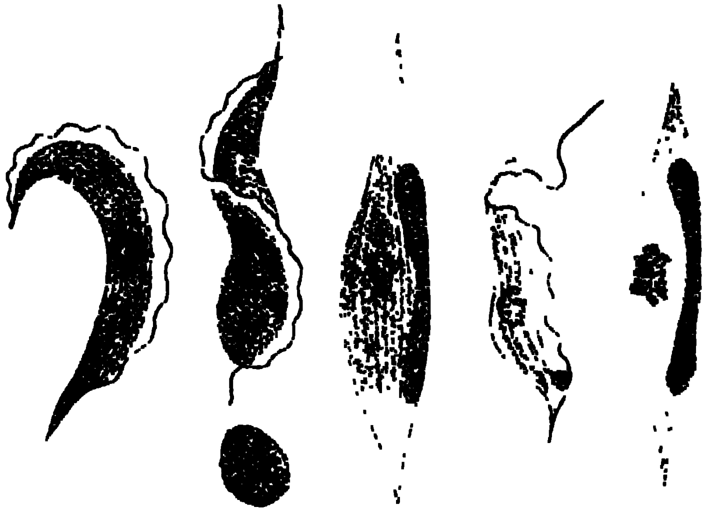


FIG. 117.—*Leucocytozoön danilewskyi* Ziemann.
(After Schaudinn.)

From the left to the right, a macrogametocyte free, same attached to a blood cell, same enclosed in a blood cell; a free microgametocyte, same enclosed in a blood cell.

He described them as spherical or oval, slightly granular bodies contained in a delicate transparent homogeneous capsule, which possessed a large elongated nucleus, compressed in the middle, and broadened at the extremities. This capsule he believed to be a degenerated leucocyte, but later he held it to be an erythrocyte. He also described macrogametes and motile oökinetes, and later he described the microgametocytes. In 1893 Sakharoff confirmed these observations and described new species in ravens, rooks, and magpies. In 1895 Theobald Smith discovered a leucocytozoön in *Meleagris gallapavo domestica* (the turkey); and in 1898 Ziemann described another specimen in *Glaucidium noctuæ* (the little owl) from Crema, in Italy. In 1902 and 1903 Laveran described forms in birds with mixed infections, and stated that he considered that they were contained in red blood cells. In 1904

Berestneff described several forms in owls, ravens, and magpies, but noted that they were in leucocytes, and in the same year came Schaudinn's paper on the development of *Leucocytozoon ziemanni*, which is given in detail later on. The Sergents, in studying the parasite in the little owl in Algeria, supported Schaudinn. In 1905 Laveran and Lucet studied Theobald Smith's parasite, and concluded that it was enclosed in a leucocyte. In 1906 Neave described a parasite in *Numida ptilorhyncha*, and in 1907 Sambon and Seligmann described one in *Lagopus scoticus* (the red grouse); and Dutton, Todd, and Tobey another in *[illegible]* (the Congo grey hawk); and lastly Sambon has reviewed the whole genus in a singularly able manner, and has described species from the capercailzie (*Tetrao urogallus*) and the pheasant (*Phasianus colchicus*). Important work has been done by Fantham, who demonstrated schizogony in *L. lovati* Sambon and Seligmann, 1907. E. H. Ross has suggested that Kurloff bodies may be Leucocytozoa, and may produce a spirochaete-like organism.

Leucocytozoon danilewskyi Ziemann, 1898.

Synonyms. *Haemamoeba ziemanni* Laveran, 1902; *Spirochaeta ziemanni* Schaudinn, 1904; *[illegible]* Blanchard, 1905; *Leucocytozoon*

FIG. 118.—INTRACELLULAR FORM OF *Leucocytozoon lovati*. (After Sambon.)

FIG. 119.—INTRACELLULAR MICROGAMETOCYTE OF *Leucocytozoon lovati*. (After Seligmann and Sambon.)

FIG. 120.—INTRACELLULAR MACROGAMETOCYTE OF *Leucocytozoon lovati*. (After Seligmann and Sambon.)

ziemanni Lühe 1906. *L. danilewskyi* is found as a parasite in the haematoblasts (or according to other authors, in the leucocytes) of the little owl, *Glaucidium noctua* (*Athene noctua* Retz.), and the wood owl, *Syrnium aluco* L.

The history of the life cycle, according to Schaudinn, may be begun with the biting of the owl by *Culex pipiens* L., and the sucking of blood containing micro- and macro-gametocytes.

Microgametocyte.—The microgametocyte may attain dimensions much larger than a leucocyte, and exists in the blood of the owl in two conditions: (1) a free active stage in the liquor sanguinis; (2) endocellular resting stage in a blood cell; and, later, when the parasite has become too large to penetrate a host cell, free in the blood stream. In this condition the parasite may engulf the cells which formerly served it for food and shelter.

(1) *Free Active Stage.*—This is the trypanosome stage (*T. ziemanni*). The anterior end is sharp-pointed, with a kinetonucleus just at its base, from which the flagellum arises, passing posteriorly along the body and projecting some distance from the posterior end. There is a well-defined undulating membrane, with sixteen myonemes arranged in four double rows or pairs on each side. The trophonucleus is well developed, and situate near the centre of the trypanosome.

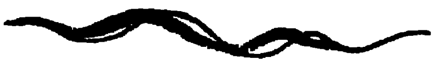


FIG. 121.—*Leucocytozoön danilewskyi* ZIEMANN: MICROGAMETE. (After Schaudinn.)

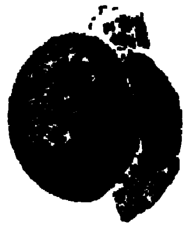


FIG. 122.—*Leucocytozoön danilewskyi* ZIEMANN: MACROGAMETE. (After Schaudinn.)

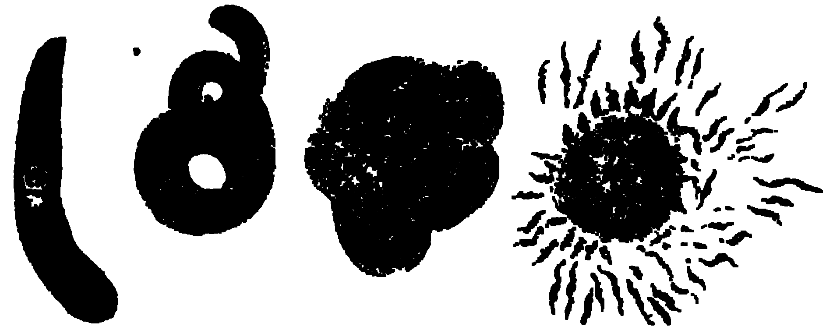


FIG. 123.—*Leucocytozoön danilewskyi* ZIEMANN: THE DEVELOPMENT OF THE OÖKINETE AND THE FORMATION OF SMALL TRYPANIFORM BODIES. (After Schaudinn.)

(2) *Endocellular Resting Stage.*—In the intracellular stage the parasite is quite spindle-shaped, the ends being composed of ectoplasm, while the endoplasm forms a dark oval central mass containing the trophonucleus, close to which the kinetonucleus is situated. The flagellum has disappeared, but the myonemes of the ectoplasm can still be seen.

Macrogametocyte.—This has also two stages—(1) free, (2) endocellular.

(1) *Free Active Stage.*—The free stage differs from the microgametocyte in being larger, in having no free projection of the flagellum, and in having smaller tropho- and kineto-nuclei, and in the myonemes not being arranged in pairs.

(2) *Resting Stage.*—This differs from the microgametocyte in being large, with smaller nuclei.

These gametocytes, called 'leucocytozoön' by Danilewsky and 'hæmamœba' by Laveran, being found in the peripheral blood of the owl, are sucked into the stomach of *Culex pipiens*, and then proceed to conjugation.

Microgamete.—The microgametocyte escapes from the capsule-like periplast, and its nucleus breaks up into eight double chromosomes, which are reduced to eight single chromosomes. These travel to the periphery, and form microgametes in the manner described for *Hæmoproteus noctuæ*, microgametes which they are said to resemble.

Macrogamete.—The macrogametocyte escapes from its enclosing cell, and the process of development of the macrogamete is the same as in *Hæmoproteus*.

Fertilization.—This is the same as in *Hæmoproteus*.

Oökinete.—There are the same three kinds of oökinetes as in *Hæmoproteus*—viz., the indifferent, the male, the female.

The ookinete, however, differs by growing in size and multiplication of its nuclei, and at the same time coiling upon itself so as to form a skein. This skein contains a large number of nuclei uniformly distributed.

Around each of these, small portions of protoplasm gather, and become finally separated off, to form small indifferent trypanosomes in the case of the indifferent ookinete, male trypanosomes from the male ookinete, female trypanosomes from the female ookinete. A large mass of residual protoplasm is left.

These trypanosomes, especially the male, are very minute, and reproduce by longitudinal division, during which they do not separate at once, but remain attached posteriorly. Couples attached to one another may extend into the same straight line, thus giving rise to a spirochæte-like form, and while in this position may undergo longitudinal division. The spirochæte forms may become pear-shaped resting forms.

In the Owl.—On entering into the owl, the indifferent forms pass through alternate endocellular and free stages. In the former there is growth, and in the latter there is division into smaller forms. After some time micro- and macrogametocytes are formed in increasing numbers.

This life-history has been doubted, but Sambon has seen forms in which a coiled trypanosome body can be detected in the blood cells.

The Enclosing Cell.—There has been great doubt as to the character of the body enclosing a leucocytozoon.

1. Ziemann, Schaudinn, Dutton, Todd, and Tobey believe that it is a portion of the parasite itself—*i.e.*, the periplast—and that it may enclose a red blood cell.

2. Danilewsky considers it to be a leucocyte, but derived his red cells from leucocytes. In considering it to be a leucocyte, he is supported by Laveran, Lucet, Sakharoff, and Berestneff, and most recent observers.

3. Laveran in his earlier observations believes it to be a red cell, and this Sambon supports, as do Keysselitz and Mayer.

It may be taken to be a much-enlarged dehæmoglobinized hæmatoblast or red cell, the spindle shape of which may be explained by the fusiform shape of the hæmatoblasts, and by the pseudopodia of the young parasites protruding into the long ends of the host cell. When the parasite contracts, these ends shrivel up, giving rise to the usual appearance.

The Spirochætes.—At first Schaudinn, after tracing out the life-history described above, thought that all spirochætes would be found to be allied to true trypanosomes; but in 1905 he stated that the spirochæte-like forms which he found in the little owl were far removed from true spirochætes, and that the relationship was only phylogenetic, and very distant at that.

E. H. Ross has brought evidence to show that Kurloff's bodies (*i.e.*, clear spherical vacuoles in the large lymphocytes of guinea-pigs) are intracorpuscular stages in the life-history of a Leucocytozoon (*Lymphocytozoön cobayæ* E. H. Ross, 1912) which ultimately give rise to spirochæte-like bodies, the development of which he traces, and which he considers to be the gametes. Later he and McDonagh described a similar origin for *Treponema pallidum*.

Recent work has tended to confirm the doubts thrown on Schaudinn's work, but the general appearance of a Leucocytozoön in its cell is sometimes remarkably similar to a trypanosome. It is possible that there may be

different parasites confused under the term Leucocytozoön, and their life-histories may be different, as Fantham's work, presently to be described, is opposed to Schaudinn's work.

Leucocytozoön lovati Sambon and Seligmann, 1907.

This leucocytozoon was discovered by Sambon and Seligmann in the red grouse (*Lagopus scoticus*), and has been recently restudied by Fantham. The microgametocyte and macrogametocyte are depicted in Figs. 119 and 120 on p. 432, and were till recently the only forms known, but Fantham has now found the schizonts, and described the process of schizogony.

Sporogony.- The microgametocytes measure 13 to 17 μ in length by 6 to 12 μ in breadth, and possess hyaline pale staining cytoplasm with a large, rather granular nucleus. The macrogametocyte measures 14 to 20 μ in length by 10 to 16 μ in breadth, and has a granular somewhat alveolar cytoplasm with a central nucleus with a karyosome. Their further development is unknown, but Fantham has found vermicules in *Ornithomyia lagopodis*, the grouse-fly, which may be the agent of transmission.

Schizogony.- The schizont is found in the spleen in cells which they almost fill and absorb, and which they do not elongate in the way in which the gametocytes deform their host cells. The schizont measures 11 to 14 μ by 8 to 11 μ, and is therefore of an oval shape, with a nucleus resembling that of the microgametocyte, and a cytoplasm like that of the macrogametocyte

The nucleus divides by rapid binary fission into some 12 to 20 small nuclei and then the cytoplasm divides, giving rise to 12 to 20 merozoites, which are small vermicules measuring 7 to 8 μ by 1 to 1·5 μ There is some residual cytoplasm after division. The merozoites now escape from the parasite and cell, and for a very brief period become free, swimming in the liquor sanguinis, and then quickly re-enter leucocytes or immature erythrocytes, and ultimately differentiate into gametocytes or schizonts.

Remarks. This process of schizogony may explain the periodical increase in the gametocytes in the blood noted by Mathis and Léger in *L. caulleryi* in Tonkin. Fantham very carefully points out that the above life-history may not take place in all Leucocytozoidæ, but, notwithstanding this, Fantham's results do not support Schaudinn's researches.

Species. Some of the species described are: *Leucocytozoön majoris* Laveran, 1902, in the great tit (*Parus major*); *L. sakharoffi* Sambon, 1908, in the raven (*Corvus corax*); *L. berestneffi* Sambon, 1908, in the magpie (*Pica pica*); *L. danilewskyi* Ziemann, 1898, in the little owl (*Athene noctua*); *L. toddi* Sambon, 1907, in the Congo grey hawk (*Asturinula monogrammica*); *L. mansoni* Sambon, 1908, in the capercailzie (*Tetrao urogallus*); *L. lovati* Sambon and Seligmann, in the red grouse (*Lagopus scoticus*); *L. macleani* Sambon, 1908, in the common pheasant (*Phasianus colchicus*); *L. smithi* Laveran and Lucet, 1905, in the domestic turkey (*Meleagris gallopavo domestica*); *L. neavei* Balfour, 1906, in the Abyssinian guinea-fowl (*Numidia ptilorhyncha*); *L. caulleryi* Mathis and Léger, 1911, *L. sabrazesi* in *Gallus ferrugineus*, *L. martini* Mathis and Léger in *Pavo cristatus*; *L. marchouxi* Mathis and Léger in *Turtur humilis*, and *L. leboeufi* Mathis and Léger in *Querquedula crecca*.

Spirochætacea Fantham, 1908.

Synonyms.- *Proflagellata* Doflein; *Spiroschaudinnidæ* Sambon, 1907; *Spiroflagellata* Krzysztalowicz and Siedlecki, 1907.

Definition.- Plasmodromata, generally parasitic, in form narrow, wavy, and thread-like, with or without an undulating membrane. The cytoplasm is divided into endoplasm and ectoplasm, and is bounded by a flexible, chitinous periplast. The nucleus consists of a spiral achromatic filament, on which are arranged transverse bars or rodlets of deeply staining chromatin.

Remarks.—The Spirochætacea are closely related to the Binucleata, and especially to the Trypanosomidæ.

The Treponemata are joined to the spirochætes because of their general resemblance, though it must be admitted that no nucleus of the nature of the spirochæte nucleus has yet been described, and the spirals are apparently not due to movement.

The Spirochætacea are potent factors in the production of disease, for *S. recurrentis* is the cause of one type of relapsing fever, *S. carteri* of another, *S. duttoni* of another, and *S. novyi* of yet another, while the Treponemata are the cause of syphilis and yaws.

The Spirochætacea may be divided into two families:—

1. With undulating membrane: Spirochætidæ.
2. Without undulating membrane: Treponemidæ.

Spirochætidæ Ehrenberg, 1883.

Definition.—Spirochætacea with an undulating membrane. Body may be ribbon-shaped on transverse section.

Type Species.—*Spirochæta plicatilis* Ehrenberg, 1833.

Remarks.—There is a difference of opinion as to whether these organisms are protozoa or bacteria. At first they were universally regarded as bacteria, but in 1904 Schaudinn's paper on the leucocytozoon in the little owl indicated that this body, after fertilization in the gut of *Culex pipiens* and subsequent asexual division, produced a large number of minute forms which he at the time considered to be spirochætes, and he further concluded that in all probability all spirochætes were stages in the life-history of intracellular parasites. In 1905, however, he came to the conclusion that the spirochæte forms which he had seen develop from *T. ziemanni* were trypanosomes. In fact, there is one great point of difference—the forms which he described possess a distinctly consolidated nucleus, whereas spirochætes do not. After this the view that spirochætes were bacteria was revived, particularly by Novy and Knapp, on the following grounds:—

1. Absence of trophonucleus.
2. Transverse division.
3. Rapid multiplication.
4. Absence of plasmolysis with distilled water.
5. Persistence of form when acted upon by heat.
6. The production of active immunity.
7. The absence of aerotropism—*i.e.*, the tendency to mass round a bubble of air.

Dobell, as a result of his prolonged inquiries, came to the conclusion that they are Schiophyta (bacteria + Cyanophyceæ), and not protozoa. He also concludes that they belong to the bacteria, and probably constitute a group of the same systematic status as the cocci, the bacilli, and the spirilla.

On the other hand, there is a growing feeling among biologists that spirochætes are really protozoa—*e.g.*, Doflein, Minchin, Sambon, Nuttall, Fantham, and Krzysztalowicz and Sisdlecki. Fantham points out that the strongest arguments in favour of their being bacteria are:—

1. Diffuse character of nucleus somewhat like *Bacillus bütschilii.*
2. The possible occurrence of transverse fission.
3. The absence of a typical kinetonucleus.

While the points in favour of their belonging to the protozoa are:—

1. The possession of an undulating membrane.
2. The occurrence of longitudinal division (denied by Schellach).
3. The non-plasmolysis.
4. Difficulty to find artificial media on which they can grow.

We consider that they are protozoa, and, further, that they are related to the trypanosomes. Spirochætes are, however, distinctly peculiar, particularly with regard to their diffuse nucleus; but there appears to be almost a series from the diffuse nucleus of the bacteria through the achromatic spiral, with its attached chromosomes of the spirochætes, to the condensed nucleus of the higher protozoa. Schellach derives them phylogenetically from the oscillatory cyanophees, genus *Spirulina.*

Morphology.—Spirochætes vary much in size, from *Spiroschaudinnia recurrentis*, which is 8 μ in length, to *Cristispira balbianii*, which may be 150 μ in length and 2 to 3 μ in thickness. The type species *Spirochæta plicatilis* was found in muddy water by Ehrenberg in 1833, and was said by Schaudinn in 1905 to possess an undulating membrane. Sambon, however, considers that this so-called type species is quite different from *S. recurrentis*, and should be placed in a different group therefrom. The most carefully studied types are *Cristispira balbianii* Certés, 1882, found in oysters, and *Cristispira anodontæ* Keysselitz, 1906, emended Schellach, 1909, both of which have been the subject of research by Fantham, whose results are here followed. These organisms are long, wavy, and thread-like, composed of cytoplasm, which can be differentiated into an ectoplasm, which is generally converted into a thin, flexible, chitinous membrane, the periplast. This is continued laterally into a spirally arranged membrane, the crista, containing longitudinally arranged fibrillæ, and having a thickened border composed of chromatin. The longitudinal fibrillæ are composed of eight to nine principal and numerous secondary fibrillæ, which are contractile, and are called 'the myoneme fibrillæ' (Fig. 124). The membrane, or crista, which does not markedly undulate, helps in locomotion, which is rapid, and takes place by a wave-like flexion of the body, which causes forward movement, and a corkscrew motion, produced by the spiral winding of the membrane, enabling the parasite to bore its way through the débris amidst which it may be living. A spirochæte can move backwards or forwards indifferently.

The endoplasm is slightly more granular than the ectoplasm, and contains a diffuse nucleus, which appears to consist of an achromatic filament with bars of chromatin.

In addition to this nucleus there is a dot of chromatin (basal granules) at each end of the periplast in *C. balbianii*, and only at one end in *C. anodontæ*; in the latter a short, stiff process of periplast projects from it, which is considered by some observers to be a flagellum.

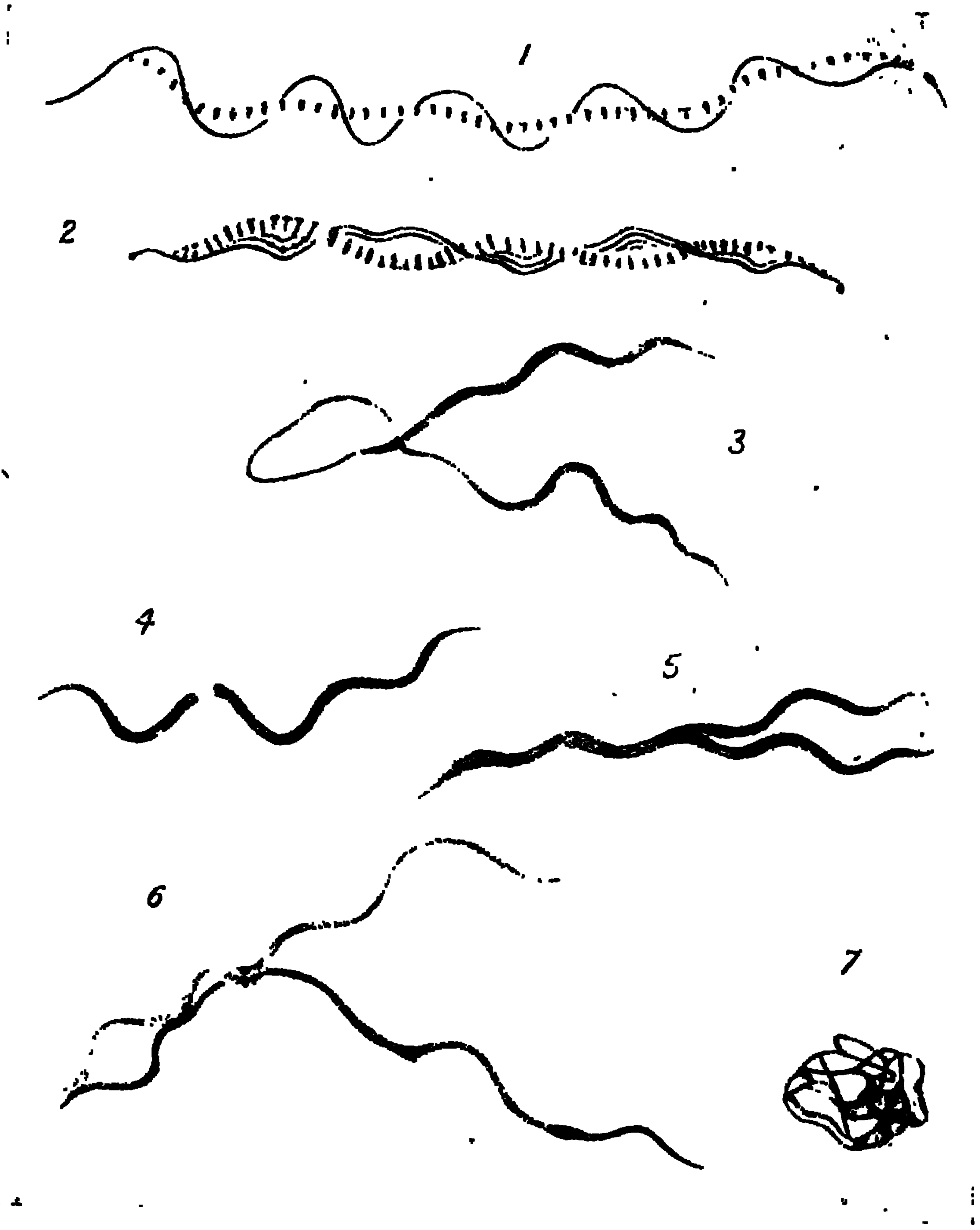


FIG. 124 – SPIROCHÆTES.

1. *Cristispira anodontæ*, showing the undulating membrane and chromatic bars (after Fantham, *Quarterly Journal of Microscopical Science*); 2, *C. balbianii*, showing fibrillæ in undulating membrane (after Fantham); 3-7, *Spiroschaudinnia duttoni* (after Breinl, *Annals of Tropical Medicine and Parasitology*); 4, shows the uncoloured transverse band; 5, longitudinal division; 6, possible male and female forms; 7, encystment.

Reproduction takes place by both longitudinal and transverse divisions; it has been described by Fantham and Porter in *C. anodontæ* Keysselitz, 1906, and *C. balbianii*. The basal granule first divides, and then the membrane, followed by the cytoplasm, as far as one end, which does not divide at once, but later, thus completing the act of asexual reproduction.

Dobell gives a very different description of *C. anodontæ*, which he states has a chambered structure, and divides only by transverse division.

Bosanquet has observed the formation of coccoid bodies in Cristispira analogous to those presently to be described in Spiroschaudinnia.

Classification.—The following genera are recognized:—

Spirochæta Ehrenberg 1838, *sensu stricto*.
Cristispira Gross, 1910.
Saprospira Gross, 1911.
Pseudospira Dobell, 1912.
Spiroschaudinnia Sambon, 1907.

But it is only the last genus which contains the forms of importance in tropical medicine.

Noguchi has created the genus *Leptospira* Noguchi, 1917, for the spiroschaudinnia found in Weil's disease and the spiroschaudinnia he has observed in yellow fever. Characteristic features would be the fine elicoid structure with persistent spirals, and the resistance to the action of saponin.

Cristispira balbianii Certés, 1882.

This spirochæte is found in the crystalline style of oysters. The oysters are apparently affected, at all events, they are poorly developed. It has a well-defined, undulating membrane, strengthened by myonemes, and also a diffuse nucleus of rodlets of chromatin on an achromatic spiral, as has already been described.

Cristispira anodontæ Keysselitz, 1906.

Synonym. *Spirochæta anodontæ* Keysselitz, 1906, *emendavit* Schellach, 1909.

S. anodontæ was found in the crystalline style of *Anodonta mutabilis* by Keysselitz in 1906, and in that of *A. cygnea* by Fantham in 1908.

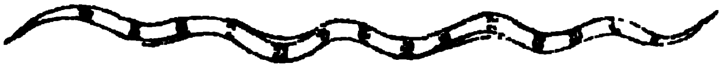


FIG. 125. DIAGRAM OF S. *duttoni*, SHOWING CHROMATIN GRANULES, POINTED ENDS, AND SLIGHT MEMBRANE EDGE. (After Fantham.)

It is 90 μ in length by 0·7 μ in breadth, with pointed ends and a spirally wound undulating membrane. The nucleus is diffuse, consisting of chromatin rodlets on a more faintly staining spiral.

S. plicatilis Ehrenberg, 1833, found in pond-water.

Spiroschaudinnia Sambon, 1907.

Spirochætidæ parasitic in the blood and tissues of vertebrates and in some blood-sucking invertebrates.

Remarks.—This genus, as we believed would happen, is now recognized by many authorities, and therefore we adopt it, though we had hesitated to do so in the previous edition.

Type Species.—*Spiroschaudinnia recurrentis* Lebert, 1874.

Morphology.—This has been most carefully studied by Fantham in *S. recurrentis*, *S. duttoni*, and *S. marchouxi*, and he finds that they have long, narrow bodies, bent into many spiral coils, enclosed in a firm periplast, with a very tenuous membrane, which is often invisible. The nucleus consists of granules of chromatin distributed along the body.

Life-History.—Multiplication can take place by longitudinal and by transverse division, and also by multiple transverse fission, in which case the protoplasm concentrates around the chromatin masses, giving rise to a number of round or oval granules, probably the same as the infective granules of Fry and Balfour, which are known to escape from one end or the other of the periplastic sheath when in the internal organs. These infective granules enter the red cells, and divide into a number of merozoites, which escape from the red cell and enter the liquor sanguinis; but their further development is unknown, though it is possible that they become spirochætes.

Fantham's observations have confirmed this granule stage of the life-history, but it must not be forgotten that every granule seen in a spirochæte is *not* an infective granule, which our own observations support.

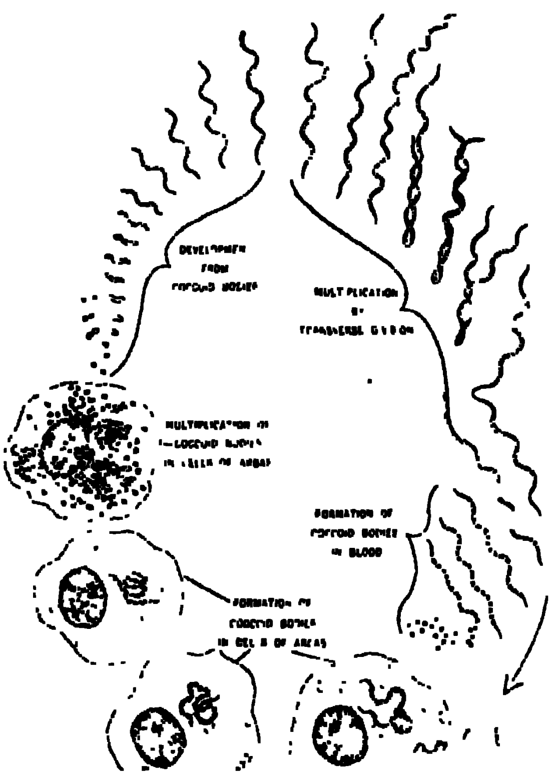

DEVELOPMENT FROM COCCOID BODIES
MULTIPLICATION BY TRANSVERSE DIVISION
MULTIPLICATION OF COCCOID BODIES IN CELLS OF ARGAS
FORMATION OF COCCOID BODIES IN BLOOD
FORMATION OF COCCOID BODIES IN CELLS OF ARGAS

FIG. 126.—LIFE-CYCLE OF *Spiroschaudinnia marchouxi* NUTTALL

(After Hindle, from the *Journal of Parasitology*.)

Minchin regarded these granules as true endogenous chromidial buds, and considered therefore that the term infective granule should be replaced by the term 'endogenous' bud formation.

The life-history of a spiroschaudinnia in the invertebrate has been traced by Leishman for *S. duttoni* in the tick *Ornithodoros moubata*, and his account has been confirmed by Balfour, Hindle, Blanc, Fantham, and others.

The *Spiroschaudinniæ*, on entering the tick, penetrate the gut wall, and on reaching the body cavity divide by multiple transverse fission into minute ovoid or rod-like bodies, which reach the ovary and become incorporated with some of the ova. In this situation they are not often infective. When laid, the egg only contains a few ovoid bodies, but in three to five days' incubation, when the Malpighian tubes have begun to develop, ovoid and more elongate bodies may be seen therein. In six to seven days' incubation these bodies have elongated and become bacillary, and may rupture the cell and appear in the lumen of the tube. It is believed that these bacillary forms give rise to spirochætes either by elongation and growth, or by fusion of rods. The recently hatched tick contains ovoid bodies, bacillary forms, and a very few fully developed spirochætes. Infection takes place towards the end of feeding by the excretion from the Malpighian tubules, which contains the spirochætes, passing into the wound caused by the bite.

Some of the *Spiroschaudinniæ*, on entering the tick, pass into the cells by the alimentary canal, and undergo multiple transverse division, while others may live for some weeks in the gut.

Cultivation.—Noguchi has successfully cultivated *S. duttoni* in sterile ascitic or hydrocele fluid, to which a piece of fresh rabbit's kidney has been added. For inoculation of this medium he uses a few drops of the citrated heart blood from a mouse forty-eight to seventy-two hours after infection.

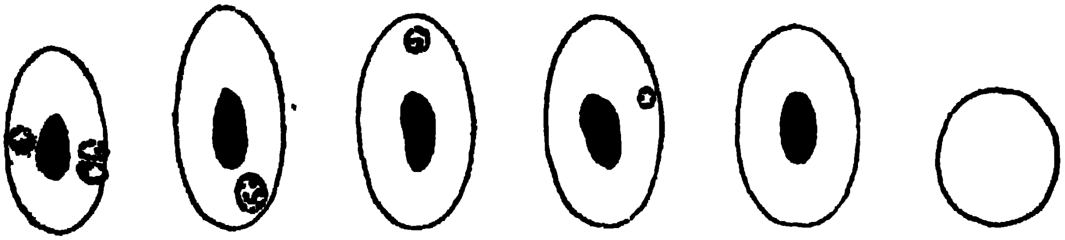


FIG. 127.—SCHIZOGONY OF *Spiroschaudinnia marchouxi* NUTTALL. (After Sambon.)

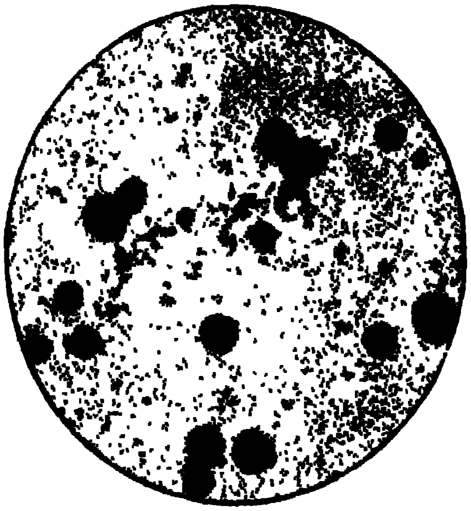


FIG. 128.—DEVELOPMENT OF *S. Duttoni*. (× 1,000.)

The small dots are chromatin bodies and the large granules are digested blood, while the pale outlines are spirochætes in the contents of the intestinal sac of a tick two days after an infective feed. (From a micro-photograph by Sir William Leishman.)

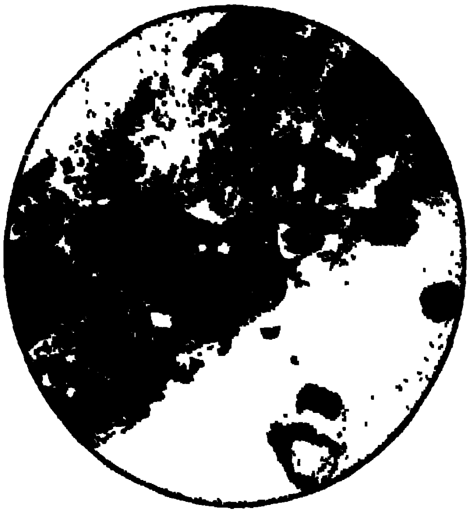


FIG. 129.—CHROMATIN GRANULES IN THE MALPIGHIAN TUBULE OF A TICK SIX DAYS AFTER INFECTIVE FEED. (× 1,000.)

(From a microphotograph by Sir William Leishman.)

At a temperature of 37° C. the maximum growth is found about the eighth to ninth day, after which disintegration sets in, resulting in total disappearance about the fifteenth day. Subcultures are best made from the fourth to the ninth day, but after that date the virulence diminishes. The subcultures do not lose their virulence even after the ninth passage.

He has also cultivated in this way *S. recurrentis* Lebert, 1874, when the maximum growth occurs on the seventh day; *S. rossi* Nuttall, 1905, with a maximum on the ninth day; and *S. novyi*, which is the most difficult, with a maximum on the seventh day. *S. marchouxi* has also been cultivated. Bronfenbrenner in 1914 simplified this method of cultivation.

Carriers. The *Spiroschaudinnia* are spread by the agency of ticks and lice.

Method of Infection. The *Spiroschaudinniæ* infect the ova of the tick, and so pass into the second generation, from which they escape in the fæces and enter the wounds made by the tick when it bites, and so infect the vertebrate host. Whether the same method of development takes place in the louse is not known, but the method of infection is thought to be due to the irritation of the louse bite causing the vertebrate host to scratch, and thus to crush the louse and at the same time to cause abrasions of the host's own skin. The *Spiroschaudinniæ* escaping from the crushed louse, enter the vertebrate host through the abrasions caused by the scratches. Both these are contaminative methods of infection. It is believed that *Spiroschaudinnia* in the vertebrate can pass from the mother via the placenta to the fœtus, thus giving rise to an hereditary method of infection, in contradistinction to the contaminative methods mentioned above.

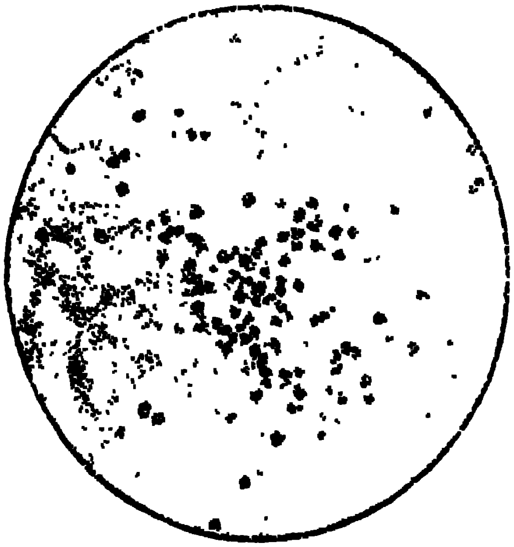


FIG. 130. GRANULES IN [illegible] INFECTED [illegible]
(From [illegible] by Sir [illegible])

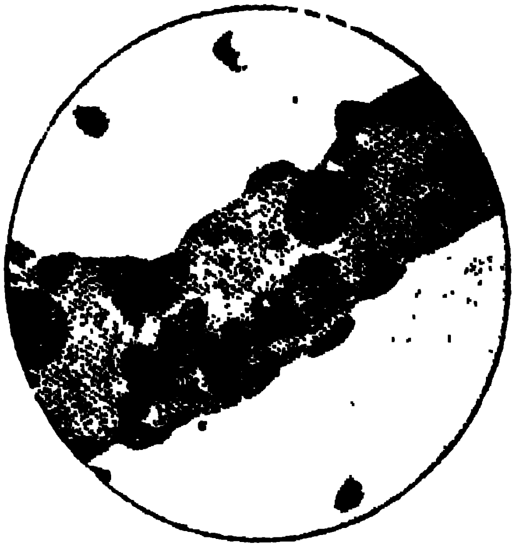


FIG. 131. MASSES OF GRANULES IN MALPIGHIAN TUBULE OF A YOUNG UNFED NYMPH. (× 1,000.)
(From a microphotograph by Sir William Leishman.)

I. HUMAN SPIROCHÆTES.

A. Blood Spirochætes.

Spiroschaudinnia recurrentis Lebert, 1874.

Synonyms.—*Spirochæte recurrentis* Lebert, 1874; *S. obermeyeri* Cohn, 1875.

This spirochæte was discovered by Obermeyer in cases of relapsing fever in Berlin.

Morphology.—It exists in the blood in short and long forms. The short forms, which are from 7 to 9 μ in length, are probably early stages. The long forms, 16 to 19 μ, result from multiplication or agglutination. The latter condition in a hyperimmune blood may lead to forms 18 to 100 μ in length, brought about by agglutination of two or more cells end to end. The width is 0·25 μ. The number of spirals in the short form, which is considered to be one cell, is two to three.

The short form is said by Novy and Knapp to have a long flagellum at one end while the other has a faint appendage. The presence of flagella in this as well as in other spirochætes is denied by Nuttall.

FIG. SCHAUDINNIA FROM CASE OF ASIATIC RELAPSING FEVER.
(From a microphotograph by J. J. Bell.)

Life-History.—This spirochæte is pathogenic to man, monkeys, rats and mice; but these latter have to be infected from a monkey. Rabbits or guinea-pigs are not susceptible. It is found in the peripheral blood during the attacks and relapses, but not in the intermission, unless occasionally after very protracted search. It can also live in the bed-bug—*Clinocoris lectularius*—for some days, and Nuttall has succeeded on one occasion in transmitting *S. recurrentis* from mouse to mouse by the bites of the same bug. Positive results have also been obtained by Sikul in Odessa. Most authorities consider lice to be the carriers.

Immunity.—The blood serum of animals immunized to *S. recurrentis* is without effect upon *S. duttoni* and *S. novyi*.

Pathogenicity.—It is the cause of European relapsing fever.

Spiroschaudinnia duttoni Novy and Knapp, 1906.

Synonyms.—*Spirillum duttoni* Novy and Knapp, 1906; *Spirochæta duttoni* Todd, 1906.

This spirochæte is the cause of the West African and the Colombian tick fever.

Morphology.—Its length is variously described; thus Novy and Knapp say that the young forms are 16 μ in length, while Breinl and Kinghorn make them 24 μ in length and 0·45 μ in width when fully grown. The number of spirals varies from two to three to eight to ten, with a width of 2·2 μ. The parasite is ribbon-shaped on transverse section, and though it is often in spirals, may be simply waved. The two ends are pointed (*vide* Fig. 125).

The central core is seen to consist of lighter and darker portions, which correspond to the chromatic and the achromatic portions of the nucleus. The chromatic portion can break up into granules, when the parasites begin to disappear from the circulation.

The periplast is well marked, but there is great doubt as to the presence of an undulating membrane. Breinl, who has studied the subject carefully, could not definitely define one, but Dutton and Todd have seen it in blood taken directly from the circulation in man, or animals, or from the gut of *Ornithodoros moubata*. A small uncoloured transverse band is often to be seen in specimens stained by Giemsa lying across the parasite, about one-third its length from one end.

Life-History.—Reproduction can take place by longitudinal and transverse division. In the former the parasite thickens and then divides from one end, while in the latter the parasite increases in length and divides in the middle. Some authors deny the occurrence of transverse division, but this is untenable after Fantham and Porter's experiments.

There is, however, another and but little known method of reproduction, which appears to be analogous to spore-formation.

Just before the crisis, when the blood is swarming with parasites, they can be seen, according to Breinl, in the spleen and bone-marrow, and more rarely in the liver, coiling themselves up, and either showing a swollen appearance, or becoming thinner and rolling themselves into more and more complicated skein-like forms, which may be engulfed by phagocytes in the spleen, but in other organs become more regular and surrounded by a thin cyst-wall, the interior of which is filled with faintly blue-staining plasma.

In this cyst the parasite becomes more and more indistinct, and at a later stage small red granules are to be seen, which are thought to be the cause of the infection in the blood when filtered through a Pasteur-Chamberland filter. Therefore, according to the investigations by Breinl, the life-history of the parasite has two well-defined stages in the vertebrate. In the first it is found free in the liquor sanguinis in its typical form; in the second it enters a cell, and, becoming coiled, its chromatin breaks up into a number of granules, each of which is believed to become a new spirochæte.

The stage in the liquor sanguinis is associated with the febrile attacks, and that in the cells with the apyrexial intervals.

Carriers.—It is spread by the agency of *Ornithodoros moubata* in Africa, and by *Argas americanus* (chinche) in Colombia.

In the Tick.—*S. duttoni* in Africa is conveyed to man and animals by fæcal infection of the bites of a tick, *Ornithodoros moubata.* Leishman has demonstrated that when *S. duttoni* enters the intestinal sac of the tick it loses its mobility and characteristic appearance, and chromatic masses escape into the lumen of the gut in the form of small rods or rounded bodies resembling micrococci. These multiply and pass into the cells of the Malpighian tubules, and also into the immature eggs in the ovary. They can be followed through all the stages of the egg into the adult tick, as small chromatin bodies lying in the cells of the Malpighian tubules. These bodies are voided with the fæces, and when the tick feeds are capable of entering the wound produced by the bite, and in this manner infecting the host.

The tick remains infective for a very long time—according to Möller as long as eighteen months—and the infection can be passed not merely through the eggs into a new generation of ticks, as has been demonstrated by Dutton, Todd, Leishman, and others, but also according to Möller into the third generation, even if the second generation have only fed on clean animals.

Pathogenicity.—It is the cause of West African and Colombian relapsing fever.

Spiroschaudinnia rossi Nuttall, 1908.

This spirochæte is distinguished from *S. duttoni* by its biological reactions, though some authorities consider it identical with *S. duttoni.* It is the cause of East African relapsing fever, and is conveyed by *Ornithodoros moubata.*

Spiroschaudinnia novyi Schellach, 1907.

History.—In 1907 Professor Manteufel, while investigating an accidental laboratory infection of relapsing fever, found that the serum of the patient agglutinated a spirochæte found by Novy in a case of relapsing fever in America in a dilution of 1 in 100, but showed no such power over the spirochæte of the European disease. Moreover, it gave Pfeiffer's reaction, being active in doses of 0·05 c.c. in experimentally infected mice. Schellach has investigated this spirochæte, and given it the specific name used above.

Morphology.—It is 17 to 20 μ in length, with six to eight undulations and a thickness of 0·31 μ. He gives the dimensions for the *S. recurrentis* as 19 to 29 μ, with eight to ten undulations and a thickness of 0·39 μ, and *S. duttoni* as 24 μ at the most, with eight to ten undulations and a thickness of 0·45 μ; which appear to be very different from Novy's table given under *S. carteri.*

The spirochæte appears to have great flexibility and activity of movement. One end has a filiform prolongation about 5 μ in length, while the other is merely pointed. No undulating membrane could be differentiated; but he states that he was able to demonstrate lateral cilia, which he considers to be artificial; but this, in our opinion, is highly suggestive of the presence of an undulating membrane. Coloured granules could be made out when stained by Giemsa. Reproduction was usually by transverse division.

Life-History. The spirochætes are found in the blood during the attacks of fever, and equally distributed in the organs in the apyrexial interval.

Inoculation.—It can be inoculated into monkeys, but small rodents are especially susceptible. Subinoculations can be made from monkey to monkey and from mouse to mouse.

Immunity.—Serum of animals immunized for *S. novyi* is without effect upon *S. recurrentis*, *S. duttoni*, or *S. carteri*.

Cultivation. It has been cultivated by Noguchi as mentioned above (see p. [illegible]).

Pathogenicity. It is the cause of North American relapsing fever.

Spiroschaudinnia carteri Manson, 1907.

S. carteri has a minimal length of 12 *μ*, with open flexures. It is thinner than *S. novyi*, and it is not agglutinated by serum of animals immunized against *S. novyi*. It can be inoculated into monkeys and with difficulty into mice, and can be subinoculated from monkey to monkey or mouse to mouse.

Novy and Knapp give the following differences between *S. carteri*, *S. duttoni*, and *S. novyi*:—

Character.	*Spiroschaudinnia novyi*	*Spiroschaudinnia duttoni.*	*Spiroschaudinnia carteri*
Length of simple cell .. .	8 *μ*	10 *μ*	8 *μ*
Length of double cell .	16-20 *μ*	30 *μ*	16-20 *μ*
Width	0·25 *μ*	0·2 *μ*	0·2 *μ*
Number of turns in a single cell	2-3 *μ*	2·5 *μ*	2-3 *μ*
Distance between the turns	1·5 *μ*	1·5 *μ*	2-3 *μ*
Movement	Vigorous	Little	--
Number in peripheral blood	Many	Few	Many

According to Strong's experiments, rats immunized against *S. recurrentis* and *S. novyi* are immune to *S. carteri*. He therefore believes these three strains to be closely allied if not identical.

They can also be distinguished by agglutination, immunization tests, by Pfeiffer's reaction, and by certain animals being susceptible to some species and not to others. Mackie has suggested that *S. carteri* may be transmitted by a pediculus. It is the cause of Asiatic relapsing fever.

Spiroschaudinnia berbera Sergent and Foley, 1910.

Spiroschaudinnia with minimal length of 12 μ and irregular open spirals or flexures. It can be inoculated into monkeys (*Macacus cynocephalus*) and with difficulty into rats and mice. Subinoculations can be made with difficulty from rat to rat and from mouse to mouse. The immune serum is without effect upon *S. recurrentis*. It produces a mild infection in animals, but a severe one in man, for whom it is the cause of North African and possibly Egyptian relapsing fever. Probably it is spread by the agency of lice.

Spiroschaudinnia morsusmuris Futaki, Takaki, Taniguchi, and Osumi, 1917.

Synonym. *Spirochæta morsusmuris.*

This spirochæte was found in the blood, skin, and lymph glands of six patients suffering from rat bite disease.

The spirochæte is mobile and shows a single flagellum at each pole, but no undulating membrane, and has generally three or four curves, but may have two to nineteen. The smaller forms occur in the blood and the larger in the tissues.

Mice and white rats become affected, but guinea-pigs and monkeys fail to do so.

Spiroschaudinnia icterohæmorrhagiæ Inada, Ido, Hoki, Kaneko, and Ito, 1915.

Synonyms.- *Spirochæte icterohæmorrhagiæ* Inada, etc., 1915; *S. icterogenes* Uhlenhuth and Fromme; *S. nodosa* Huebener and Reiter.

Nomenclature. Noguchi has created a new genus (see p. 139) for this parasite, calling it *Leptospira icterohæmorrhagiæ*, and this will probably be generally accepted.

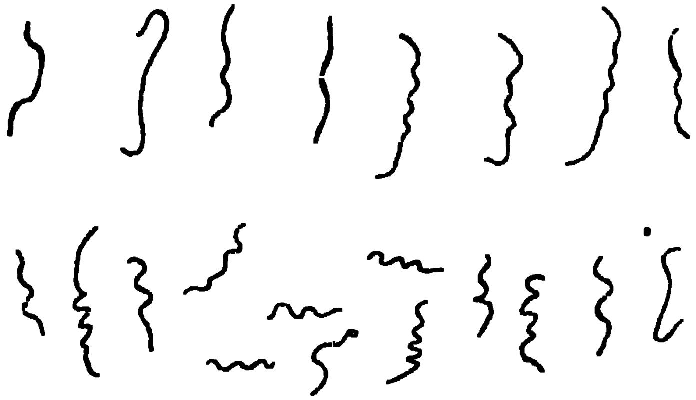


FIG. 133. *Spiroschaudinnia icterohæmorrhagiæ* Inada, etc.

This spirochæte is found during the first four weeks in the blood and urine of patients suffering from infective jaundice (Weil's disease) of the spirochætal type, and can be inoculated into animals, producing jaundice. These observations have been confirmed by French, Italian, and German workers. The spirochætes found in Japan and Belgium have been shown by Noguchi to be identical morphologically and serologically. The parasite seems to occur in the kidneys and urine of wild rats in Japan, in the rats in the trenches in Belgium, in those in France, where the disease in unknown, and in America, where it is rare.

The organism can enter through the alimentary canal, via abrasions on and even through the healthy skin, and, as it can live in water, this is thought to be the principal means of infection—*i.e.*, by walking barefoot or in sandals on wet earth or in stagnant water.

The spirochætes are 6-9 microns long on an average, but may reach to 20 microns and about 02·5 micron in breadth, with two to three large or four to five small waves. It often contains refractile granules, to the number of twenty-five to forty (these may in reality represent small waves, as shown by Dobell).

Guinea-pigs may be infected orally, subcutaneously, or intraperitoneally, with the blood of patients up to the seventh day of the illness, but usually not later, though there are exceptions to this. The incubation period in these animals is seven to eight days, and the symptoms resemble those produced in man. Rabbits cannot be infected. Ito and Matsuzaki obtained it in pure culture from the heart blood of subinoculated guinea-pigs, by sowing this on blood agar or blood gelatine and incubating from 20°-25° C., though it can grow from 15°-37° C. It produces neither odour, gas, nor liquefaction of the medium. The organism so cultivated remains pathogenic for guinea-pigs. A good medium is a mixture of rabbit blood-serum and 0·85 per cent. saline in the proportion of 1 to 5.

Spiroschaudinnia hebdomadis Ido, Ito, and Wani, 1918.

Morphologically similar to *S. icterohæmorrhagiæ*, differs serologically. Found by Ido, Ito, and Wani in cases of a seven-day fever called Nanukayami, which somewhat resembles atypical Weil's disease.

The field mouse (*Microtus montebelli*) seems to be the normal host of the spirochæte.

Spiroschaudinnia in Yellow Fever.

Stimson in 1909 described a spirochæte in the organs of persons who had died of yellow fever (*S. interrogans* Stimson 1909), but little importance was given to this observation. In 1918 Noguchi cultivated from the blood of several yellow fever patients a spirochæte similar to *S. icterohæmorrhagiæ* (*Leptospira icterohæmorrhagiæ*), and by inoculating cultures of the organism he produced in monkeys the same hæmorrhagic lesions as seen after the successful inoculation of blood of yellow fever patients.

B. CUTANEOUS SPIROCHÆTES.

Spiroschaudinnia vincenti Blanchard, 1906.

Synonym.—*Spiroschaudinnia schaudinni* Prowazek, 1907.

This is a very active motile spirochæte 10 to 20 μ in length, with a well-marked undulating membrane and one rather short flagellum. Male and female forms can be seen, according to Prowazek. Division is longitudinal.

It is, according to Prowazek, the cause of ulcus tropicum, and is possibly transmitted by a leech. Induces formation of pseudo-membranes.

It is often associated with the so-called fusiform bacilli causing angina Vincenti and, according to certain authors, hospital phagedæna and noma.

Spiroschaudinnia aboriginalis Cleland, 1909.

This spirochæte was found by Wise in British Guiana in 1906, and by Cleland in West Australia in 1909 in cases of granuloma inguinale. Its length is 6 to 18 μ, and it possesses but few coils, which vary in depth. The extremities, according to Cleland, are blunt. Similar spirochætes have been found by Wise and others in a peculiar granulomatous affection, which attacks the genital organs of dogs and bitches. It is believed at the present time that this *Spiroschaudinnia* is not the cause of granuloma inguinale, but merely a saprophyte.

Spiroschaudinnia phagedenis Noguchi, 1912.

Noguchi discovered this spirochæte in an indurated and ulcerated swelling of the labium which had lasted ten days. It has been cultivated by him on ascitic agar medium, and is a strict anaerobe. Length varies from 4 to 30 μ. and the curves from 1 to 8 μ, while young forms may be quite straight. Inoculated into monkeys and rabbits it causes transient inflammation.

S. acuminata Castellani, 1905, and **S. obtusa** Castellani, 1905.

Found in the open sores of yaws.

S. pseudopallida Mulzer, 1905.

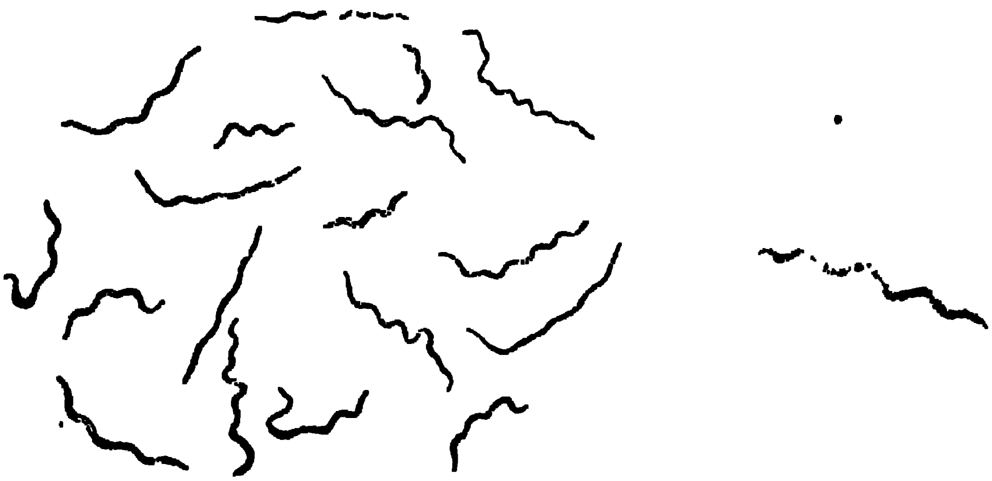
Found in ulcerating carcinomata.

Unnamed forms of cutaneous spirochætes have been seen by von Prowazek in cases of psoriasis.

C. RESPIRATORY SPIROCHÆTES.

Spiroschaudinnia bronchialis Castellani, 1907.

The presence of this spirochæte and the disease which it causes was first described by Castellani in 1906. They have been confirmed by Branch in the West Indies, by Chalmers and O'Farrell in the Sudan,



FIGS. 134 AND 135.—*Spiroschaudinnia bronchialis* CASTELLANI.

by Macfie in West Africa, by Castellani and Jackson in the Balkans, by Toro Villa in Colombia and South America, by Ragazzi in Bengazi, by Galli-Valerio in Switzerland, by Lurie in Serbia, by Violle in France, and by Broughton-Alcock in North Italy (see p. 1882).

It was originally found by Castellani in cases of bronchitis in Ceylon, and its morphology has been carefully studied by Fantham in the Anglo-Egyptian Sudan.

S. bronchialis is an organism with marked polymorphism, varying in length from 5-25 microns and in breadth from 0·2-0·3 micron. The variations indicate different stages of growth and division. As a rule the ends, though varying considerably, are acuminate. Its movements are active, but cease shortly after removal from the body, and are succeeded by a granule stage, as described by Fantham, and from these granules new spirochætes are believed to be formed. The granules are probably the infective agent, and spread the infection from man to man by the air.

It is believed to be different from *S. dentium* and *S. buccalis*, the mouth spirochætes, of which the former measures 4-10 and the latter 9-22 microns in length.

Chalmers and O'Farrell's experiments tend to show that monkeys can be infected.

Spiroschaudinnia minuta Castellani, 1916.

Found in cases of rhinopharyngitis (p. 1881). With Romanosky it stains a pinkish red, and has very few spirals. Length 3-10-12 microns.

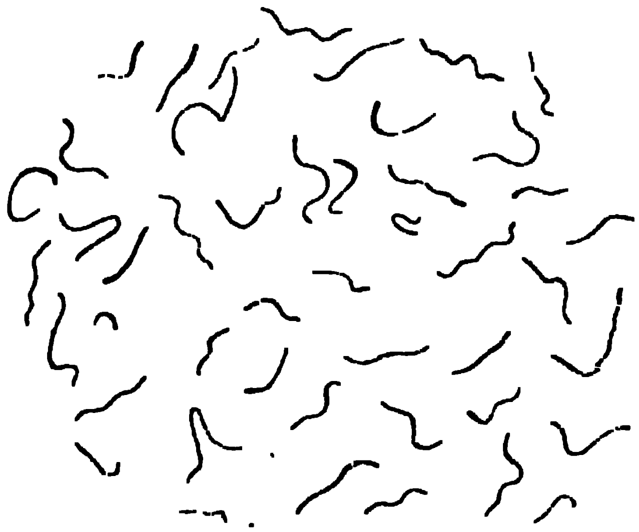


FIG. 136.—*Spirochaudinnia minuta* CASTELLANI.

D. ALIMENTARY CANAL SPIROCHÆTES.

Spiroschaudinnia subtilis Castellani, 1907.

Found in scrapings from oral mucosa and in intestinal contents.

Spiroschaudinnia eurygyrata Werner, 1909, *emendavit* Fantham, 1916.

Synonyms.—*Spirillum hachaizæ* Kowalski (perhaps); *S. eurygyrata* Werner, 1909.

The spirochæte was first noted under the name spirillum in cholera motions in 1884-86 and 1893-94. In 1903 Le Dantec saw them in cases of so-called spirochætal dysentery. In 1909 Werner gave them the two names mentioned above, which Fantham in his 1916 researches considers to be the same.

The spirochætes were found by Fantham in the fæces of soldiers suffering from diarrhœa or dysentery in Gallipoli and Flanders, and also in healthy people. It has pointed ends, and varies from 3-15 microns in length by about 0·25 micron in breadth. The number of waves is from two to nine, while chromatin granules can be seen along the body. It is actively motile, and has been seen to enter the shed epithelial cells found in the fæces, where it produces coccoid bodies.

NOTE.—It is essential not to confuse true spirochætes found in the fæces with vegetal organisms with pseudo-spirochætal shapes, as has occurred—*e.g.*, *Spirobacillus* (*Bacillus*) *zeylanicus* Castellani, 1910, has often been mistaken for a true spirochæte (see p. 1838).

E. URINARY SPIROCHÆTES.

Spiroschaudinnia urethræ Macfie, 1917.

These spirochætes have been seen by Macfie in urine in natives on the Gold Coast, where it caused an acute urethritis.

The parasite was found free in large quantities in the pus and also in the pus cells. It measured from 5-20 microns in length, and showed a membrane or crest. The cytoplasm, which was homogeneous, contained chromatin granules or rodlets at intervals. Some pus cells contained coccoid granules.

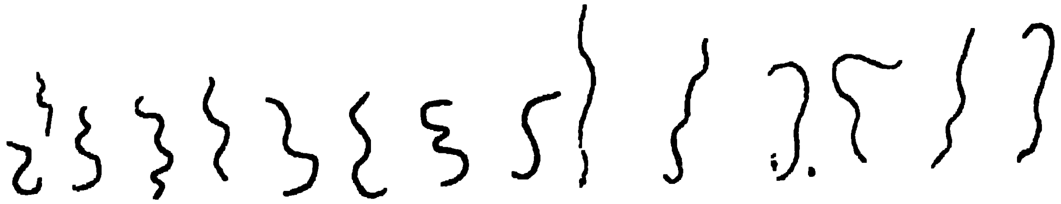


FIG. 137.—*Spiroschaudinnia mitis* CASTELLANI.

Spirochætes have been found in the normal urethra by various authors—*e.g.*, Mendelson.

S. mitis was found by Castellani in the centrifuged urine of certain cases of camp jaundice of mild type. It is thicker than *S. icterohæmorrhagiæ*, and has larger and better defined waves. Of doubtful pathogenicity.

THE DIFFERENTIATION OF HUMAN SPIROCHÆTES.

The differentiation of spirochætes is exceedingly difficult, as morphological characters seldom help, and measurements with wave formations are useless for this purpose.

As many of the so-called species are probably only variants produced by environment, it seems correct to classify them according to site in the human body, according to their action on man and animals, and according to immunity experiments.

The following is an attempt on these lines:—

A. Found in the blood:—
- I. In cases of relapsing fever:—
  - (*a*) Clinical symptoms in man mild, but in animals severe —*S. novyi*.
  - (*b*) Clinical symptoms in man severe:—
    - 1. In animals severe—*S. duttoni*.
    - 2. In animals mild:—
      - (1) Berbera immune serum protective—*S. berbera*.
      - (2) Berbera immune serum ineffective and recurrentis immune serum protective; closely allied forms:—
        - (*a*) Found in Europe—*S. recurrentis*.
        - (*b*) Found in India—*S. carteri*.
- II. In cases of infectious jaundice—*S. icterohæmorrhagica*.
- III. In cases of rat-bite disease—*S. morsusmuris*.

B. Found in the skin:—
- I. In ulcus tropicum:—
  Not cultivated, with undulating membrane and short flagellum—*S. vincenti*.
- II. In granuloma inguinale:—
  Not cultivated without undulating membrane or flagellum —*S. aboriginalis*.
- III. In cutaneous inflammation:—
  - (*a*) Cultivated, strictly anaerobic; causes transient inflammation in animals—*S. phagedenis*.
  - (*b*) Not cultivated; found in open yaws ulcers:—
    - 1. Acuminate—*S. acuminata*.
    - 2. Obtuse—*S. obtusa*.
  - (*c*) Not cultivated; found in ulcerating carcinomata—*S. pseudopallida*.

C. Found in the respiratory passages:—
- I. In bronchial spirochætosis—*S. bronchialis*.
- II. In rhinopharyngitis—*S. minuta*.

D. Found in the alimentary canal and skin lesions:—
- **I. In the mouth:—**
  - **(*a*) Produces pseudo-membranes. In cases of angina and ulcus tropicum—*S. vincenti*.**
  - **(*b*) Non-pathogenic:—**

1. Short forms—*S. dentium.*
2. Long forms—*S. buccalis.*

II. In vomit:—
Rather doubtful forms in vomit of Belyando spew in Queensland—*Unnamed.*

III. In fæces:—
In health and disease—*S. eurygyrata.*

E. Found in the urethra:—

I. In free and in coccoid form in pus cells from urethritis. With crest or membrane—*S. urethræ.*

II. In urine from cases of mild camp jaundice. With well-marked waves—*S. mitis.*

ANIMAL SPIROCHÆTES.

Spiroschaudinnia macaci Castellani and Chalmers, 1910.

Synonym.—*Spirochæta macaci* Castellani and Chalmers, 1910.

This spirochæte was found by us in monkeys in Ceylon in 1906. In length it measures about 12 *μ*, and closely resembles *S. carteri* Manson, 1907. It can be easily inoculated from monkey to monkey. Spirochætes which may be of a different species have also been found by Leishman, Balfour, and by Plimmer in *Cercopithecus sebæ* from Sierra Leone.

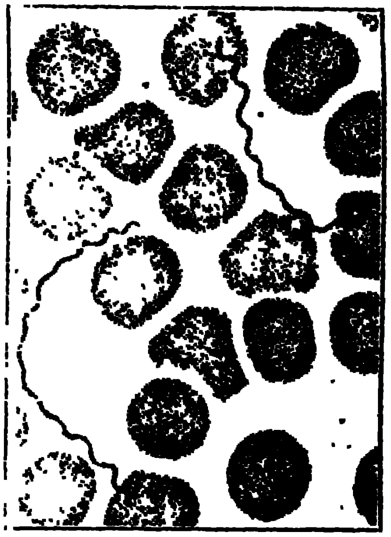


FIG. 138.—SPIROCHÆTES IN THE BLOOD OF *Cercopithecus sebæus* FROM SIERRA LEONE. (× 1,000.)

(From a microphotograph by H. G. Plimmer.)

Spiroschaudinnia anserina Saccharoff, 1891.

Found in enormous numbers in the blood of geese in the Caucasus and Tunis. It causes fever, diarrhœa, tenderness of the feet, and death in about a week, the mortality being 80 per cent. It can be inoculated into other geese.

Spiroschaudinnia marchouxi Nuttall, 1904.

Synonym.—*Spirochæta gallinarum* R. Blanchard, 1905.

This spirochæte, which has been discovered by Marchoux and Salimbeni, and studied by Balfour, is about 10 to 20 *μ* in length, causes disease in fowls in many countries—*e.g.*, Brazil, the Sudan, Egypt, Tunisia, and Serbia. The symptoms are fever, diarrhœa, anæmia, somnolence, convulsions, and death in four to five days, or in chronic cases cachexia and death in fourteen days. As first observed by Sambon, it appears to enter the red corpuscle, and to break up within it in a way which reminds one of the description already given for *S. duttoni.* Balfour has made an important investigation on granule spreading and the infective granules. It is spread by *Argas persicus* and other Argasidæ, as Fulleborn has shown with *Ornithodoros moubata.* Balfour has made the important observation that in the infected ticks chromatic granules are present as described by Leishman in *S. duttoni.*

* Recent researches by Balfour tend to show that the Sudan strain is a separate species: *S. granulosa* Balfour, 1910. Aragão has attempted to obtain a serum and a vaccine with a certain degree of success.

Spiroschaudinnia neveuxi Brumpt, 1909.

Brumpt describes this spirochæte as morphologically identical with *S. marchouxi*, but cross immunization shows that the two species are different. It is the cause of fowl spirochætosis in Senegal, and is spread by *Argas persicus*.

Spiroschaudinnia theileri Laveran, 1904.

This spirochæte, discovered by Theiler in 1902, is found in cattle in Africa about Pretoria, in the Cameroons, and in East Africa. The symptoms are not clear, as babesia has also been seen in the same animals. It is spread by *Margaropus decoloratus*, the blue tick.

Spiroschaudinnia ovina R. Blanchard, 1906.

This spirochæte may be the same as *S. theileri*. It was found by Martoglio and Carpano in sheep in Erythræa, on the Red Sea, and by Theiler in the Transvaal.

Spiroschaudinnia equi Novy and Knapp, 1906.

Found by Theiler in the Transvaal, and by Martin in French Guinea, and may be the same as *S. theileri*.

Other Spirochætes.—*S. vespertilionis* Novy and Knapp, found by Nicolle and Comte in 1905, in *Vespertilio kuhli*.

S. gracilis Levaditi and Stanesco, 1909, very like *Treponema pallidum*.

S. culicis Jaffé, 1907, found in the gut and Malpighian tubules of *Culex pipiens* and the larva of *Anopheles maculipennis*.

S. muris Wenyon and *S. laverani* Breinl and Kinghorn, in mice.

S. bufonis Dobell, 1908, found in the rectum of a frog.

S. glossinæ Novy and Knapp, 1906, in the stomach of tsetse-flies.

S. microgyrata Gaylord and Calkins, 1907, in cancer of the breast in mice.

S. balanitidis Hoffmann and Prowazek, 1906, found by Hoffmann and Prowazek in balanitis.

S. lutræ Prowazek, 1907, found by Prowazek in the otter.

Sambon has found spirochætes in scrapings from gastric ulcers in a fox.

Various spirochætes have also been observed in the stomach of normal cats, dogs, and rats (Bizzozzero, Salomon), in the intestinal ulcers of dogs and monkeys affected with trypanosomiasis (Balfour), in the intestine of normal mice (Wenyon) and birds (Kent).

Treponemidæ Schaudinn, 1905.

Definition.—Spirochætacea with a minute thread-like body twisted into numerous fine coils, with pointed tapering extremities. The body is cylindrical on section, and not flattened, and the spirals appear preformed. There is no undulating membrane. Transverse and longitudinal division have been observed, the latter type being the only one found in cultures.

Classification.—Only one genus.

Treponema Schaudinn, 1905.

Synonym.—*Spirochæta* Ehrenberg *pro parte; Spironema* Vuillemin, 1905, von Klebs, 1892.

Treponemidæ with the characters of the family.

Type Species.—*Treponema pallidum* Schaudinn, 1905.

Treponema pallidum Schaudinn, 1905.

Synonyms.—*Spirochæta pallida* Schaudinn, 1905; *Spironema pallidum* Vuillemin, 1905; *Microspironema pallidum* Stiles and Pfander, 1905; *Trypanosoma luis* Krzysztalowicz and Siedlecki, 1905.

History.—This treponema was discovered by Schaudinn in syphilis in 1905. The history of the finding of parasites in syphilis is interesting, for as long ago as 1546 Frascastorius considered syphilis to be a parasitic disease. In 1879 Klebs, and, later, Losdorfer and Döhle in 1901, described parasites, and saw cell inclusions in the disease, and in 1905 Siegel described an organism, *Cytoryctes luis*, in which there are flagellate bodies very closely resembling spirochætes. In 1905 Schaudinn, after investigating and reporting unfavourably on Siegel's work, found the *Treponema pallidum*, which is accepted as the cause of the disease. Korté in 1906 described free round bodies and cysts with threads in primary sores. E. H. Ross has described an intracellular formation allied to his *Lymphocytozoon cobayæ*, which develops into spirochætes, and these researches have in part been confirmed by Jennings. McDonagh also has described a complicated life-cycle.

FIG. 13[illegible].—*Treponema pallidum* SCHAUD.
(From a microphotograph by J. J. Bell.)

Morphology.—It varies from 4 to 10 μ in length, average 7 μ, with a width up to 0·5 μ. It is twisted into spirals, which vary from six to twelve and more in number, the average being eight to ten, and are to a certain extent preformed—*i.e.*, not due to the parasite's movements. It moves by rotation on a long axis by gliding movements, forwards and backwards, and also by flexion of the whole body. The periplast is continued as long delicate processes at each end, which are considered by some to be flagella.

Krzysztalowicz and Siedlecki say that not far from the middle the body may be nearly straight, and a clear spot can be observed which they think is a nucleus; but it might correspond to the similar area in *S. duttoni*. They also describe male and female gametes and conjugation, which they think leads to the formation of a cyst or spore, which may be carried via the blood stream to different parts of the body, and there develop into Treponemata.

The parasite is found in the primary sores and in the secondary lesions, but is very difficult to detect in tertiary eruptions, though it is abundantly present in the liver, spleen, decidua, the placental villi, the umbilical cord of syphilitic fœtuses, and infants.

It is distinguished from other spirochætes (*S. refringens*) which may be met with on ulcerated surfaces by difficulty in staining; number, character, and permanence of the spirals; the terminal prolongations; absence of an undulating membrane; minute size and delicacy.

Inoculation.—Syphilis can be inoculated into chimpanzees (as shown by Metchnikoff and Roux) and other monkeys, and *T. pallidum* can be found in the lesions so caused, the incubation being fifteen to forty-nine days, average thirty days, for the primary sore; and nineteen to sixty-one days, average thirty-three days, for the secondary eruption after the primary have appeared. In the lower monkeys the lesion remains localized to the seat of the inoculation.

Cultivation.—Schereschewsky has cultivated, with a certain degree of success, *T. pallidum* on a medium of horse serum, brought to a gelatinous consistence by heating to 60° C., and partly autolyzed by keeping in an incubator at 37° C. for three days. Later Muhlens and Hartmann also cultivated it, Hartmann inoculating a pure culture with success in the testicles of a rabbit, and more recently it was grown by Noguchi quite successfully, as described above for Spiroschaudinnia, and he has also been successful in reproducing the disease in monkeys by inoculation of the pure culture. The monkeys present a positive Wassermann reaction two weeks after inoculation. Noguchi has made the important observation that there are several varieties of *T. pallidum*; he distinguishes a normal type of medium thickness, a thick type, and a thin type. Inoculated in the testicles of rabbits, the normal type gives rise to a diffuse induration, which develops the third week after inoculation; the thick type gives rise to several small hard nodules, which develop slowly; the thin type induces a diffuse swelling, which develops very quickly, ten to fourteen days after inoculation. It is interesting to note that Mott, several years ago, suggested—on clinical and pathological grounds—that there might be more than one variety of *T. pallidum*.

Biological Reactions.—By heating the cultures to 60° C. Noguchi has produced a product which he calls luctine, by means of which a cutaneous reaction can be obtained in syphilitic patients.

Life-History.—Unknown.

E. H. Ross found cellular inclusions resembling Kurloff's bodies in mononuclears in non-ulcerated Hunterian chancres, and examined them in detail by placing the blood from such a chancre upon H. C. Ross's coefficient jelly.

Similar bodies have been described by McDonagh, who has given an account of a complicated life-cycle for *T. pallidum* (see second edition of this book, p. 409).

Pathogenicity.—*T. pallidum* is the cause of syphilis.

Treponema pertenue Castellani, 1905.

Synonyms.—*Spirochæta pertenuis* Castellani, June, 1905; *Spirochæta pallidula* Castellani, November, 1905.

History.—It was discovered by Castellani in 1905 in the scrapings from yaws papules.

Morphology.—*Treponema pertenue* is an extremely delicate spiral-shaped organism, varying in length from a few microns to 18 and 20 μ and even more. It is very slender. Some individuals are, however, thicker than others. It does not stain easily, but good results may be obtained with Giemsa's method, and also with Leishman's stain, provided the alcoholic solution is allowed to act for five minutes, and the subsequent admixture with distilled water for from one half-hour to several hours. Using either of these methods, the Treponemata stain purplish. Occasionally a few more deeply stained granules may be seen in the body of the organism. The extremities of the parasite are often pointed, but forms may be met with presenting blunt extremities, or one extremity pointed and the other blunt. In some individuals one of the extremities may present a large pear-shaped expansion or a loop-like formation. The number of coils varies from six to twenty or more, but they are, as a rule, numerous, uniform, and of small dimensions. Occasionally a portion of the *Treponema* shows numerous close uniform coils, while the rest of its body shows no coils at all. Sometimes two Treponemata may be attached end to end, or apparently twisted together. Castellani has not been able to detect any undulating membrane, though its presence has been asserted by other observers (Blanchard). Occasionally, in preparations stained by Löffler's method of flagella staining, it has seemed to several observers that some of the organisms present an extremely delicate flagellum at one end. Prowazek has described a resting form, oval or round, produced by a coiling up of the spiral. Ranken, by means of the dark-ground illumination, has been able to observe the extrusion from the parasite of small, highly-refractile granules, which are apparently shot out by free lateral motion. These granules immediately after extrusion remain stationary, then begin to rotate and move about, though apparently not supplied with flagella.

Intracellular Stage.—Castellani in 1905 described some peculiar bodies, free and intracellular, in leucocytes, which possessed an oval or roundish shape, and contained chromatin dots. At the time he was inclined to consider them to be stages in the development of the parasite, but later he held that they were cell inclusions of non-parasitic origin. In view, however, of the work of E. H. Ross and McDonagh on the organism of syphilis, it is possible that they are in reality a stage in the development of *T. pertenue*.

Comparison with T. pallidum.—From the above description it is evident that the frambœsia organism is morphologically very similar to that of syphilis. Blanchard, Martin, Prowazek, and others seem to have been able to make out some slight morphological differences between the two. Martin states that the frambœsia *Treponema* is even more slender and more difficult to stain than the *T. pallidum* of Schaudinn. On the other hand, some authorities consider it to be thicker. Rivas states that it has closer coils. Prowazek, Levaditi, and Nattan-Larrier state that *T. pertenue* shows less regularly shaped coils, and one extremity terminates in a loop much more frequently than in *T. pallidum*. Moreover, according to Levaditi and Nattan-Larrier, in fresh preparations *T. pertenue* displays whip-like lateral movements rather than translatory ones. Russell and Archibald consider that *T. pertenue* is slightly thicker than *T. pallidum*; the distance from crest to crest of the waves and the dip from the crest to the hollow is greater; the parasite has greater tendency to curl up into a loop at one end. Ranken states that the parasite does not show any corkscrew-like motion, nor any progressive motion. We believe that the differentiation of the two organisms, and in general of spirochætes and Trypanosomata, is to be based more on the results of the biological tests than on slight morphological differences. The animal tests clearly show that *T. pertenue* and *T. pallidum* are two different species, inasmuch as monkeys immunized with *T. pertenue* do not become immune for *T. pallidum*.

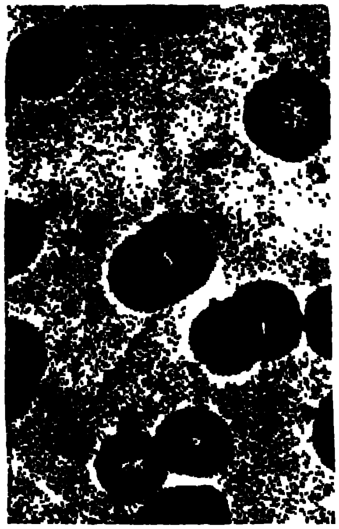


FIG. 140.—*Treponema pertenue* CASTELLANI.

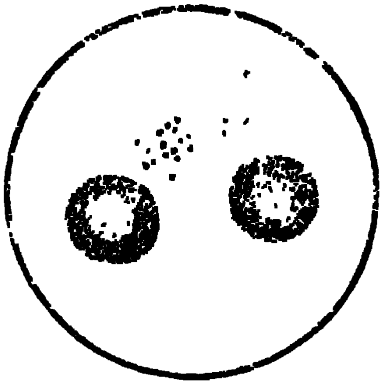


FIG. 141.—BASOPHILE CELL, WITH CHROMATIN DOTS, IN A CASE OF FRAMBŒSIA.

Incidence of the T. pertenue in Frambœsia Lesions.—The presence of the *Treponema* is constant in the primary lesion and in the unbroken papules of the general eruption. It may be found in the spleen, lymphatic glands, and bone-marrow. In the blood it has not yet been demonstrated microscopically, though there is no doubt that the blood of the general circulation is infectious, inasmuch as monkeys inoculated with it develop typical yaws lesions, in which the *Treponema* is abundantly present. The *Treponema* is absent in the cerebro-spinal fluid, and generally in the tertiary lesions.

Bacteriological Flora found in Open Sores of Framboesia.—While *T. pertenue* is the only germ found in the non-ulcerated lesions, the ulcerated lesions of framboesia are soon invaded by all kinds of germs. Apart from innumerable bacteria, various kinds of spirochætes are present. One form is rather thick, and takes up the stain easily. It is morphologically similar to the *Spiroschaudinnia refringens* of Schaudinn. Another form is thin, delicate, with coils varying in size and number, and with blunt extremities—*S. obtusa* Castellani. A third form is likewise thin and delicate, but tapers at both ends—*S. acuminata* Castellani; *T. pertenue* is also present in many cases.

Inoculation Experiments of Framboesia in Man.—Paulet, in 1848, inoculated fourteen negroes with the secretion taken from framboetic granulomata. All of them developed framboesia, the inoculation period varying from twelve to twenty days, when at the seat of inoculation in ten cases the first nodule appeared, soon followed by a typical general eruption. In two cases apparently the eruption did not start from the seat of inoculation.

Charlouis, in 1881, inoculated thirty-two Chinese prisoners, who had never suffered from the disease, with crusts and scrapings from a case of yaws. The disease developed in twenty-eight of them, beginning invariably at the seat of inoculation. Moreover, he inoculated a native suffering from typical yaws with syphilis. The inoculation was quite successful, a primary syphilitic sore developing, followed by all the usual types of secondary eruption. That yaws patients are not immune against syphilis is proved also by Powell and Nicolas and others, who have described several cases of syphilis supervening on yaws. Syphilitic patients may contract framboesia naturally and experimentally.

Inoculation Experiments in Monkeys.—Neisser, Prowazek, Halberstadter in Java, and shortly afterwards Castellani in Ceylon, have shown that monkeys are susceptible to framboesia. According to their experiments, the inoculation period varies from a minimum of sixteen days to a maximum of ninety-two. The appearance of the lesions developing at the seat of inoculation is practically the same in all cases—viz., an infiltrated spot slowly increasing in size, and soon becoming moist, the secretion drying into a thick crust. Removal of the crust exposes a raw, granulating, red surface.

In the monkeys of a low class (genus *Macacus*, genus *Semnopithecus*) the eruption is, as a rule, localized to the seat of inoculation. The infection, however, is general, as is proved by the presence of *T. pertenue* in the spleen and lymphatic glands besides the local lesions. Halberstadter has obtained a general eruption in ourang-outangs. According to Castellani's experiments, splenic blood, obtained by puncturing the spleen of a patient affected with frambœsia, can reproduce the disease in monkeys. The inoculation of the blood of the general circulation also may occasionally produce the disease. The inoculation of cerebro-spinal fluid into normal monkeys has always proved negative.

Neisser, Halberstadter, J. Prowazek in Java, and later Castellani in Ceylon, have proved that monkeys successfully inoculated with frambœsia do not thereby become immune to syphilis, and, *vice versa*, monkeys successfully inoculated with syphilis do not thereby become immune to frambœsia. According to Levaditi, monkeys immunized for frambœsia do not acquire any immunity for syphilis, but monkeys immunized for syphilis may acquire a partial immunity for frambœsia. According to Ashburn and Craig, monkeys of the species *Cynomolgus philippinensis* are susceptible to frambœsia, but not to syphilis.

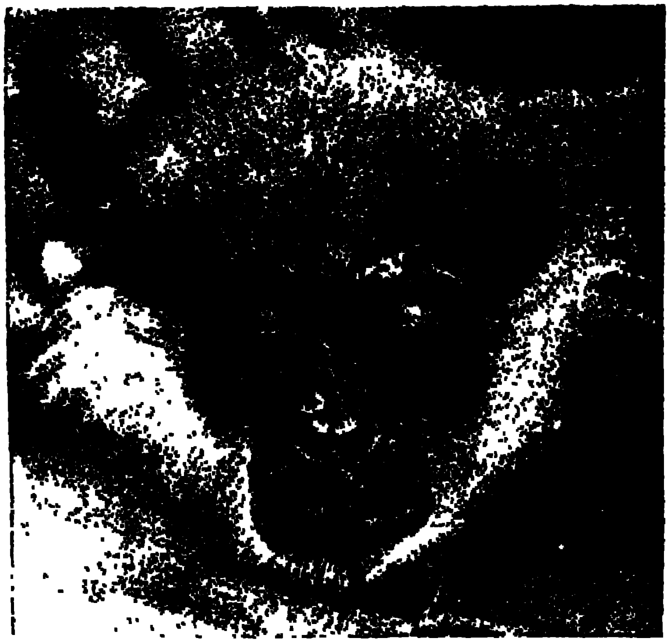


FIG. 142.—MONKEY INOCULATED WITH FRAMBŒSIA.

The following facts are in favour of the *T. pertenue* being the specific cause of frambœsia:—

1. In the non-ulcerated papules, in the spleen, in the lymphatic glands of frambœsia patients, as well as in inoculated monkeys, the *T. pertenue* is the only organism present. No other germ can be demonstrated, either microscopically or by cultural methods.

2. The extract of frambœsia material containing the *T. pertenue*—but, so far as our present methods of investigation permit us to say, no other germs—is effective when inoculated into monkeys.

3. The extract of frambœsia material from which the *T. pertenue*

has been removed by filtration becomes inert, and monkeys inoculated with it do not contract the disease.

Inoculation Experiments in Rabbits.—Nichols has inoculated rabbits successfully, and finds that the incubation period is shorter than that for *T. pallidum* in the same animal. He finds that 4·5 milligrammes of salvarsan per kilogramme of the animal's weight injected intravenously will effect a cure, which is less than for *T. pallidum.* Complement fixation is positive by the fourteenth day, but after administration of salvarsan it becomes negative. He has not been able to produce immunity, and he finds that if reinoculation is unsuccessful it is because the animal is still infected; whereas, if it is cured, reinoculation can be successfully performed. It is possible to demonstrate the difference between syphilis and framboesia by the reinoculation of rabbits after treatment by salvarsan. Castelli has inoculated rabbits intravenously, and states that the general clinical symptoms, papules, etc., are so different from those obtained after a similar injection of *T. pallidum* that this method may be of use for differentiating them.

Cultivation.—*T. pertenue* has been successfully cultivated by Noguchi, as described for Spiroschaudinnia (p. 441).

Pathogenicity.—It is the cause of framboesia tropica (*vide* Chapter LXI., p. 1535).

Treponema mucosum Noguchi, 1912.

This *Treponema* was isolated from the pus of a case of pyorrhœa by Noguchi. It closely resembles *T. pallidum* and *T. microdentium,* but differs in certain biological properties. It can be cultivated in citrate dilution of ascitic agar. Cultures have a strong fœtid odour, and mucin is produced in the medium, but this property is lost by repeated subcultures. It is a strict anaerobe. Inoculated into monkeys or rabbits it causes transitory local inflammation.

Treponema calligyrum Noguchi, 1913.

Found by Noguchi in condylomata—cultivated by the same observer. It shows deep, regular curves, not so closely set as in *T. pallidum.* It is also thicker.

Other species are: *T. microdentium, T. refringens, T. termitis* Leidy, 1881, in *Calotermes militaris*; *T. minei* Prowazek, 1910; *T. vivax* Dobell, 1911, in *Oscillatoriæ*; *T. stylopygæ* Dobell, 1911, in *Stylopyga orientalis*; *T. parvum* Dobell, 1911; *T. minutum* Dobell, 1911; *T. dentium* Koch, 1877. *T. buccale* Cohn, 1872; *T. intermedium* Dobell, 1911, in the human mouth.

A rather doubtful *Treponema* has been described by Dobell in the intestine of *Bufo vulgaris* L.

T. urethrale Castellani, 1915, found in the mucopurulent discharge from the urethra. It is very delicate and has numerous spirals all equal. Length, 6-12 microns. The patient had no sign of gonorrhœa or syphilis.

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CHAPTER XX

DIPLOZOA AND OCTOMITIDÆ

Preliminary—Diplozoa—Octomitidæ—Octomitus—Giardia—References.

PRELIMINARY.

WE now return to the classification of the Protomonadina given on p. 332, where the order is divided into two suborders, Monozoa and Diplozoa. The Monozoa we have just considered, and in the present chapter the Diplozoa are described.

SUBORDER 2. DIPLOZOA Hartmann and Chagas, 1911.

Definition.—Protomonadina with more or less tendency to bilateral symmetry in *undividing forms*, as shown by the arrangement of the flagella, by the duplication of the axostyle, with sometimes the nucleus and more rarely of the cytostome. An undulating membrane is absent.

Classification.—This suborder may be divided into two families, of which one is of importance in tropical medicine.

A. Cytostome single or absent; flagella eight in number—Family 1, *Octomitidæ* Minchin, 1912.
B. Cytostome double; flagella variable in number—Family 2, *Distomatidæ* Senn, 1900.

Only the first of these families concerns us.

FAMILY 1. OCTOMITIDÆ Minchin, 1912.

Definition.—Diplozoa with eight flagella and with or without a cytostome.

Type Genus.—*Octomitus* Prowazek, 1904.

Classification.—The family is divisible into several genera as follows:—

- A. Anteriorly three pairs and posteriorly one pair of flagella; nucleus single, bilaterally lobed or doubled; sucker absent.
  - I. Parasitic—*Octomitus*.
  - II. Free living—*Hexamita*.
- B. Antero-laterally one pair, mesially two pairs, and posteriorly one pair of flagella; nucleus usually double; sucker present—*Giardia*.

Octomitus and Giardia concern us; Hexamita does not.

GENUS I. OCTOMITUS PROWAZEK, 1904.

Definition.—Octomitidæ, parasitic with anteriorly three pairs and posteriorly one pair of flagella; nucleus single, bilaterally lobed or doubled; sucker absent.

Type Species.—*O. intestinalis* Prowazek, 1904, found in rats.

Classification.—The known species of Octomitus may be recognized as follows:—

A. Nucleus situate close to the anterior end:—
  I. Nucleus often bilobed—*Dujardini*.
  II. Nucleus double:—
    (*a*) Measurements 8-12 × 5-7 microns—*Intestinalis*.
    (*b*) Measurements 4-6 × 2 microns—*Muris*.
B. Nucleus not situate close to the anterior end:—
  Nucleus single and rounded; size 6 × 3 microns—*Hominis*.

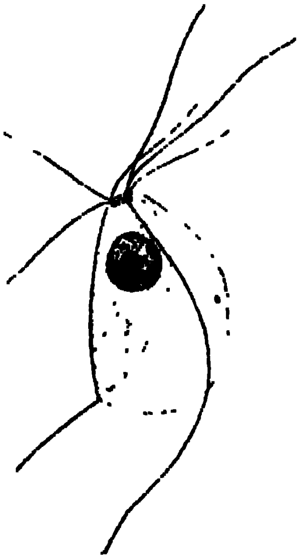

FIG. 143.—*Octomitus hominis* CHALMERS AND PEKKOLA, 1916. (× 2,000.)

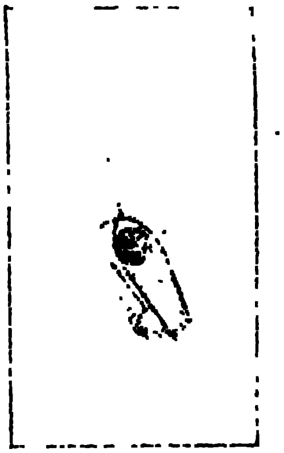

FIG. 144.—*Octomitus hominis* CHALMERS AND PEKKOLA, 1916. (× 2,000.)

Octomitus hominis Chalmers and Pekkola, 1916.

Definition.—Octomitus with single rounded nucleus, not situate close to anterior end.

Morphology.—Small fusiform or pear-shaped flagellates, in size 5·6-6·0 × 2·8-3·0 microns.

When examined in the stained condition it showed a circular clearly defined nucleus (Figs. 143 and 144), measuring about 1·4 microns in transverse diameter, and lying near the junction of the anterior third with the posterior two-thirds of the body. This nucleus is bounded by a well-marked membrane, which limits the homogeneous dark staining contents, in which there is often a centrally or excentrically placed karyosome.

In front of the nucleus and closely approximated to the anterior end of the body is a well-defined blepharoplast, which, though typically single, may have a secondary smaller blepharoplast associated with it. No sign of a rhizoplast could be seen.

From this blepharoplast there arise six anteriorly directed flagella, though occasionally one accidentally appears as though directed backwards. When there are two blepharoplasts, then three flagella arise from each.

These flagella vary considerably in length, being generally much longer than the body, but it is exceedingly difficult to be certain where they end, and in the specimens drawn only such portions as could be clearly seen are portrayed, though in other specimens the length was clearly much greater, in some instances quite three times the length of the parasite.

Directed backwards, and also arising from the blepharoplast or blepharoplasts, there are two chromatic lines, which, diverging and running on either side of the nucleus, may or may not converge, but in either case end near the posterior margin of the body in very minute chromatic particles, which are generally very difficult to see. From each of these chromatic particles there arises a posteriorly directed flagellum.

The chromatic rods are obviously axostyles, and the little particles in which they end may be termed axoplasts.

It is not often that the axostyles are seen together, as the parasite usually lies so that only one is visible, while the other is almost invisible; but at times they are seen as described above, or at other times when the parasite has shrunk into a rounded mass they may be observed crossing one another.

No cytostome has been observed, while the periplast is thin and without markings.

The cytoplasm is vacuolated with food vacuoles.

Life-History. Nothing is known of the life-history.

Pathogenicity. Believed to cause diarrhœa.

Genus Giardia Künstler, 1882.

Synonyms. *Lamblia* R. Blanchard, 1888; *Dimorphus* Grassi, 1879, *nec* Haller, 1878; *Megastoma* Grassi, 1881, *nec* de Blainville.

Definition. Octomitidæ with one antero-mesial pair, two pairs of mesial and one pair of posterior flagella; nucleus usually double; sucker present.

Type Species. *Giardia intestinalis* (Lambl, 1859).

Giardia intestinalis (Lambl, 1859).

Synonyms.— *Lamblia intestinalis* Lambl, 1859; *Cercomonas intestinalis* Lambl, 1854; *Hexamitus duodenalis* Davaine, 1875; *Dimorphus muris* Grassi, 1879; *Megastoma entericum* Grassi, 1881; *Megastoma intestinale* Blanchard, 1886; *Lamblia intestinalis* Blanchard, 1888.

This parasite lives in the intestine of different species of the genera Mus and Epimys (*M. musculus, E. rattus, E. norvegicus, M. silvestris*); also in species of Arvicola (*A. arvensis* and *A. amphibius*); also in the rabbit, the cat, the dog, the sheep, and man.

It was first observed by Lambl in the mucous intestinal evacuations of children in Russia; then by Grassi in Italy, who made a complete study of the parasite; by Moritz in Germany; by Jaksch in Austria; by Kruse in Egypt; and we have observed it several times in Ceylon; while it has been carefully studied by Werner in 1901, and more especially by Wenyon in 1907 and 1910, and his account is classical. It is common in the Anglo-Egyptian Sudan.

It occurs in the small bowel of man, and it and its cysts can be found in the fæces. Infection is brought about by swallowing the encysted forms. This has been proved experimentally by Grassi, and as it occurs in mice, it is quite easy to see how infection of foodstuffs is possible.

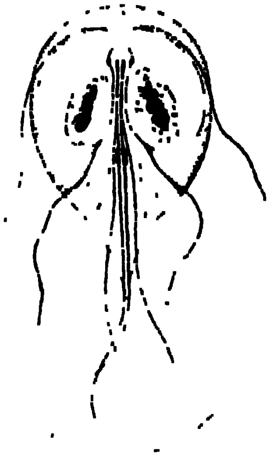

FIG. 145. — *Giardia intestinalis* (LAMBL, 1859).
(After Wenyon.)

G. intestinalis is an actively motile organism about 12 to 21 μ in length, and about 5 to 12 μ in breadth. It is pear-shaped, being surrounded by a thin periplast (ectoplasm), which keeps its form. The under surface (when attached) is excavated with a well-defined border, which is interrupted at the site of the cytostome. This hollow is probably a kind of peristome, and is useful in fixing the parasite to the intestinal epithelium.

There are two oval nuclei, with definite nuclear membranes and with large irregular karyosomes in their centres. There is no connection between these nuclei, but between them lie two darkly staining rods with expanded ends, and which posteriorly are continuous with the prolongations of the posterior flagella into the body. From the thickened posterior ends of the two rods spring the mesial pair of flagella, while at their anterior ends is a small granule, from which arises the anterior pair of flagella, which, running forwards and inwards, cross one another and pass across the peristome, or sucking disc or sucker, to its raised margin, around which they run, forming a kind of membrane, till nearly at the level of the nucleus they become free on each side.

From the same anterior pair of granules there arise the second and finer pair of mesial flagella, running down on the mesial aspect of the nuclei, behind which they turn outwards along the margin of the sucker and finally become free.

Sometimes there is a row of granules extending from the anterior granules to the nucleus on the same side.

Behind the two nuclei there is a triangular area, which forms a groove running towards the tail. Dorsal to this groove lie two darkly staining masses.

In addition in the living animal refractile granules can be seen lying in the anterior part of the animal on each side of the mesial line. From each of these granules a fine line runs posteriorly, and all these lines converging, as it were, into the handle of a fan, end in the tail, with the movements of which they may be concerned.

Life-History.—Reproduction may take place by binary fission. The process is very complicated, the whole system of sucking disc and flagella being reproduced dorsally, and then the flagellate splits longitudinally, the fissure passing from before backwards between the sucking discs.

Kofoid and Christiansen have described multiple fission in the lamblia of mice, but this has not been seen in those in man.

Encystment begins by a thin wall being excreted, inside which the flagellate can be seen moving. Later the cyst becomes ovoid and the wall tougher, and the contained lamblia may or may not have undergone division. Conjugation is not known to occur.

The cysts are oval and measure 13-14 × 6-7 microns; the wall is smooth and transparent. Later the nuclei divide, giving rise to four nuclei in all, which are crowded together.

Method of Infection.—The cysts escape in fæcal matter and are taken into house-flies, Musca and Fannia etc., and passing into the intestine, eventually escape in the flies' droppings, and so can infect human food.

Pathogenicity.—It is usually believed to be the cause of the diarrhœa with which it is associated.

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CHAPTER XXI

TELOSPORIDIA

Telosporidia—Gregarinida—Coccidiidea—Hæmosporidia—Hæmogregarinidæ—Toxoplasmidæ—Piroplasmidæ—Plasmodidæ—Hæmoproteidæ—References.

PHYLUM III. TELOSPORIDIA Schaudinn, 1900.

Synonym.—*Eimerioinea* Poche, 1913.

Definition.—*Parasitic plasmodromata* without motile organs, in which the reproductive phase of the life-cycle, which produces spores, is distinct from and follows after the trophic phase.

Remarks.—All the Telosporidia are parasitic, and usually begin their life-cycle as small amœboid bodies, with a single nucleus, called trophozoites, which absorb nutriment and grow, and when fully developed show a cuticle, an ectoplasm, and an endoplasm. The endoplasm is granular, and contains a vesicular nucleus with chromatin karyosomes. The nucleus of the fully-grown trophozoite now begins to divide, and the parasite is known as a schizont, which reproduces by spore-formation. These spores, called merozoites, complete the cycle of asexual reproduction called schizogony. At some stage in the life-history of the parasite, generally when conditions of life are not favourable, some merozoites are produced, which, instead of developing into trophozoites, become sexual gametocytes, male and female. These forms, which are often resistant, are the means of transmitting the given species from one host to another. They produce gametes, which conjugate and form bodies called sporoblasts, and, lastly, spores called sporozoites.

Classification.—The Telosporidia are divided into three orders: Gregarinida, Coccidiidea, and Hæmosporidia, while the two latter are often put together into the Coccidiomorpha.

These may be recognized as follows:—

A. Only young trophozoites intracellular—*Gregarinida*.
B. Full trophozoite stage intracellular—*Coccidiomorpha*.
    I. With resistant spores in the sporocysts—*Coccidiidea*.
    II. Without resistant spores in sporocysts—*Hæmosporidia*.

ORDER I. GREGARINIDA Lankester, 1866.

Synonyms.—*Gregarinidea* Lankester, 1885; *Gregarinæ* Haeckel, 1866.

Definition.—Telosporidia, in which only the young trophozoites are intracellular, the fully-grown forms being extracellular.

Reproduction by Schizogony or Sporogony.— The gregarines are essentially parasites of the invertebrata, not being found in true vertebrates, though known in Amphioxus and Ascidians. They are generally found in the Arthropoda and worms, and appear to be non-pathogenic.

Their life history may be briefly described as follows: The young trophozoite enters a cell, generally of the alimentary canal, in which it grows, apparently causing considerable damage, for the cell first swells and afterwards degenerates.

In the meanwhile the parasite has found its way either wholly or partially out of the cell, to the remains of which, however, it is attached until all nourishment is extracted, when it becomes cœlozoic—*i.e.*, it leaves the remains of the cell, and dwells either in the alimentary canal, the cœlome, or the blood stream. The young parasite is unicellular, having its cytoplasm divided into ectoplasm and endoplasm. The ectoplasm is hyaline, and when fully developed has three layers—(1) external epicyte, (2) middle sarcocyte, (3) internal myocyte.

The last named contains contractile fibrils called myonemes. The endoplasm is granular, and contains a well-developed vesicular nucleus. A unicellular gregarine, such as this, belongs to the suborder Acephala, and is illustrated by *Monocystis agilis* Stein, which is found in the vesiculæ seminales of *Lumbricus terrestris*.

On the other hand, in such a gregarine as *Pyxinia frenzeli* Laveran and Mesnil, a part of the sporozoite grows out from the cell, and into this external portion the nucleus travels. The portion left in the cell is known as the 'epimerite,' while the external portion, growing considerably, is divided by a septum into a 'protomerite' near the cell, and a 'deutomerite' away from the cell.

The parasite in this condition is called a cephalont, and belongs to the suborder Cephalina.

In due course the trophozoite, whether entirely or partially in the cell, is set free, either by bursting its way out, or by a separation between the epi- and protomerite. The cell now degenerates, and the parasite may be called a sporont. Sporogony takes place by two sporonts or gametocytes lying side by side becoming enclosed in a cyst with two walls—an external epicyst and internal endocyst.

The karyosomes of the nuclei of the gametocytes now break up into chromidia, which collect to form the generative nucleus. This divides by mitosis to form a large number of nuclei, which, travelling to the surface and surrounding themselves with cytoplasm, become detached as gametes, the rest of the cell forming a *masse de reliquat* or residual mass. Thus, inside the cyst-walls there are gametes from two separate parasites and two residual masses.

Gametes presumably from different individuals fuse and form a true zygote with a synkaryon. Each zygote represents a sporoblast, and each sporoblast becomes a single spore by the secretion of a chitinous cuticle and the contraction of its protoplasm (called by Minchin the 'sporoplasm'). This sporoplasm divides by amitosis into eight sporozoites and a residual mass. During this process the two residual masses of the original cyst disappear. The cyst now contains only the spores which used to be called pseudonavicellæ. These spores are intended to convey infection to a new host, in the intestine of which they set free the sporozoites, which promptly attack either the cells of the intestine or some other organ, thus completing the cycle of sporogony.

Schizogony. This is uncommon in the gregarines, being only found in the Schizogregarinidæ. It is typically seen in *Schizocystis*, in which the trophozoite grows into a schizont, whose nucleus divides into a large number of daughter nuclei, round each of which a portion of cytoplasm gathers, forming a merozoite. This, escaping from the schizont, infects another cell, thus completing the cycle of schizogony. Some of the merozoites may develop by sporogony.

Classification.— The gregarines are classified as follows:

SUBORDER I. SCHIZOGREGARINARIA Doflein, 1909.

Synonyms.—*Schizogregarinæ* Minchin, 1903, *Schizocystina* Poche, 1913.
Reproduction by schizogony and sporogony.
Genera.—*Schizocystis* Léger, 1900, in the intestine of *Ceratopogon*; *Ophryocystis* Schneider, 1884, in the Malpighian tubules of beetles.

SUBORDER II. EUGREGARINARIA Doflein, 1901.

Reproduction as usual by sporogony. Schizogony very rare, if present at all, and only in the earliest cytozoic stages. The Eugregarinida are divided into two tribes.

TRIBE 1. ACEPHALINA Delage Hérouard, 1896.

Synonym.—*Monocystidea* Haeckel, 1866. No epimerite and no septa.
Genera (eighteen described by Minchin).—*Monocystis* Stein, 1848, parasite in the vesiculæ seminales and body cavities of the Oligochætæ and Cyclopidæ: *Zygocystis* Stein, 1848, in *Lumbricus agricola*; *Zygosoma* Labbé, 1899, *Lankesteria* Mingazzini, 1891, in *Ascidians*

TRIBE 2. CEPHALINA Delage Hérouard, 1896.

Synonym.—*Polycystidea* Haeckel, 1866. With epimerite, and with or without a septum in the body.

SUBTRIBE 1 GYMNOSPOREA Léger. Cyst with naked sporozoites (gymnospores).
FAMILY 1: AGGREGATIDÆ Labbé, 1899.
Genus. *Aggregata* Frenzel, 1885 Sporozoites grouped about residual masses.
FAMILY 2 POROSPORIDÆ Labbé, 1899 Each sporoblast giving rise to numerous sporozoites grouped round a residual mass.
Genus.—*Porospora* Schneider, 1875. *P. gigantea* in the lobster.
SUBTRIBE 2: ANGIOSPOREA Spores well developed
FAMILY 1 GREGARINIDÆ Greene, 1859 Trophozoites with simple epimerites.

Genera. *Gregarina* Dufour, 1828. Epimerite conical or knobbed. Species found in cockroaches, earwigs, meal-worms, and in the intestines of other insects. *Gamocystis* in the cockroach, also *Eirmocystis*, *Hyalospora*, *Lasperia*, *Sphærocystis*, *Cnemidospora*, *Stenophora*.
Other families are Didymophyidæ, Dactylophoridæ, Actinocephalidæ, Acanthosporidæ, Monosporidæ, Stylorhynchidæ, and Dolichocystidæ.

ORDER II. COCCIDIIDEA.

Synonyms. *Coccidiomorpha* Doflein, 1901; *Eimeridea* Poche, 1913.
Definition. Telosporidia, parasitic, as a rule, in epithelial cells of vertebrates and invertebrates. Reproduction always by both schizogony and sporogony.
Remarks.—The Coccidiidea were recognized as long ago as 1839 by Hake, who did not know that they were animals, that discovery being made by Remak (1845); while Lieberkühn in 1854 showed that they were allied to Gregarines. Leuckart (1879) gave them the name Coccidium, while Schaudinn in 1900 first described a full and complete life-history of *Coccidium schubergi*, which will be taken as the type.

Coccidium schubergi Schaudinn, 1900.

Coccidium schubergi begins its life-history in the intestinal cell of the centipede (*Lithobius forficatus* L.) by a sporozoite pressing its anterior end against an intestinal cell, and thus forcing a way into its interior.

Inside this cell it becomes the young trophozoite, an oval body which grows rapidly at the expense of the protoplasm of the cell, and in twenty-four hours attains its full size.

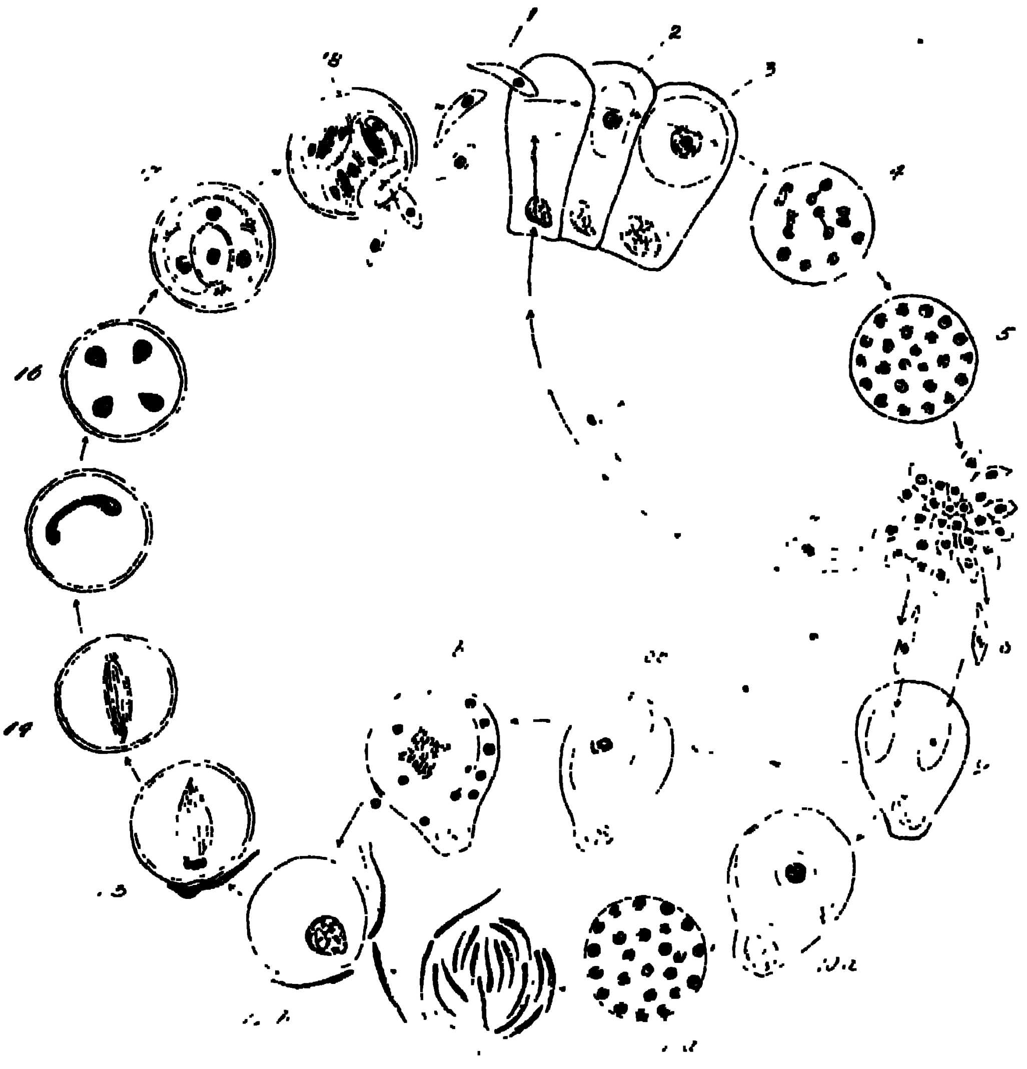


FIG. 190 - DIAGRAM OF THE LIFE-HISTORY OF *Coccidium schubergi* SCHAUDINN. (After Schaudinn)

1, Sporozoite entering an intestinal canal; 2-3, trophozoites; 4-5, schizonts; 6-8, merozoites; 9, young gametocyte; 10a-11a, microgametocyte; 10b-11b, macrogametocyte; 12a, microgametes; 12b, macrogamete; 13-16, oöcyst; 17, sporocysts; 18, sporozoites.

It is now called a schizont, because its nucleus divides into a number of daughter nuclei, which are formed into merozoites in the usual way. These merozoites, set free by the breaking up of the schizont, attack new intestinal cells, thus increasing the infection of the host.

This process cannot, of course, go on for any length of time, for a limit to the nutritive power of the host is reached in five days, when the parasite must attempt to infect a new host, and this is done by sporogony.

Some merozoites now become differentiated into micro- and macro-gametocytes. The former consist of finely granular cytoplasm, with little reserve material, while the latter are bean-shaped and have much food-material. The microgametocyte forms the microgametes by its nucleus becoming irregular, and forming fine achromatic paths through the cytoplasm to the periphery of the parasite, along which chromidia travel from the nucleus. At first, scattered evenly along the periphery, these chromidia gather into patches, and finally fuse into masses, enclosing in each a vacuole. The masses of chromatin lengthen, and by bending project from the cytoplasm, which now forms two flagella, whose active movements set free the microgamete.

In the meanwhile the macrogametocyte becomes a macrogamete by expulsion of the karyosome of the nucleus.

Micro- and macro-gametes now fuse and form a zygote with a synkaryon. The oöcyst, as it may be called, now passes out of the body of the host, and divides into four sporoblasts. Each sporoblast now develops two vacuoles and a cyst-wall, the sporocyst, so that the sporoblast is often called the spore. The nucleus of the spore divides into two, while the two vacuoles fuse and the cytoplasm divides, forming two sporozoites which are capable of infecting a new host, being set free by the acid of the digestive juices.

Sporogony takes about two to three days for completion.

It may be as well at the present time, when so much disputation is taking place *re* Schaudinn's work on trypanosomes, to mention that he worked out this life-history, which has never been refuted, though the parasite was found in company with *C. lacazei* Labbé and *Adelea ovata* A. Schneider.

Classification of the Coccidiidea.—The usual classification is that by Léger in 1900, and is based upon the number of sporozoites in each cyst.

FAMILY 1. ASPOROCYSTIDÆ.—Sporozoites naked, no sporocysts inside the oöcyst.

FAMILY 2. DISPOROCYSTIDÆ.—Oöcyst has two spores.

FAMILY 3. TETRASPOROCYSTIDÆ.—Oöcyst has four spores.

FAMILY 4. POLYSPOROCYSTIDÆ.—Oöcyst has many spores.

FAMILY ASPOROCYSTIDÆ Léger, 1900.

The genus included in this family is *Eimeriella* Stiles, 1902, of which there is only one species. *Eimeriella nova* Schneider, 1819 in the Malpighian tubules of Glomeris.

FAMILY DISPOROCYSTIDÆ Léger, 1900.

The genera of this family are: *Cyclospora* A. Schneider, 1881 (spores dizoic); *Diplospora* Labbé, 1893 (spores tetrazoic); *Isospora* A. Schneider, 1881 (spores polyzoic).

Isospora A. Schneider, 1881.

Definition.—Disporocystidæ with polyzoic spores.

Isospora bigemina Stiles, 1891

Synonym.—*Cytospermium villorum intestinalium canis et felis* Rivolta, 1874.

This parasite lives in the intestinal villi of dogs and cats, and is distinguished because it is small and because it is in pairs, the oocyst dividing into two equal portions, which become encysted and form two spores (*vide* Coccidiosis in man *infra*).

FAMILY TETRASPOROCYSTIDÆ Léger, 1900.

Type Genus.—*Eimeria* A. Schneider, 1874.

Synonym.—*Coccidium* Leuckart, 1879 (the dizoic spores are spherical or oval). **Other Genus:** *Crystallospora* Labbé, 1896 (the dizoic spores have the form of a double pyramid).

Eimeria A. Schneider, 1875.

Telosporidia with the formation of an oocyst after fecundation; sporoblasts in the form of a pyramid; spores globular or oval, provided with a micropyle.

Eimeria stiedæ Lindemann, 1865.

Synonyms.—*Psorospermium cuniculi* Rivolta, 1878; *Coccidium oviforme* Leuckart, 1879, *C. perforans* Leuckart. *Pfeifferia princeps* Labbé, 1896.

This is the common species found in the liver of rabbits. The spores swallowed by the rabbit are opened by the action of the acid of the gastric juice, and the sporozoites set free ascend the bile-duct, and pass into the cells lining the small bile ducts. Here they propagate vigorously by schizogony, causing proliferation of the epithelium and connective tissue of the ducts, so that thick-walled nodules, more or less isolated and containing caseous material (consisting of detritus, pus, epithelial cells, and coccidia), are formed. The inflammation may be severe enough to kill the rabbit.

Sporogony proceeds with the formation of macrogametocytes with macrogametes, and the microgametocytes with microgametes, which conjugate and form zygote, sporoblast, spores, and sporozoites (*vide* Coccidiosis in man, *infra*).

FAMILY POLYSPOROCYSTIDÆ Léger.

Comprises a large number of genera: *Adelea* A. Schneider, 1875 (dizoic); *Klossia* (tetrazoic) A. Schneider, 1875, *Minchinia* Labbé, 1896; *Klossiella* Smith and Johnstone, 1902, *Barrouxia* (monozoic); *Benedenia* (trizoic).

Coccidiosis in Man.

The utmost confusion has existed as to this infection of man, but now, thanks to the labours of Dobell, whose writings we have followed, the subject is more defined.

In 1841 Johannes Muller introduced the name 'psorosperms' for the spores of the myxosporidia, and as the coccidia were believed to resemble these bodies, they were called 'oviform psorosperms' until Leuckart in 1879 gave them the name *coccidium*. The various diseases and cases rightly or wrongly called coccidiosis at any time in man may be considered as follows:—

Diseases now known not to be Coccidiosis. These are (1) a form of blastomycosis (granuloma coccidioides); (2) rhinosporidiosis; (3) Darier's disease, (4) molluscum contagiosum.

Cases wrongly diagnosed as Coccidiosis.—These are the cases described by Virchow (1860), Rivolta (1873 and 1878), Grassi (1879), Podwyssoki (1889), Giles (1890), Jurgens (1895), Quincke (1899), Thomas (1899), Grunow (1901),—and probably by Künstler and Pitres (1884).

Cases correctly recognized as Coccidiosis.—Dobell considers that over seventy cases, mostly from the Near East, have recently been recognized as coccidiosis. The earlier cases are:—

Hepatic.—Gubler in Paris (1858), Dressler in Prague (recorded by Leuckart in 1863), Sattler in Vienna (recorded by Leuckart in 1879), Perls in Giessen (recorded by Leuckart in 1879); Perls and von Sömmering (?) (recorded by Leuckart in 1879), and Silcock in London (1890).

Intestinal.--Kjellberg (recorded by Virchow in 1860) and two cases by Eimer (1870).

Fæcal.--These are numerous. The earliest are Woodcock (1915), Low (1915), Wenyon (1915), Woodcock and Penfold (1916), Dobell (1916), Roche (1917), Cragg (1917), Wenyon and O'Connor (1917), Savage and Young (1917), Castellani and Richards (1917), Martin, Kellaway, and Williams (1918), Boney, Crossman, and Boulenger (1918), while Dobell (1918) has found a new form.

Coccidia found in Man.--The coccidia found in the above cases may be classified as:--(1) *Isospora hominis* Rivolta, 1878, *emendavit* Dobell, 1918; (2) *Eimeria wenyoni* Dobell, 1918; (3) *Eimeria oxyspora* Dobell, 1918; (4) the hepatic coccidium of man. These species may be described as follows:—

Isospora hominis Rivolta, 1878, *emendavit* Dobell, 1913.

Synonyms.--*Psorospermien* Virchow, 1860, Leuckart, 1863, Eimer, 1870; *Cytospermium hominis* Rivolta, 1878, *Coccidium perforans* Leuckart, 1870; *Coccidium bigeminum* var. *hominis* Railliet and Lucet, 1891, *Coccidium perforans* var. *kjellbergi* Labbé, 1896, *Coccidium hominis* Rivolta, 1878, *emendavit* Labbé, 1896, *Eimeria stiedæ* Lindemann, *pro parte* Luhe 1906, *Isospora bigemina* Stiles, 1891, *pro parte* Luhe, 1906.

Definition.--Isospora with oöcysts elongate, ovoid in form, narrow end drawn out into a neck, 25-33 × 12·5-16 microns, with clear, colourless, and porcellaneous wall, with two or more layers and an inconspicuous micropyle at narrow end. Development of spores takes place outside of host, and requires several days for completion. Oöcyst forms two round sporoblasts, from which arise two sporocysts, which form four vermiform sporozoites and leave a large granular sporocystic residue. Habitat, man.

History.--*I. hominis* was discovered by Kjellberg about 1860, in the villi of the small intestine, it was seen in 1870 by Eimer, and was named in 1878 by Rivolta. Its oöcysts were probably first found in human fæces by Railliet and Lucet in 1890, but the first clearly recognizable account is that given by Wenyon in 1915, since when some fifty cases of infection have been recorded, making in all, with the cases seen by Castellani and Richards in the Balkans, about seventy infections.

Distribution.--It has been found in people coming from Gallipoli, Salonika, Egypt, Mesopotamia, and in the Balkans.

Pathogenicity.--This is believed to be nil, as most cases showed merely a small and transitory infection. Animals have so far not been infected with this parasite.

Eimeria wenyoni Dobell, 1918.

Synonyms.--*Eimeria* (Coccidium) Wenyon, 1915; *Coccidium* (Eimeria) Wenyon, 1916; *Eimeria* sp. Dobell, 1917.

Definition.--Eimeria with a spherical oöcyst, 20 microns in diameter, with outer surface rough and rugose, inner smooth and lined by a delicate membrane. Four oval spores measuring 10 × 7 microns. External surface of sporocyst rough. No oöcystic residual body. Each spore contains two typical sporozoites and one or two sporocystic residua. Habitat, man.

History.—This parasite was found by Woodcock and Wenyon, in 1915, in the fæces of a British soldier from Gallipoli. It was again found by Roche in 1917 in three cases at Salonika, so that the total infections up to date (1918) are four.

Distribution.—Shores of the Eastern Mediterranean.

Pathogenicity.—Unknown and no attempts so far made to infect animals.

Eimeria oxyspora Dobell, 1918.

Definition.—Eimeria with spherical oöcyst 36 microns in diameter, with faintly yellow transparent wall, composed of at least two distinct layers, containing four dizoic spores and a small oöcystic residue. Spores long, sharply pointed at both ends, 30-32 × 7·5 microns. Sporocyst has a tough endospore and deciduous epispore, the remains of which give the spore a frilled appearance. There are two sporozoites in each spore, with pointed anterior and rounded posterior ends which contain the nucleus.

History.—The parasite was found by Dobell in a young man who had been in South Africa, Ceylon, and India.

Distribution.—Unknown.

Pathogenicity.—Infection small, but pathogenicity not certainly known, because the patient was infected with *E. histolytica* and *Ancylostoma*. Believed not to be pathogenic.

The Hepatic Coccidium of Man.

Synonyms. *Cellules ovoides* (?) *œufs d'helminthes* Gubler, 1858; *Corps oviformes* Davaine, 1860; *Psorospermien* Leuckart, 1863; *Psorospermi* Rivolta, 1873; *Coccidium oviforme* Leuckart, 1879; *Coccidien leberpsorospermien* Butschli, 1882; *Coccidium cuniculi* (Rivolta) Blanchard, 1896; *Eimeria stiedæ* (Lindemann) Lühe, 1906; *Eimeria* (?) sp. Dobell, 1918.

Definition.—Not at present capable of definition.

History.—It was first recorded by Gubler in 1858, in a quarryman, aged forty-five, in Paris. This man is said to have died from peritonitis. He suffered from digestive troubles, anæmia, and had an enlarged liver. Post-mortem the liver contained many tumours of a cancerous appearance, in which were numerous ovoid cells or eggs of helminthes, at least four times the size of the largest cells of the surrounding tissue. Some had a distinct double contour, and were completely filled with granular contents. One end was rather blunter than the other, which showed a slight constriction, and had a small depressed surface, as though an operculum or micropyle were present.

The second case was found by Dressler of Prague, and consisted of three small nodules in the margin of a human liver. These nodules contained a whitish pulp, which surrounded oval bodies 18-20 microns in length, and his drawings show four oöcysts. The third case was discovered by Sattler of Vienna in a pathological preparation. It showed a dilated bile-duct with greatly proliferated epithelium and coccidia.

The fourth case is by Perls; it was from a preparation made by von Sömmering, and is said by Leuckart to have contained coccidia.

The fifth and last case is that described by Silcock in 1890 at St. Mary's Hospital, London. A woman aged fifty had enlargement of the liver and spleen, with fever and slight diarrhœa. At the post-mortem the liver was much enlarged and showed a number of caseous foci. The ileum contained six papule-like elevations surrounded by an inflammatory zone, and the large intestine had deeply congested patches of mucosa.

In the caseous nodules were agglomerations of small oval, egg-like bodies, with granular contents and a well-marked capsule, and were considered to be identical with Leuckart's coccidia. They were kept in water, and psorosperms freely developed. He considered them to be *Coccidium oviforme*, and to be present in the spleen, but does not state anything definite as to the intestine.

In all, therefore, up to 1918, five cases have been recorded.

Dobell does not consider this parasite to be *Eimeria stiedæ*, judging from Dressler's drawings.

Gubler's case was considered to be a hydatid cyst. Dobell's conclusions are that there is a coccidial parasite which very rarely occurs in the human liver, and resembles *E. stiedæ*, but is considerably smaller and is probably a distinct species, though perhaps belonging to the same genus.

Distribution.—Europe.

Pathogenicity.—It causes cyst-like swellings of the liver, with enlargement of that organ.

ORDER III. HÆMOSPORIDIA Doflein, 1901.

Synonym.—*Hæmocytozoa* Mesnil, 1915.

Definition.—Telosporidia, Coccidiomorpha without resistant spores in the sporocysts and with the trophozoite stage intracellular. With alternations of generation, schizogony in a vertebrate and sporogony in a blood-sucking arthropod or leech.

Remarks.—Mesnil considers that the family Hæmogregarinidæ is related to Léger's Adeleidea division of the Coccidiidea, and the Plasmodidæ to the *Eimeridea* division, and that they should find their places in that group. He considers that the genus Leucocytozoön should come into the Hæmosporidia, and that the Piroplasmidæ require more study in the invertebrate before being classified. There is no doubt that Hæmosporidia is merely a temporary order in which to place forms pending a fuller classification, which will probably be on the lines indicated by Mesnil.

Classification.—The following families may be temporarily placed in this order for convenience, and can be differentiated as follows:—

A. *Without hæmozoin* :—
  I. Live in red and white blood cells in the peripheral blood—*Hæmogregarinidæ*.
  II. Live in white cells in the organs—*Toxoplasmidæ*.
  III. Live in red cells in the peripheral blood—*Piroplasmidæ*.

B. *With hæmozoin* :—
  I. Oökinete encysts and forms an oöcyst—*Plasmodidæ*.
  II. Oökinete is not known to encyst—*Hæmoproteidæ*.

FAMILY HÆMOGREGARINIDÆ Neveu-Lemaire, 1901.

Synonyms.—*Hæmosporidia* Labbé, 1894; *Hæmosporea* Minchin, 1903.

Definition.—*Telosporidia*, in which either the gametocytes or the schizonts, or both, are present in red or white cells in the peripheral blood of vertebrates, and in which schizogony takes place either in the cells of the peripheral blood, or in those of some organ, while sporogony takes place in the body of some blood-sucking invertebrate, such as a leech, a tick, a mite, or an insect. Neither schizonts nor sporonts contain hæmozoin.

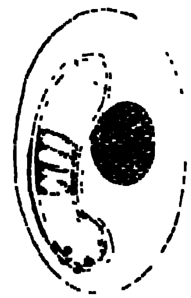


FIG. 147.—*Hæmogregarina canis* SAMBON. (After Sambon.)

History.—Although the first hæmogregarine was discovered in a frog as far back as 1850 by Chaussat, who thought it was a nematode, it is only quite recently, owing to the labours of Sambon, Miller, Miss Robertson, Christophers, and others, that any accurate knowledge has been obtained.

The evolution of the knowledge concerning these parasites may be briefly stated.

Discovered, as mentioned above, by Chaussat, they were next seen by Ray Lankester in 1871, and thought to be a stage in the life history of the frog trypanosome, *T.* (*Undulina*) *rotatorium*, and then by Gaule in 1880, who mistook them for cell inclusions. In 1885 Danilewsky first applied the name 'Hæmogregarina' to the parasites he found in the blood of tortoises and lizards. In 1894 Labbé classified them, according to the relationship between the length of the parasite and that of the blood cell, into (1) *Drepanidium*, parasite not more than three quarters of the length of the host cell; (2) *Karyolysus*, parasite not exceeding host cell in length, and destroying the nucleus; (3) *Danilewskya*, parasite exceeding the host cell in length, and bent upon itself.

The term *Drepanidium* having been previously employed for one of the Heterokaryota, it was necessary to alter it to *Lankesterella*, and the term *Danilewskya* was also altered by Danilewsky in 1897 to 'Hæmogregarina' (*sensu stricto*); but since Sambon and others have described so many new species this classification no longer stands, nor can a natural arrangement be proposed until the life-histories of the various species are fully known; therefore the suggestion of Laveran is being universally adopted, which consists of arranging them according to the classes, orders, and genera of the hosts, and distinguishing only one genus, *Hæmogregarina* Danilewsky, 1885, the various species of which are arranged into four groups: (1) Hæmogregarinida of mammals; (2) Hæmogregarinida of reptiles; (3) Hæmogregarinida of amphibia; (4) Hæmogregarinida of fish. With regard to the Hæmogregarinida of mammals, they were first discovered by Bentley in the blood of a pariah dog (*Canis familiaris*) in Assam, and confirmed by James in 1905. In 1905 Balfour discovered *Hæmogregarina jaculi* Balfour, 1905, in *Jaculus gordoni* in Khartoum, and described the cycle of schizogony, but though numerous experiments were conducted with *Xenopsylla cleopatræ*, species of *Dermanyssus* (mites), and *Clinocoris rotundatus*, only the liberated gametocytes have been traced. A danger is to mistake *Crithidia pulicis* of the flea for a developmental stage of the *H. jaculi*.

In 1905 Christophers discovered *H. gerbilli* in the Indian field rat (*Gerbillus indicus*), and traced its schizogony and later cyst formation in a louse (*Hæmatopinus stephensi*); but he did not observe conjugation, nor did he reinfect rats from the louse, and finally in 1907 he appears to think it probable that the cysts he described may have nothing to do with the hæmogregarine.

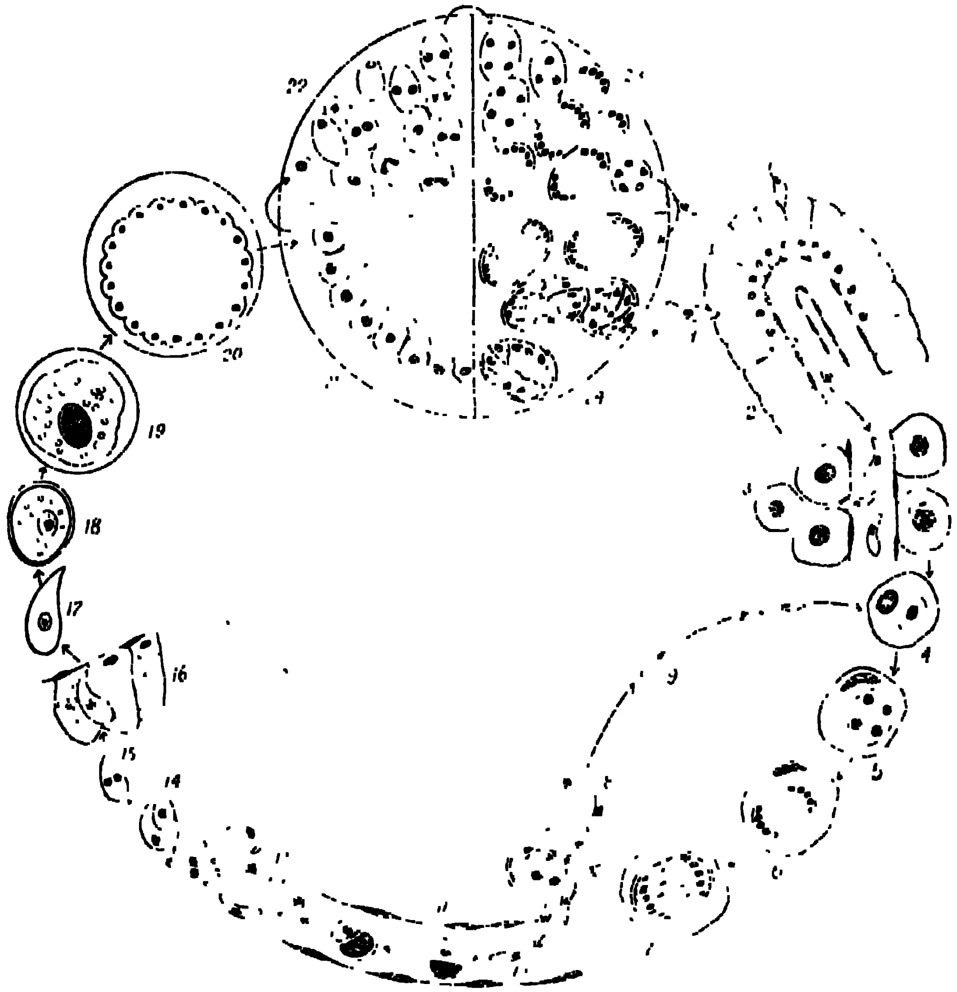


FIG. 198.—LIFE-CYCLE OF *Hæmogregarina muris* BALFOUR.
(After Miller.)

1, 2, Free sporozoites in the intestine of the rat penetrating the villus and entering the blood; 3, entering the liver cells; 4-8, schizogony in the liver; 9, merozoite about to reinfect a liver cell; 10-11, merozoite infecting a white blood cell; 12, free vermicules in the stomach of the louse; 13, conjugation; 14, the zygote; 15, ookinete in the stomach; 16, ookinete in the wall of the stomach; 17, oökinete; 18-19, oöcyst; 20, sporoblasts appearing; 21, early sporoblasts; 22, sporoblasts; 23, late sporoblasts; 24, formation of sporozoites

In 1906 Adie discovered a hæmogregarine in *Epimys rattus*, Balfour one in *E. norvegicus*, Christophers another in *Felis domestica*, Patton another in *Funambulus pennantii*.

In 1907 Christophers traced the sporogony of *H. canis* in *Rhipicephalus sanguineus*. In 1908 Miller contributes a most valuable paper on *H. muris* Balfour, 1905, under the term *Hepatozoon perniciosum* Miller, 1908, in which he not merely traced out the cycle of schizogony, but also fully that of sporogony. This was the first description of the full life-history of a hæmogregarine ever given. This paper is also of the greatest importance in arranging the classification of the Hæmogregarinida, for, as already stated, Ray Lankester in 1871 believed that *H. minima* might be a stage of *Trypanosoma rotatorium*, and in this was supported by Billet in 1904, who considered that he could infect clean frogs with hæmogregarines by the bites of leeches containing trypanosomes.

Brumpt's experiments in 1904 on the sporogony of *H. bagensis* in the leech (*Placobdella catenigera*) also supports this theory by finding a binucleate condition in the oökinetes. Miss Robertson believes that hæmogregarines have a trypanosoma stage. These observers would therefore classify the Hæmogregarinida with the Binucleata; but against this Brumpt in 1907 has shown that Billet was probably mistaken, for if leeches infected with *T. inopinatum* are placed on a 'clean' frog a trypanosomiasis results, and the fact that though Sambon has often seen hæmogregarines in snakes and lizards, trypanosomes are absent or rare.

The life-history of *H. muris* as worked out by Miller shows no trypanosome stage, and clearly indicates that the Hæmogregarinida belong to the Telosporidia, and are related to the Gregarinida and Coccidiidea, as was pointed out by Laveran in 1898.

With regard to the Hæmogregarinida of reptiles, a very complete work is that of Sambon in 1908 on the parasites in snakes, where a full history will be found. Those which occur in tortoises and crocodiles have been studied by Danilewsky, Castellani and Willey, Miss Robertson, Dobell, and others, while Siegel has worked out fully the schizogony and sporogony of *H. stepanowi* in the leech.

The Hæmogregarinida of lizards have been studied by Danilewsky, Laveran, Minchin, C. França, and others, and those of amphibia by Chaussat, Lankester, Billet, Durham, Brumpt, Labbé, Lesage, and others.

Life-History.—The most accurately known life-history is that given for *H. muris* Balfour by Miller.

Schizogony.—The asexual reproduction takes place in the cells of the liver, in which the young trophozoite appears as a small spherical organism with a large vesicular nucleus containing a well-defined karyosome. The trophozoite grows at the expense of the liver cell, the nucleus of which is pushed to one side, and in due course becomes a schizont, which divides into twelve to twenty merozoites, and a 'rest' body.

Some of these merozoites on liberation enter fresh liver cells, and continue the cycle of schizogony, while others enter mononuclear leucocytes, in which they become encysted, and develop into gametocytes.

Sporogony.—Sexual reproduction takes place in a mite belonging to the Gamasidæ called *Lelaps echidninus* Berlese, which lives on the blood of the rat.

The gametocytes, liberated from the leucocytes by the digestive action of the juices of the mite's gut, arrange themselves in couples, which are at first exactly similar, but which later differentiate into a large encircling form, which is more granular, and which is probably the macrogamete, and a smaller, more rounded, and less granular microgamete. Zygosis now takes place, forming an oökinete, which grows, and leaving the gut by piercing the wall, forces its way into the body cavity, which consists of a series of small spaces between the organs, and further into the sheaths of the muscles, and into the investing membrane of the salivary glands.

In the tissues the oökinete encysts and becomes the oöcyst, which grows rapidly in size, and undergoes nuclear division.

The daughter nuclei migrate to the periphery, which becomes covered with 50 to 100 bud-like projections, in each of which a nucleus is to be found. These buds break off from the central mass, and form the sporoblasts, the nuclei of which divide, forming daughter nuclei, which gather at the poles, while the whole sporoblast encysts. Short rod-like processes of cytoplasm, each containing a nucleus, now break off from the sporoblasts, each of which becomes a sporozoite, of which there are on an average sixteen to each sporoblast.

Infection of the rat takes place by ingestion of the mite, when the sporozoites are liberated by the juices of the duodenum, and become actively motile striated vermicules, which penetrate the intestinal villi, enter the blood stream, and are carried to the liver, into the cells of which they penetrate, and start the cycle of schizogony.

As the mites leave the rats during the day-time, and only feed on them during the night, it is easy to understand the manner in which the disease spreads from the sick to the healthy.

Variations in the Life-Cycle.—The life-history of *H. muris* is peculiarly interesting, because it is fully known, but it is not quite typical for all hæmogregarines, for in it the gametocytes alone are found in the peripheral blood, and they are enclosed in leucocytes.

Other species, however, show marked differences from *H. muris*, for the majority are found in red, not white, corpuscles, while in some the whole process of schizogony is completed in the blood stream; therefore a few more general remarks are necessary to supplement the life history given above.

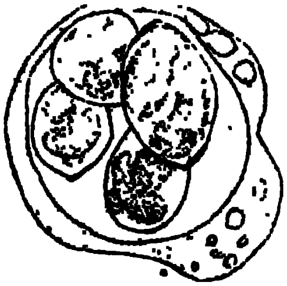


FIG. 149.—*Hæmogregarina nicoriæ* ROBERTSON, SHOWING SCHIZOGONY.

(After Miss Robertson.)

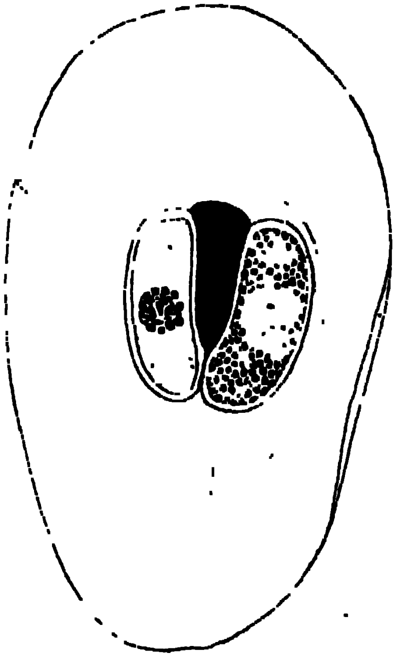


FIG. 150.—*Hæmogregarina rarefaciens* SAMBON, SHOWING MALE AND FEMALE SCHIZONTS.

(After Sambon.)

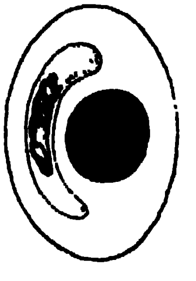


FIG. 151.—*Hæmogregarina rarefaciens* SAMBON: YOUNG GAMETOCYTE.

(After Sambon.)

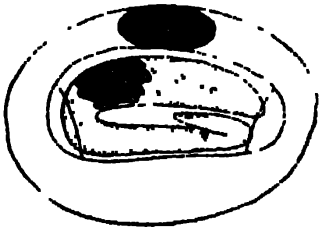


FIG. 152.—*Hæmogregarina seligmanni* SAMBON, SHOWING CAPSULE AND CLEAVAGE LINES.

(After Sambon.)

The peripheral blood of the vertebrate can contain trophozoites, schizonts, and gametocytes lying either in red or white corpuscles, the two latter being contained in a double capsule, which is probably formed by the parasite, and which is always in close attachment to the nucleus of the host cell.

Schizogony begins with the young trophozoite lying free in the enclosing cell, as an oval, fusiform, or club-shaped mass of cytoplasm with a large, homogeneous nucleus. As this trophozoite grows it becomes encapsuled, and forms the schizont, which, when fully grown, is a large oval or rounded body, with a central nucleus, and with the cytoplasm filled with spherules. This schizont usually lies in an enlarged and dehæmoglobinized cell, in which it is seen to be surrounded by a thick capsule, which shows three definite cleavage lines, of which two cross it transversely a short distance from either pole, while the third is longitudinal.

There are two varieties of schizonts, one which gives rise to relatively few large merozoites called ' macromerozoites,' while the other breaks up into relatively many small micromerozoites.

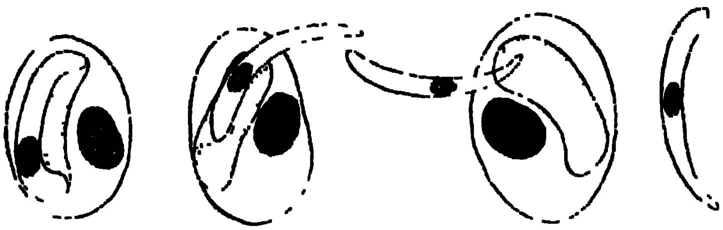


FIG. 153.—*Hæmogregarina mirabilis* CASTELLANI AND WILLEY, SHOWING THE ESCAPE OF THE GAMETOCYTE FROM ITS CAPSULE.

(After Castellani and Willey.)

This differentiation is considered to be a prelude to the formation of macro- and micro-gametocytes. Usually the schizont divides into eight, twelve, or sixteen merozoites, which may escape from the enclosing cell in the peripheral blood, but more generally do so in an organ, such as the liver, lung, or bone-marrow. Other hæmogregarines, like *H. jaculi* and *H. muris*, undergo segmentation in the cells of an organ such as the liver.

The gametocytes are easily recognizable from the schizonts, as they lie bent up in the capsule, and because the enclosing cell is not affected by the parasite. It is not possible at present to differentiate between the macro- and the micro-gametocyte.

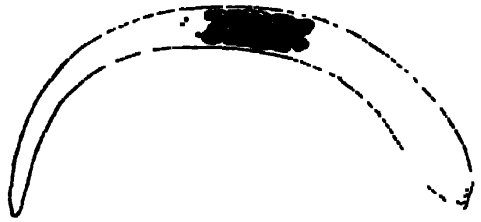


FIG. 154.—*Hæmogregarina seligmanni* SAMBON: FREE SPORONT.

(After Sambon.)

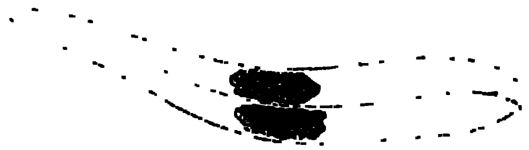


FIG. 155.—*Hæmogregarina seligmanni* SAMBON.

According to Sambon, this figure probably represents conjugation.

(After Sambon.)

In shed blood they quickly escape from the capsule, which may be seen to be double, for Sambon depicts a gametocyte which has escaped from the outer wall of the capsule, but has the inner wall still adherent.

When free, they are seen to be of an elongated, club-shaped form. At the thicker end, which is anterior, there projects a small retractile rostrum or beak, from which a clear line, probably a cytostome or pharynx, runs backwards through the cytoplasm, and ends near the nucleus.

The ectoplasm shows at times a differentiation into three layers—epicyte, sarcocyte, and myocyte—while the endoplasm is granular, and about its middle is found the round or oval nucleus.

According to Sambon, conjugation can be seen taking place in blood spread on an ordinary slide. The further history of the cycle of sporogony is only known in *H. muris* and *H. canis*; the former has already been described, and the latter will be mentioned later.

Recently Henry has shown that Balfour's infective granule is a phase in the life-history of *H. simondi*. Hæmogregarines can be cultivated in Nicolle's blood-agar medium.

No hæmogregarines are at present known in birds nor, until recently, in man, but some peculiar parasites have been seen by Castellani and Willey and others in the peripheral blood of man (p. 538); whether these will prove to be hæmogregarines, or whether they belong to some other order of the protozoa, remains to be seen. Krempf has recently described a hæmogregarina in the spleen of a Chinese.

Classification.— As already mentioned, the species of the genus *Hæmogregarina* Danilewsky, 1885, will be arranged according to their hosts. Some authors recognize *Hepatozoon* Miller, 1908, with *H. muris* Balfour, 1905, as a type, and distinguish it by living in leucocytes, and sometimes undergoing schizogony in the cells of the internal organs.

HÆMOGREGARINES OF THE MAMMALIA.

Hæmogregarina hominis Krempf, 1917.

Definition.— *Hæmogregarina* found only in the spleen of man suffering from splenomegaly, in China.

Remarks.— The infection appears to have been acquired in China.

Morphology.— The parasite lives in red cells which increase in size. Inside the red cells the organism lies in a capsule, 10 × 5 microns, and is vermicular in shape, being bent or twisted. There is a granular nucleus, mostly central in position. Parasites which have escaped from the red cells and lie free in the plasma are identical with those found in the cells.

Life-History.—Unknown.

Pathogenicity.—Believed to cause splenomegaly.

Hæmogregarina muris Balfour, 1905.

Synonyms.—*Leucocytozoon muris* Balfour, 1905; *Hepatozoon perniciosum* Miller, 1908.

H. muris is found in the mononuclear leucocytes of *Epimys norvegicus* in Khartoum, and in white rats in Washington, D.C. Its schizogony and sporogony in *Lelaps echidninus* have already been described (p. 479). It caused anæmia, severe illness, and death in the rats.

Hæmogregarina canis James, 1905.

Synonym.— *Leucocytozoon canis* James, 1905.

Hæmogregarina canis was discovered by Bentley in the blood of a pariah dog, *Canis familiaris*, in Assam, and this discovery was fully confirmed by James in 1905. Christophers was the first investigator to trace out its full life-history in 1906-07.

It appears to be common in pariah dogs in Assam and Madras, but more particularly in the puppies and less common in the adults. It is also found in Ceylon, and, according to Dutton, Todd, and Tobey, it probably occurs in dogs in the Gambia.

Morphology.—The parasite is seen in the white corpuscle of the peripheral blood as an oval, unpigmented mass which is difficult to stain, and which lies in two envelopes—an outer formed from the cytoplasm of the corpuscle, and an inner formed by itself. The cell in which it lies is not typical of any corpuscle, though at first sight it resembles a polymorphonuclear leucocyte. When stained, it is seen to possess a nucleus in the shape of a mass of chromatin stretching across the body at one end.

Schizogony.—Schizogony appears to take place only in the bone-marrow, and has not been seen in the liver or spleen. It begins by the parasite gathering into schizonts in liver cells. The schizont divides into a large number of merozoites, leaving no residual mass of undivided cytoplasm. The merozoites probably infect the red blood cells, and after a time can escape into the liquor sanguinis as free trophozoites, and invade the liver cells.

What happens to the free vermicule is not known.

Hæmogregarina funambuli Patton, 1906.

Synonym.—*Leucocytozoon funambuli* Patton, 1906.

This parasite was found by Patton in the large mononuclear leucocytes of *Funambulus pennatii* (the Kathiawar palm-squirrel).

It is found in cysts in the leucocytes, and as free forms in the plasma. No evidence of schizogony could be found. In the gut of the louse (*Hæmatopinus* sp.) parasitic on these squirrels vermicules could be found, and also in the cœlome, but no further development took place.

Hæmogregarina ratti Adie, 1906.

This is a hæmogregarine found in the leucocytes of *Epimys rattus*.

Hæmogregarina felis Christophers, 1906.

Like *H. can* only found in cats. It was discovered by Patton. Schizogony and spor

HÆMOGREGARINES OF REPTILIA.

Hæmogregarines of the Crocodilia.

H. hankini Simond, 1901, in *Gavialis gangeticus* Gmel; *H. crocodilinorum* Börner, 1901, in *Osteolæmus tetraspis* Cope, and in C *cataphractes* Cuv.

Hæmogregarines of the Chelonia.

A very large number of hæmogregarines are known in Chelonia, but the best-studied life-history is that of *H. stepanovi*

Hæmogregarina stepanovi Danilewsky, 1889.

H. stepanovi is a parasite in the red blood-corpuscles of tortoises—*e.g.*, *Emys orbicularis* L. and *Cistudo*

It appears in two forms—one kidney-shaped, and the other long and thin, and bent upon itself

The young trophozoite is club shaped, and grows into the broad kidney form, which in the bone marrow, liver, or spleen breaks up into merozoites, which, escaping from the red cell, complete the cycle by entering new cells.

The trophozoite grows into a large oval form, which elongates until it gives rise to the long thin form which is bent upon itself. If blood containing this form is sucked by a leech (*Placobdella catenigera* Moqu.-Tand), it escapes from the corpuscle in the intestine, and, entering between the epithelial cells, develops into a macrogamete or a microgamete, and forms an oökinete, which wanders into the bloodvessels around the intestine, and so gets to the pharyngeal glands, in which it becomes an oöcyst forming numerous sporoblasts and sporozoites, which complete the cycle of sporogony by entering the tortoise, when it is again bitten by the leech. There is also evidence of the infection of the ova of the leech in the finding of sporozoites in the pharyngeal glands of immature embryo leeches.

Hæmogregarina nicoriæ Castellani and Willey, 1904.

This parasite is common in the tortoises (*Nicoria trijuga* Schweigg) which are found in the ditches and marshy lands round Colombo, and also in Colombo Lake. The young trophozoite grows into the schizont, which divides into merozoites.

Other parasites are:- *H. laverani* Simond, 1901, in *Emyda granosa* Schoepff, *H. mesnili* Simond, 1901, in *Kachuga tectum* Gray; *H. billeti* Simond, 1901, in *Trionyx cartilagineus* Boddert; *H. stepanoviana* Laveran and Mesnil, 1902, in *Damonia reevesii*; *H. rara* Laveran and Mesnil, 1902, in *Damonia reevesii*; *H. mauretania* Sergent, 1904, in *Testudo ibera* Pall.; *H. bagenesis* Ducloux, 1904, in *Clemmys leprosa* Schweigg. Its sporogony is said to occur in *Placobdella catenigera* Moqu.-Tand. *H. vittatæ* Robertson is *Emyda vittata* (Figs. 149, 157, and 158).

Hæmogregarines of the Ophidia.

The hæmogregarines of Ophidia are numerous, but their life-history has not been properly studied. They have mostly been described by Sambon.

Hæmogregarina mirabilis Castellani and Willey, 1904 (Fig. 153).

H. mirabilis is a parasite in the red cells of *Tropidonotus piscator* Schn.

The trophozoite is vermicular and large (12 μ), and stains uniformly blue, leaving no clear pole. The nucleus is dense, and placed near the anterior end, and is enclosed in a well-developed cytocyst, which is stippled with Schüffner's dots.

Other forms are: *H. pythonis* Billet, 1895, in *Python reticularis* Schn.; *H. pococki* Sambon and Seligmann, 1907, in *P. molurus* L.; *H. shattocki* Sambon and Seligmann, 1907, in *P. spilotes* Lacep.; *H. najæ* Laveran, 1902, in *Naja tripudians* Merr.; *H. mocassini* Laveran, 1902, in *Ancistrodon piscivorus* Pal.; *H. crotali* Laveran, 1901, in *Crotalus confluentus*; *H. seligmanni* Sambon, 1907, in *Lachesis mutus*; *H. zamenis* Laveran, 1902, in *Zamenis hippocrepis* L.; *H. mansoni* Sambon and Seligmann, 1907, in *Zamenis flagelliformis* L.; *H. refringens* Sambon and Seligmann, 1907, in *Pseudaspis cana* L.; *H. rarefaciens* Sambon and Seligmann, 1907, in *Coluber corais* Holb.; *H. cantliei* Sambon, 1907, in *Eryx conicus*; *H. terzii* Sambon, 1907, in the boa-constrictor; and many others.

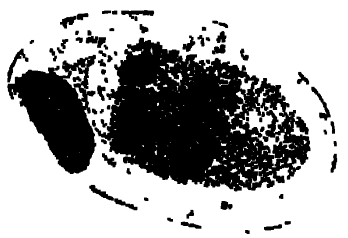


FIG. 157.—*Hæmogregarina vittatæ* ROBERTSON: A BROAD FORM, SHOWING PECULIAR RED BODIES.

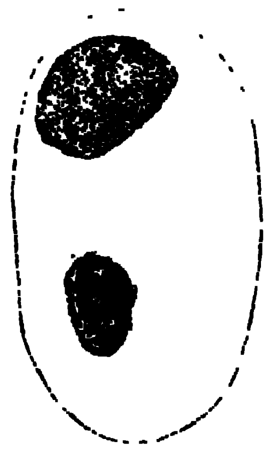


FIG. 158.—*Hæmogregarina vittatæ* ROBERTSON: GAMETOCYTE.

(After Miss Robertson.)

Hæmogregarines of the Sauria.

The best known of these is *H. lacertarum* Danilewsky, 1885, in the red cells of *Lacerta muralis* Laur., *L. viridis* Laur., *L. agilis* L., and *L. ocellata* Daud.

The young trophozoite grows into a schizont, which is enclosed in a cytocyst, and which breaks up into merozoites in the liver, spleen, or kidney.

Among the merozoites there may be macromerozoites or micromerozoites, which are thought to be precursors of the macro- and micro-gametocytes which develop in *Ixodes ricinus* L. This tick may infect the lizard in the adult stage, though this must be rare, as it usually attacks mammals, and then only by its nymphæ and larvæ.

A number are described: *H. thomsoni* Minchin, 1907, in the Himalayan lizard (*Agama tuberculata*); *H. schaudinni* C. França, in *Lacerta ocellata* Daud.

HÆMOGREGARINES OF THE AMPHIBIA.

The best studied of these is *Hæmogregarina minima* Chaussat.

Synonyms. —*Drepanidium ranarum* Lankester, *Laverania ranarum* Grassi, *H. ranarum* Kruse, *Lankesterella ranarum* Labbé.

This parasite is found in the red cells, leucocytes, and tissue cells of *Rana esculenta* L.

Schizogony takes place in the spleen, liver, kidney, and bone-marrow, where the cytocysts containing round schizonts, which break up into five to eight macromerozoites (5 to 8 μ) or numerous micromerozoites (3 to 4 μ).

The sporont is club-shaped, and sporogony takes place, according to Billet, in the leech (*Helobdella*), but his account is very doubtful, and will require confirmation.

Hintze gives a quite different development in the intestine of the frog, but it is possible that he mistook a coccidial parasite for the sporogenic stages.

Durham notes a *Drepanidium* (hæmogregarine) in the blood of a toad in Pará, and a *Dactylosoma* (Labbé) in the internal organs—the former is the schizont, and the latter the sporont—and found evidences of conjugation and cyst-formation in ticks fed on these toads.

H. splendens Labbé, 1908, is found in *Rana esculenta* in Portugal. *H. leptodactyli* Lesage, 1908, is found in *Leptodactylus ocellatus* in Argentina; *Lankesterella tritonis* Fantham, 1905, in *Triton cristatus*.

HÆMOGREGARINES OF THE PISCES.

Fish of all kinds and in all parts of the world appear to contain these parasites.

Hæmogregarina simondi Laveran and Mesnil, 1901.

H. simondi is a parasite in *Solea vulgaris* (the sole). Schizogony takes place in the red corpuscles, the schizont dividing longitudinally into two, four, or eight merozoites. Sporogony takes place in *Platybdella soleæ* Kroger, a leech found on the sole in which ookinetes have been found.

Hæmogregarina anarrhichadis Henry, 1912.

H. anarrhichadis is found in the catfish *Anarrhichas lupus*.

Other fish hæmogregarines are *H. bigemina* Laveran and Mesnil, 1901, in *Blennius pholis*, *H. quadrigemina* in *Callionymus lyra*, *H. platessæ* Lebailly, 1904, in *Pleuronectes platessa*, *H. rovignensis* Minchin and Woodcock, 1910, in *Trigla lineata*.

FAMILY *Toxoplasmidæ* França, 1917.

Definition. Hæmosporidia without hæmozoin generally living in white cells in the organs of vertebrates.

Type Genus. *Toxoplasma* Nicolle and Manceaux, 1908.

Remarks. Only two genera. It is possible that some authors might place *Elleipsisoma* França, 1911, and some allied genera therein. At present we have classified these with the Piroplasmidæ. Ovoplasma may also come here.

Classification. The genera of the Toxoplasmidæ may be recognised as follows:

A. With a definite nucleus—*Toxoplasma*.
B. Without a nucleus—*Ovoplasma*.

Genus Toxoplasma Nicolle and Manceaux, 1908.

Definition.—Toxoplasmidæ of oval or reniform shape, reproducing by longitudinal division or by multiple division inside cells. Live usually in mononuclear and polymorphonuclear cells in the spleen and internal organs. Rarely seen in the blood.

Type Species.—*Toxoplasma gondii* Nicolle and Manceaux, 1908.

Other Species.—*T. cuniculi* Splendore, 1909, found in *Oryctolagus cuniculus* in Brazil, and *T. canis* Mello, 1910, found in the dog in Italy, Germany, and Brazil. These two forms and *T. pyrogenes* Castellani, 1913, found in man are all pathogenic.

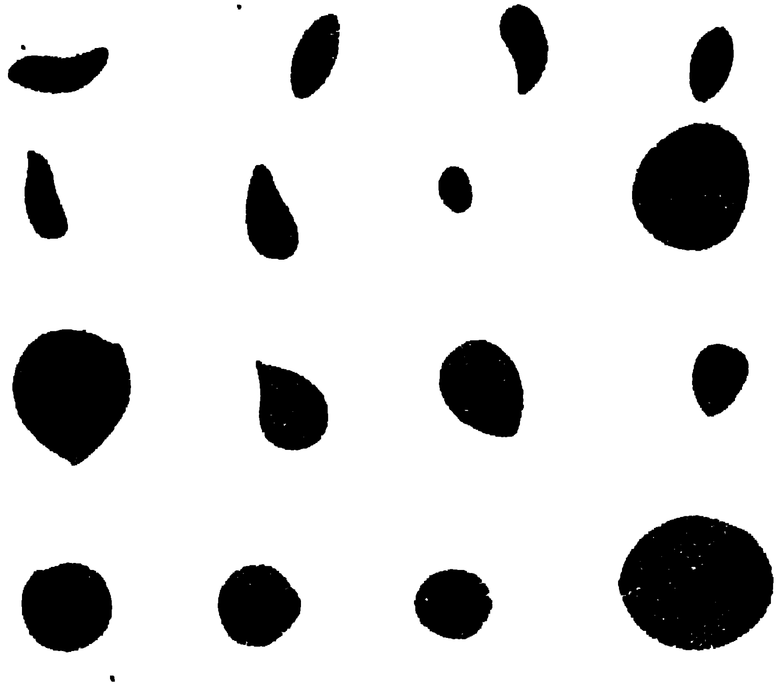


FIG. 159.—*Toxoplasma pyrogenes* CASTELLANI, 1913.

T. talpæ Prowazek, 1910, in Japan, *T. musculi* Sangiorgi, 1913, in *Mus musculus* in Italy; *T. sciuri* Coles, 1914, in England; *T. ratti* Sangiorgi, 1915, in *Mus rattus* in Italy; *T.* sp. (?) Plimmer, 1915, in *Cryptoprocta ferox*; *T. caviæ* Carini and Migliano, 1916; *T.* sp. (?) Thézé, 1916, in *Myceles seniculus* are mammalian parasites.

FIGS. 160-162. *Toxoplasma pyrogenes* CASTELLANI, 191

A number of forms are known in birds—*e.g.*, *T. avium* Adie, 1909; *T. sporophilæ* (Aragão, 1911); *T. neophrontis* Todd and Nolbach, 1912; and *T. françæ* de Melo, 1915; with two unnamed species by Plimmer, 1916, and five by Carini and Maciel in 1916. In snakes one species unnamed was found by Plimmer in 1916.

Toxoplasma gondii Nicolle and Manceaux, 1908.

Endoleucocytic crescentic parasites 6 to 7 μ by 3 to 4 μ, found in the spleen and other organs of *Ctenodactylus gondii*.

Toxoplasma cuniculi Splendore, 1909.

Found by Splendore in the spleen and other organs of the rabbit, in which it produces lesions resembling kala-azar. Shape, oval or reniform; length 5 to 8 μ, breadth, 2·5 to 4 μ.

Toxoplasma pyrogenes Castellani, 1913.

Definition.—Toxoplasma pathogenic to man.

History.—Found by Castellani in 1913 in a case of splenomegaly in the tropics. In 1916 a similar parasite was found by Fedorovitch in the peripheral blood of a case of splenomegaly in a child on the Black Sea coast, and also in the blood of a dog from the same neighbourhood.

Morphology. Roundish oval or crescentic bodies 2·5-6·0 microns in diameter, with blue staining cytoplasm, and with one large roundish mass of chromatin at one pole or in the centre. In one instance the faintest appearance of a flagellum seemed to be present. Occasionally the bodies were larger, roundish or pear-shaped, and possessed two chromatin masses, one at each pole or close together. The bodies were generally free, and only in one specimen were a few found in a leucocyte.

While in the spleen numerous bodies of this description were found in this case, in the peripheral blood they were absent. In the peripheral blood some peculiar structures were observed of roundish or pyriform appearance. They were mostly vacuolated, and took a pale blue colour with Romanowsky, and showed several large masses of chromatin. Castellani at first thought that these might be related to Koch's bodies or *plasmakugel*, which are roundish, oval, or irregularly shaped cells 8-12 microns in diameter, found by Koch in African cattle suffering from East Coast fever. Koch's bodies were later classified under Piroplasma by Gonder who believed them to represent a stage in the life cycle of *Theileria parva*.

Against this hypothesis Castellani observed that they were only present in the blood and not in the spleen, and the chromatin masses were much larger than those in typical Koch's bodies. Castellani was inclined to believe that these bodies found in the blood were related to Toxoplasma found in the spleen in some similar manner to that by which Koch's bodies are related to Theileria. It must be remembered that Castellani's slides were examined by a number of protozoologists and medical men, all of whom agreed as to the parasitic and protozoal nature of the bodies; but while the majority regarded them to be *Toxoplasma*, others held the view that they might represent a new genus between Toxoplasma and Leishmania, and a few thought that they might be a mixture of Toxoplasma with Theileria and Anaplasma.

Life-History.—Unknown.

Cultivation.—So far not cultivated.

Pathogenicity.—Probably the cause of a splenomegaly in man.

Genus Ovoplasma De Raadt, 1913.

Definition.—Toxoplasmidæ without definite nucleus.

Remarks.—Some doubt has been thrown upon this genus and its species.

Type Species.—*Ovoplasma anucleatum* De Raadt, 1913.

Ovoplasma anucleatum De Raadt, 1913.

Definition.—Ovoplasma ring-like, with large vacuole, found in man.

History.—This parasite was found in Borneo in the spleen of a Madurese with splenomegaly, who was born in Java.

Morphology.—The organisms were generally found in mononuclear leucocytes, though rarely they were in the red cells. They were ring-like, with large vacuoles and without any nucleus, but the cytoplasm collects on one side of the vacuole. Sometimes it was pyriform.

Life-Cycle. It reproduces by budding and by binary fission.

Pathogenicity.—May be harmless, but in certain cases pathogenic.

FAMILY *Piroplasmidæ* França, 1909.

Definition.—Hæmosporidia without hæmozoin living in red blood-corpuscles.

Classification.—*Paraplasma* Seidelin, 1911, is the resultant of certain blood conditions, and is not a parasite. *Globidium* Neumann, 1909, and *Immanoplasma* Neumann, 1909, require further investigation.

The following genera can be differentiated:—

1. *Piroplasma* Patton, 1895.
2. *Smithia* França, 1909.
3. *Nuttallia* França, 1909.
4. *Theileria* Bettencourt, França, and Borges, 1907.
5. *Achromaticus* Dionisi, 1900.
6. *Rangelia* Carini and Maciel, 1914.
7. *Rossiella* Nuttall, 1910.
8. *Elleipsisoma* França, 1910.
9. *Nicollia* Nuttall.
10. *Anaplasma* Theiler, 1910.
11. *Bartonella* Strong, Tyzzer, Brues, Sellards, and Gastiaburu, 1915.

A. *Cytoplasm voluminous*:—
   I. Rounded forms in red cells with circular nucleus. Schizogony by binary division inside red cells. Division may continue and form a number of large merozoites—*Rossiella*.
   II. Oval forms in red cells, which they dehæmoglobinize. Nucleus large at one side of parasite. Schizogony in the lung—*Elleipsisoma*.

B. *Cytoplasm easily visible :—*

I. Schizogony known:—

(*a*) Large pear-shaped solitary forms. Numerous merozoites—*Achromaticus*.

(*b*) Small oval or pear-shaped forms, often in pairs, 30-100 merozoites—*Rangelia*.

II. Schizogony unknown:—

(*a*) Division in pairs—*Piroplasma*.

(*b*) Division in fours:—

1. Nucleus without dimorphism—

(A) Pear-shaped swollen parasites occupying the whole breadth of the corpuscle—*Smithia*.

(B) Small oval forms, no bacillary forms—*Nuttallia*.

(C) Bacillary forms—*Theileria*.

2. Nucleus with dimorphism—*Nicollia*.

C. *Cytoplasm usually invisible :—*

I. Coccus-like bodies found in animals—*Anaplasma*.

II. Rounded and rod-like bodies:—

Extremely small, and found in man in Oroya fever—*Bartonella*.

Genus Piroplasma Patton, 1895.

Synonyms.—*Hæmatococcus* Babès, 1888 (*non* Agardh); *Pyrosoma* Smith and Kilborne, 1893 (*non* Péron); *Ixodioplasma* Schmidt, 1904; *Apiosoma* Von Wandollek, 1875 (*non* Blanchard, 1855); *Babesia* Starcovici, 1893; *Amœbosporidium* Bonome, 1895.

Definition.—Piroplasmidæ living inside red cells, without voluminous, but with easily visible, cytoplasm, not possessing any pigment, and multiplying by division.

Type Species.—*Piroplasma bovis* (Babès, 1888).

Classification.—There are a number of species.

A. *In bovines :—*

1. *P. bovis* (Babès, 1888), spread by *Boophilus annulatus*, *B. australis*, and *B. decoloratus*—America, Australia, Asia, and Africa.

2. *P. divergens* MacFadyean and Stockman, spread by *Ixodes ricinus*—Europe.

B. *In sheep :—*

3. *P. ovis* Starcovici, 1893, spread by *Rhipicephalus bursa*—Europe.

C. *In dogs :—*

4. *P. canis* Piana and Galli-Valerio, 1895, spread by *Rhipicephalus sanguineus* everywhere.

D. *In horses :—*

5. *P. caballi* Nuttall, 1910—Europe.

E. *In rodents*:—

6. *P. muris* Fantham, 1905 -England.
7. *P. avicularis* Wenyon, 1908- -Sudan.

F. *In monkeys*:

8. *P. pitheci* P. H. Ross, 1905—-Uganda.

Piroplasma canis Piana and Galli Valerio, 1895.

Synonym.- *Babesia canis* Piana and Galli Valerio, 1895

In 1895 Piana and Galli Valerio found a characteristic hæmatozoon in the red blood corpuscles of a dog which was infested by ticks (*Ixodes reduvius* L.), and which was suffering from fever, weakness, and slight jaundice, after having hunted in marshy localities. This hæmatozoon occupied 3 to 4 per cent. of the corpuscles, and also occurred free in the plasma. In the corpuscles the parasites appeared as pyriform bodies, as many as two, three, four, or five in one corpuscle, and showed amœboid movement. The dog in question recovered, but in other dogs the post-mortem showed fluid blood, congested liver and spleen, with icteric staining of the tissues and necrotic foci in the omentum near the pancreas. Other symptoms noted by them in dogs were hæmoglobinuria, anorexia, prostration, and emaciation.

In 1899 Hutcheon described the disease caused by this parasite as ' malignant jaundice ' or ' bilious fever ' in dogs. It is also known as ' malignant malaria,' ' hondziekté,' and ' malarial fever,' and is said to have often been mistaken for distemper. The disease is by no means uncommon in dogs in the tropics, and should be called ' canine piroplasmosis.'

Geography.- It is known in Europe, especially in Lombardy and other parts of Italy; also in France. In Africa it is found in South Africa, East Africa, Senegal, and other parts of West Africa, and also in North Africa, including Egypt. Nuttall suggests, however, that the African Piroplasma may be different from the European. In Asia it is found in India and Ceylon.

Place and Season. -It appears to be more common in coast towns and districts, and less common in higher inland places. It seems to have a seasonal variation, but this is not properly understood.

The Parasite. The life-cycle in the dog has been most carefully studied by Nuttall and Graham Smith.

In the fresh blood it is noted that the infected corpuscles are pale and enlarged, and contain irregular, dark coloured, pear shaped bodies, possessing a central refractive portion. Amœboid or globular non motile bodies may be noted, and also many free forms.

In specimens stained by Leishman's method the parasites seem to consist of a blue-coloured cytoplasm, with a delicate vacuolated or trabecular structure centrally, but more condensed around the periphery. This cytoplasm may contain a single homogeneous nucleus, which has a vivid red colour, and is often connected by a thin strand with a loose mass of chromatin, which is situated near the blunt end. The parasite contains a vacuole.

Schizogony.- A free pyriform parasite (pyriform stage) enters a normal red blood-corpuscle and becomes rounded (ring stage) in shape, while the loose mass of chromatin is drawn near to the original nucleus, where it condenses. Finally it fuses with that nucleus, forming a single chromatin mass.

The parasite now throws out pseudopodia and appears as an amœba (amœboid stage), and the chromatin subdivides into two unequal masses, connected with a thin strand.

This amœboid stage lasts for a long time, at the end of which the parasite enters upon a quiescent stage, in which the vacuole appears in a subcentral position, and the chromatin, which lies along its margin, has its two masses widely separated, though still connected by the thin strand already referred to. The smaller mass has divided into two, making in all three masses of chromatin connected together by chromatin strands.

Two small symmetrical processes of cytoplasm protrude from the parasite in the neighbourhood of the two small chromatin masses, which they carry with them.

The processes enlarge at the expense of the rest of the cytoplasm, and the vacuole divides, and the so-called trefoil stage is reached, in which the main mass of the chromatin, much reduced in size, lies at the base of the two processes.

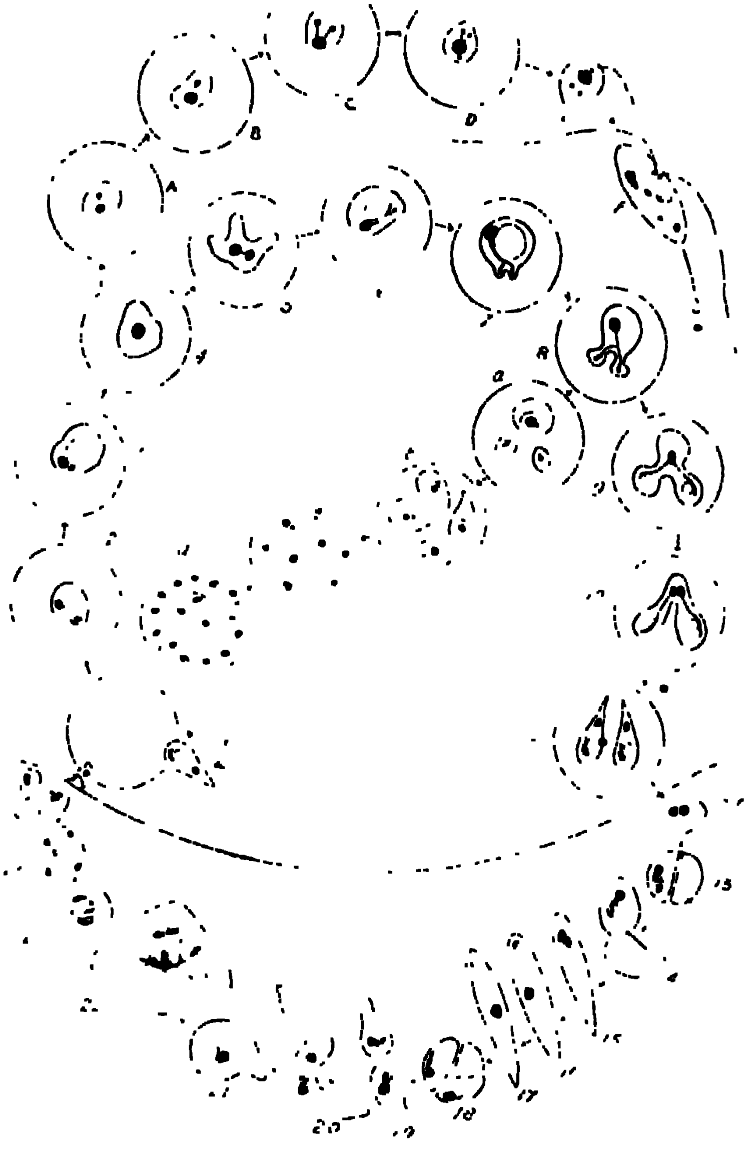


FIG. 163.—DIAGRAM OF THE LIFE-CYCLES OF *Piroplasma canis*.

(After Nuttall and Graham-Smith, Christophers and Breinl and Kinghorn.)

1-12*x*, Reproduction by simple division, *a-a*, reproduction by multiple division, A-F development of a flagellate form; 12*y*-25, sporogony in the tick.

The single strand connecting the two smaller chromatin particles has shortened and disappeared, so that the strand of each small mass now rises directly from the principal chromatin mass. This now divides into two nuclei, connected by a strand, while the cytoplasmic processes become large. Finally, the cytoplasm divides, and two pyriform parasites are found lying side by side in one corpuscle, an arrangement considered typical of a piroplasma. In each parasite is a vacuole, and a principal chromatic nucleus situated near the pointed extremity, from which a tail of loose chromatin runs alongside the vacuole towards the blunt extremity.

The corpuscle now ruptures and liberates the two parasites and some granules, representing residual matter, from the parasite or the corpuscle, or both.

Two slight variations of the process have been described by Nuttall and Graham-Smith; in one the two nuclei and their strands form an hourglass-shaped mass, and in the other the strand and second nucleus form a reticular mass; but both develop into the stage depicted in the diagram. Four pyriform parasites may be found in a corpuscle instead of two, and this may come about by an invasion of the corpuscle by two pyriform shapes, which proceed to division, or by the division of the uninuclear shape into two, both of which proceed to develop regularly. Reproduction by gemmation with the formation of one or two buds has been described by Breinl and Hindle, and of many buds by Kinoshita.

Flagellate Forms.—Nuttall and Graham Smith in 1905 described large forms in the blood of the first dog which they infected in Cambridge by ticks from South Africa. These forms were found on the fourth, fifth, and tenth days, and occurred in the peripheral blood and in that from a kidney. They were sausage-shaped, with rounded or tapering extremities. In some the chromatin was almost entirely concentrated in the middle, while in others it appeared to be of loose texture. Kinoshita has seen similar parasites in blood from the heart, the pancreas, and the lungs after death. The significance of these parasites is not yet understood.

Free parasites with flagella-like processes have been seen by Pound, Bowhill, Le Doux, Nuttall and Graham-Smith, Kinoshita, Fülleborn, and Breinl and Hindle, the last-mentioned observers describing the development of large biflagellate forms from the normal intracellular parasite.

The significance of these forms is not understood, Breinl and Hindle considering that they are such very transient stages in the life-history that they may easily be overlooked.

The development as given by Breinl and Hindle is associated with a binucleated form.

Cultivation.—Kleine, Nuttall, and Graham-Smith have attempted to cultivate *Babesia canis* in defibrinated blood. Kleine has observed elongated forms with radiating processes, similar to those found by Koch in ticks.

Nuttall and Graham-Smith have observed the same forms, but consider them to be intracellular, the hæmoglobin having nearly disappeared from the red cells.

Inoculation.—It was first shown by Dr. Corrington Purvis in 1900 that the disease could be spread from dog to dog by blood inoculation.

Infection from Tick-Bites.—Piana and Galli Valerio, when they discovered the parasite in 1895 in Italy, suspected that it was transmitted by the tick *Ixodes reduvius* L., but the first actual demonstration that this really took place was by Loundsbury in 1901, by the bites of the tick *Hæmophysalis leachi* Audouin, in South Africa.

Dermacentor reticulatus Fabr. is suspected as the spreader of the disease in France.

This subject has been carefully investigated by Loundsbury, who finds that the parent tick, having gorged with blood, falls to the ground and lays her eggs, which develop into six-legged larvæ.

These larvæ do not infect the dog, which they attack as soon as possible, and on whom they remain two days sucking blood. After dropping off, they in due time shed their larval skin, and become eight-legged nymphs, which again bite the dog, but do not infect it.

The nymph, after dropping off, undergoes metamorphosis, and sheds its nymphal skin and becomes the sexually mature tick, which is the only form that spreads the infection, a fact confirmed by Nuttall.

Christophers has traced out the development in *Rhipicephalus sanguineus* Latreille, thus finally confirming the idea of the transmission through the tick.

Development in the Tick.—When an adult tick or a nymph bites a dog and takes in blood containing the oval parasites already described, these parasites develop in the gut into round or oval bodies, 4 to 5 μ in diameter, the chromatin remaining undisturbed.

The cytoplasm now partially divides into a portion with and a portion without chromatin, the latter turning round to form a tail to the former, thus constituting a club-shaped body, which gradually becomes an oökinete.

In the adult these wander into the ova, while in the nymph they simply pass into the embryonic tissue.

In either case they become rounded, and form the zygote, which breaks up into sporoblasts, and these, again, into sporozoites, which infect the salivary glands of the nymph and the adult of the second generation. This development explains Lounsbury's experiments.

Pathogenicity.—The pathological effects are divided by Nocard and Leclainche into two types—the acute, always fatal, and the subacute, ending in recovery.

Acute Form.—In the severe attack the dog quickly becomes ill with high fever ([illegible] C.), accompanied with great weakness. After the attack of fever comes a stage of subnormal temperatures. The mucous membrane becomes pallid, bluish, or icteric. Respiration is laboured, and the movements of the animal are shaky. Vomiting is frequent. The spleen is enlarged, the urine albuminous, and in 3·5 per cent. of cases there is hæmoglobinuria. The blood is pale and watery, and the serum stained with hæmoglobin or bile pigments; the red corpuscles are reduced (in one dog, according to Wright, from 5,800,000 to 1,000,000) and altered, some becoming larger, others smaller, than normal, and often nucleated. The hæmoglobin is diminished, the smallest amount observed being 17 per cent. Usually the leucocytes are increased up to even 60,000, but in some cases they are reduced. Polymorphonuclear and mononuclear leucocytes share the general increase. Phagocytosis is not energetic, being rarely met with. The animal dies in from three to six days.

Subacute Form.—This is characterized by progressive anæmia and feebleness, with sometimes a little hæmoglobinuria or a little icterus. Fever may at first be high, but generally falls to normal. The anæmia is very pronounced, and is accompanied with paralysis, etc.

The attack lasts six weeks, and the convalescence takes three months.

Post-Mortem Appearances.—The mucous membranes are pale, and there is icteric staining of the tissues. Congestion and enlargement of the spleen, more rarely of the liver, œdema of the lungs, congestion of the kidneys, and inflammation of the stomach and intestines may be noted, but sometimes no macroscopical lesions are to be seen.

Histological.—The capillaries of the alveoli are dilated, and their walls show some proliferation of the cells, and there may be leucocytes and red corpuscles in the lumen of the air-cell.

In the heart the capillaries are dilated, and there may be slight hæmorrhages. There is no change in the skeletal muscles. The liver has the central vein and the interlobular capillaries much dilated, as are the intralobular vessels. The fibrous tissue is normal, but the liver cells are distorted, and in many cases destroyed. The spleen contains a large quantity of blood in its pulp. The kidneys only show dilatation of the bloodvessels, especially those of the glomeruli. The suprarenal capsules have all the capillaries (cortex and medulla) dilated, as has the pancreas. In the brain and spinal cord there is only slight dilatation of the capillaries, and slight excess of cerebro-spinal fluid. In the small intestine the vessels of the villi are congested and crowded with infected corpuscles, as are those of the mesentery and omentum. The lymphatic glands are normal, except dilatation of their smaller vessels. The general histological condition is engorgement of the organs by dilatation of the capillaries.

Treatment.—Quinine, benzoate of soda, calomel, etc., have all been advised. Nuttall and Hadwen have introduced Trypanbleu treatment with success.

Piroplasma gibsoni Patton, 1910.

This Piroplasma has been found in dogs and in the jackal (*Canis aureus*) in India by Patton.

Morphology.—In films from the peripheral blood it is seen as small rings 0·1 µ in diameter, with one or two chromatin masses, of which the second is much smaller than the first, to which it is often joined by a pink thread Oval parasites, with a long amœboid process, are also seen.

Division.—Division is by binary fission, giving rise to a number of forms enclosed in one leucocyte.

Pathogenicity.—It causes one variety of canine piroplasmosis.

Piroplasma bigeminum Smith and Kilborne, 1893.

Synonyms.—*Pyrosoma bigeminum* Smith and Kilborne, 1893; *Apiosoma bigeminum* Wandollek; *Babesia bovis* Chauvelot; *Ixodioplasma specificum bovum* Schmidt.

P. bigeminum is the cause of Texas fever in oxen, and appears as pyriform, round, or amœboid cells, and also as flagellate forms. It can be cultivated on artificial media.

Koch has traced the development in the tick, in whose gut the parasites leave the red cell and become long and club-shaped, at the broad end of which is found a round chromatin mass. From the club pseudopodia project.

This club then becomes spherical, and immense numbers of amœba-like forms appear, which are said to grow into clubs.

Pathogenesis.—The disease may exist in two forms, a grave and a benign.

The usual symptoms of high fever, hæmoglobinuria, icterus, anæmia, paralysis, constipation, and death in a week or less, are exhibited in the grave form, in which the mortality is 60 to 80 per cent.

In the benign form there is anæmia without hæmoglobinuria as a rule, and the duration is about fourteen days

The disease can be spread by inoculation or naturally by the bites of infected ticks *Margaropus australis* Fuller in South America, Cuba, Porto Rico, Australia, and the Philippines, and by *M. decoloratus* Koch in South Africa.

Post-Mortem. The usual post mortem signs are visible.

Treatment.—There is no specific treatment. Krägerud advises intravenous injections of 1 in 100 of protargol or formol, and afterwards a beverage of 10 grammes of lysol and carbolic acid in 500 grammes of distilled water.

Lignières recommends chloride of sodium and purgatives. Quinine has also been advised. Nuttall and Hadwen's treatment should be tried.

Piroplasma bovis Babès, 1888.

Synonyms.—*Piroplasma annulatum* Dschunkowsky and Luhe, 1888, *Piroplasma bigeminum* Babès, *Hæmatococcus bovis* Babes.

P. bovis is the cause of red water or hæmoglobinuric fever in European cattle and in red deer (*Cervus elaphus* L.), and is spread by the ticks *Ixodes reduvius* L. and *Margaropus annulatus* Say.

The disease produced may be acute or chronic. In the acute form about 90 per cent. of the red cells are infected by bacillary or ring-like parasites, which cause high fever, quick pulse and respirations, seldom hæmoglobinuria, with convulsions and death in one or two weeks; or a chronic form, with minute coccus-like parasites in 10 to 40 per cent. of the red cells, producing weakness, jaundice, and anæmia. The post-mortem shows hæmorrhages into many organs.

Piroplasma ovis Babes, 1880.

Synonyms.—*Hæmatococcus ovis* Babès, *Piroplasma ovis* Laveran, *Amœbosporidium polyphagum* Bonome.

P. ovis is found in sheep in Europe, Africa, and the West Indies, as large intracorpuscular and extracorpuscular forms, and causes anæmia, hæmoglobinuria, hæmaturia, and bile in the urine, and also blood in the motions. The mortality is 50 per cent.

The post mortem shows œdema of the tissues, enlargement of the spleen, inflammation of the liver, kidney, and bowels, in the last of which there may be ulcers.

The *Piroplasma* is spread by the daughter adult tick developed from the *Rhipicephalus bursa*, which sucked the infected blood. It is inoculable into other sheep.

Piroplasma pitheci P. H. Ross, 1905.

This organism caused piroplasmosis in a species of *Cercopithecus* from Kikuga, in Uganda.

The parasite is a non-pigmented, pear-shaped, oval, or round endocorpuscular body, being 1·5 μ in diameter when round, and 3 by 2 μ to 2·5 by 1·5 μ in the pyriform shapes. It may be single, double, or in multiples of two, four, eight, or sixteen.

Nuttall and Graham Smith have investigated the parasite carefully, and conclude that it is a true *Piroplasma*, and multiplies in the same manner as *P. canis*, and they figure one body in a corpuscle very like the peculiar free forms noted in *P. canis*.

Ross tried inoculation into dogs twice, but though one of the dogs showed a temporary rise of temperature, the experiment failed. No ticks were found on the monkeys, or in the box in which they lived. The disease causes fever, and killed four out of twelve monkeys.

Piroplasma muris Fantham, 1906.

P. muris causes a chronic disease in mice, in which it exists as pyriform intracorpuscular parasites, singly and in pairs (as many as four and six have been seen). The secondary mass of chromatin has not been observed, and no typical dividing forms have yet been seen.

Piroplasma cervi França and Borges, 1907.

This *Piroplasma* is found as bacillary and cross forms in the blood of *Cervus dama* L. Its development is not known.

Piroplasma minense Yakimoff, 1909.

Found in Russia in hedgehogs, and spread by *Dermacentor reticulatus* (?).

Piroplasma aristotelis Denier, 1907.

This parasite is found in *Cervus aristotelis* in Annam.

Genus Theileria Bettencourt, França, and Borges, 1907.

Synonym. *Lymphohæmatocytozoon* Meyer, 1913.

Definition.—Bacilliform or rod shaped forms arranged at times in the form of a cross.

Type Species. *Theileria parva* Theiler, 1903.

Theileria parva Theiler, 1903.

Synonyms.—*Piroplasma theileri*, *Babesia parva* Theiler, 1903; *Lymphohæmatocytozoon parvum* Meyer, 1913.

This is the cause of East Coast fever in cattle in Rhodesia, and is also found in India and Japan.

Parasite.—The parasite appears in the blood as minute bacillary forms or as small rings, which later become larger, and give the typical pyriform appearance, being frequently arranged in the form of a cross. Very large forms, consisting of protoplasmic masses containing numerous chromatin particles, may be found in the endothelial cells of the spleen and lymphatic glands.

Schizogony.—According to Gonder, the large multinucleated plasmodial masses divide into minute merozoites, and lead to the breaking up of the enclosing lymphocyte. The merozoites penetrate into another lymphocyte in the spleen or lymphatic glands, in which they grow and become the multinucleated masses, and so complete the process of schizogony.

Sporogony.—After a time merozoites are produced with a different nuclear structure; these multiply and produce the gametocytes, which, penetrating into the red blood cells, appear in the peripheral circulation. The microgametocytes are the bacillary forms, and the rounded or pear-shaped forms are the macrogametocytes. In Eurhipicephalus these come out of the corpuscles, and the male forms creep about like little amœbæ, while the nucleus undergoes reduction, forming the microgamete. In a similar manner the macrogamete is formed. Copulation takes place, and a zygote in the form of an active oökinete is formed, which enters the salivary glands and breaks up into sporozoites.

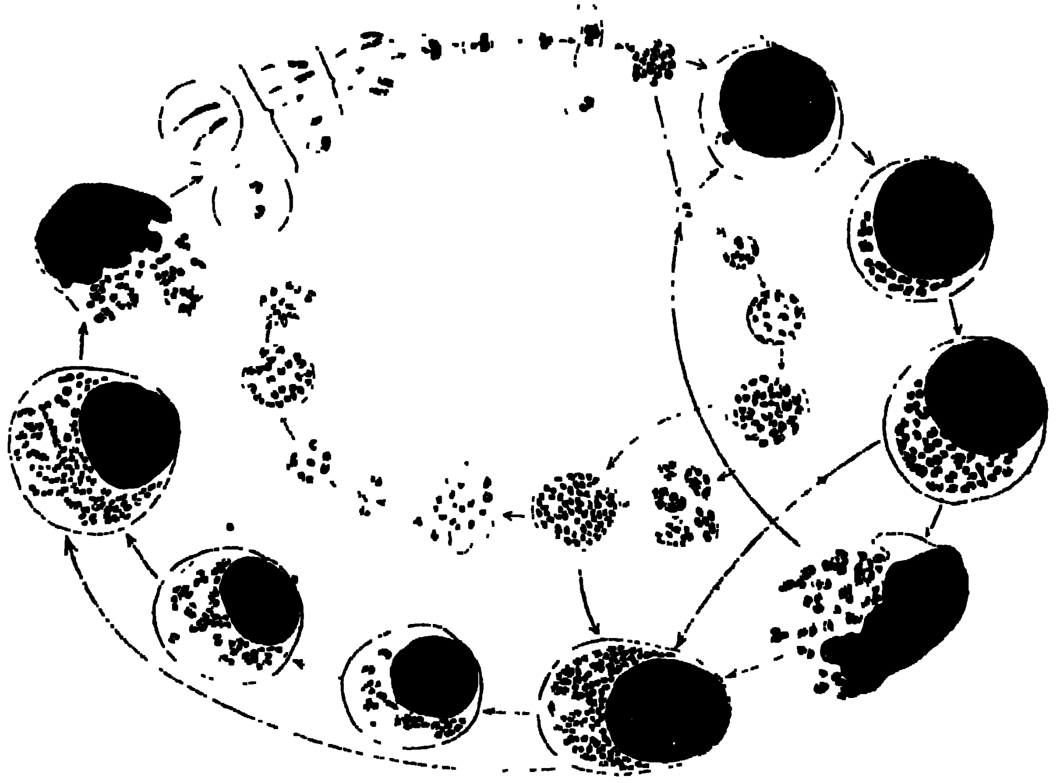


FIG. 164. LIFE CYCLE OF *Theileria parva* (THEILER, 1903).
(After Gonder, from the Report of the First Expedition of the Harvard School of Tropical Medicine to South America in 1913.)

It is spread by *Eurhipicephalus appendiculatus* Neumann, by the nymphs and the adults.

Cultivation.—Miyajima states that he has cultivated the parasite in broth, producing trypanosome-like bodies, but this has not been confirmed.

Inoculation.—It cannot be inoculated successfully.

Incubation.—Fourteen days.

Symptoms.—The symptoms produced are very similar to those caused by *P. bigeminum*, but there is very little anæmia and no hæmoglobinuria.

Mortality.—The mortality is about 90 per cent.

Post-Mortem.—The autopsy shows œdema of the lungs, inflammation of the lymphatic glands, and infarcts in the lungs, liver, and kidneys.

Theileria mutans Theiler, 1907.

Synonym.—*Piroplasma mutans* Theiler, 1907.

This *Piroplasma* is found along with *P. bigeminum*, in cattle in the Transvaal, and produces forms like *Theileria parva*, but distinguished by being inoculable. It is not known how it is spread.

Theileria celli Castellani and Chalmers, 1910.

This parasite is found in *Macacus pileatus* in Ceylon, in bacillary and pear-shaped forms, lying side by side in the same erythrocyte. The development has not been traced.

Theileria buffali Neveu-Lemaire, 1912.

This parasite was discovered by Shein in 1908 in the buffalo in Nha-Trang in Indo-China, and is seen in two forms—an ovoidal, which is most frequently met with, and a bacillary. Its mode of transmission is unknown.

Genus Nicollia Nuttall.

Definition.—Oval or pear-shaped parasites, with an oval nucleus with two karyosomes, one near the centre and another close to the surface of the body, with quadruple division.

Nicollia quadrigemina Nicolle, 1907.

This parasite is found in *Ctenodactylus gondii* in North Africa, and Nuttall and Graham-Smith point out that its method of division and its chromatin are so peculiar that its position is doubtful.

Genus Nuttallia França, 1909.

Definition.—Oval or pear-shaped parasites with multiplication in the form of a cross.

Type Species.—*Nuttallia equi* Laveran, 1899.

Nuttallia herpetedis França, 1908.

N. herpetedis is found in considerable numbers in *Herpestes ichneumon* L., the mongoose, as small spheres, with the chromatin arranged as a cross, or as pyriform shapes, or in fours arranged in cross form.

Nuttallia equi Laveran, 1899.

Synonym.—*Piroplasma equi* Laveran, 1899.

Nuttallia equi is the parasite of piroplasmosis in horses, mules, donkeys, and zebras in Africa, Germany, Italy, and Venezuela.

The disease appears to have been first differentiated by Wiltshire, in 1883, as anthrax fever, which name was changed to bilary fever by Hutcheon. The parasite was first seen by Guglielmi, in Italy, in 1899.

It differs from *P. canis* in existing in large and small spherical forms, in large and small pyriform shapes, in large and small rod-like bodies, in rosettes of four, and sometimes as free flagellate forms. Koch believes that this list includes two different types of parasite—one of parasites arranged in groups of four, and the other like *P. canis*.

It is very difficult to inoculate, and is believed to be spread by the blue tick (*Eurhipicephalus decoloratus*).

The incubation period is not known. The disease begins with high fever, but becomes subnormal before death. The appetite varies. The animal is very weak, and in the later stages becomes paralytic and comatose. Anæmia and jaundice are noted. The pulse varies, being often weak and irregular. The respirations are accelerated. Bowels often constipated; urine is highly coloured, and hæmoglobinuria may occur. The disease may be acute or chronic.

In acute cases death may take place in from two to five days, but the mortality is not high. Secondary and terminal infections may take place.

The post-mortem reveals emaciation and icteric staining, and anæmia of the tissues, enormous enlargement of the spleen, and thin, watery blood. The liver is yellow and congested; the kidneys are enlarged and anæmic; the lymphatic glands are hæmorrhagic, as may be the mucosa of the intestines. The heart is sometimes enlarged. The lungs are usually normal.

Other species are *N. ninensis* Yakimoff, 1910, in *Erinaceus europæus; N. muris* Coles, 1914; *N. decumani* Macfie, 1915; *N. microti* Coles, 1914.

Genus Smithia França, 1910.

Definition.—Pear-shaped forms, not in pairs, occupying the whole diameter of the corpuscles. Forms crosses.

Type Species.—*Smithia microti* França, 1910.

Other Species.—In addition to *Smithia microti* França, 1910, found in *Microtus arvalis*, there is *S. talpæ* Galli-Valerio, 1913, in *Talpa europæa*

Genus Anaplasma Theiler, 1910.

Definition.—Coccus-like parasites, round or oval in form, apparently consisting wholly of chromatin, and devoid of cytoplasm. Flagellate forms said to exist.

Dias and Aragão consider these organisms to be degenerations of red cells.

Type Species.—*Anaplasma marginale*.

Anaplasma marginale Theiler, 1910.

Coccus-like parasites situated near the margin of the corpuscles.

Morphology.—Round or oval parasites consisting only of chromatin substance, sometimes situated in a paler zone of the corpuscle. Multiply rapidly, and invade 40 to 50 per cent. of the corpuscles.

Life-History.—It is spread by the ticks *Eurhipicephalus decoloratus* and *E. simus*, and possibly passes through the egg.

Cultivation.—Veglia claims to have cultivated this organism on defibrinated blood media.

Pathogenicity.—It causes a disease like red water, but different therefrom in that animals immune against red water are susceptible to it. Clinically, it causes a severe type of illness, with fever, anæmia, and diarrhœa, with yellow fæces and urine. The blood shows anisocytosis, poikilocytosis, polychromasia, and basophilia. The post-mortem appearances are anæmia with jaundice, enlarged and yellow liver, inspissated bile, and enlarged spleen.

Anaplasma marginale var. centrale Theiler, 1912.

Like *A. marginale*, but situate towards the centre of the cell. Type of illness milder than the above form.

Anaplasma canis Basile, 1912.

Cocci-like forms and crescent-shaped bodies free and enclosed in corpuscles found in peripheral blood, liver, spleen, and lungs of dogs around Messina. Large form 4·9 by 2·3 μ observed, provided with a flagellum measuring 5 μ.

Pathogenicity.—Causes canine anaplasmosis.

Genus Achromaticus Dionisi, 1898.

Definition.—*Piroplasmidæ* with easily visible but not voluminous cytoplasm, sickle shaped, pyriform or rounded. Schizogony in red cells. Many merozoites. Large solitary parasites.

Type Species.—*A. vesperuginis* Dionisi, 1898.

Achromaticus vesperuginis Dionisi, 1898.

This parasite was found by Dionisi in the noctule in 1898. Sambon classifies it as a Piroplasma but this is doubted by Nuttall and Graham-Smith, as well as by Dionisi, though they report pyriform endocellular parasites from blood films from bats of the genus *Vesperugo*, and Nuttall and Graham-Smith report four pyriform parasites in a corpuscle. Gonder, however, believes that it is in some intermediate position between the Plasmodidæ and the Piroplasma, and Nuttall and Graham-Smith consider that further investigations are necessary before it can be classified. We agree with Gonder, and consider the parasite to be neither a Piroplasma nor a plasmodium, and therefore return to Dionisi's original idea of a separate genus. Recently it has been studied by Yakimoff, Stolnikoff, and Kohl-Yakimoff, who believe that it is a true Piroplasma. Another species is *A. gibsoni* Patton, 1910.

Genus Rangelia Carini and Maciel, 1914.

Definition.—Piroplasmidæ, often in pairs, with rounded, oval, or pyriform appearance, with easily visible cytoplasm. Schizogony in endothelial cells in internal organs. Merozoites very numerous.

Type Species.—*Rangelia vitalli* Pestana, 1910.

Rangelia vitalli Pestana, 1910.

This is the cause of a disease in dogs in Brazil called nambiavú

Genus Rossiella Nuttall, 1910.

Definition.—Piroplasmidæ of unusual type with voluminous cytoplasm, not pigmented; rounded form and rounded nucleus, which is not peripherally placed. Schizogony in red cells, division first into two and subsequently in more merozoites.

Type Species.—*Rossiella rossi* Nuttall, 1910.

Rossiella rossi Nuttall, 1910.

Parasite of *Canis adustus* in Africa.

Genus Elleipsisoma França, 1910.

Definition. Piroplasmidæ of unusual type, with voluminous cytoplasm, not pigmented; living in red blood cells which become dehæmoglobinized. Schizogony in the lungs.

Type Species.—*Elleipsisoma thomsoni* França, 1910.

Elleipsisoma thomsoni França, 1910.

Parasite of *Talpa europæa* and *T. cæca*.

Genus Bartonella Strong, Tyzzer, Brues, Sellards, and Gastiaburu, 1915.

Definition.—Piroplasmidæ with rounded or rod-shaped dividing forms, sometimes in chains; reproduction by binary division, cytoplasm and chromatinic substance often differentiated with difficulty. Motile. Habitat, red blood-corpuscles.

Type and Only Species.—*Bartonella bacilliformis* Strong, Tyzzer, Brues, Sellards, and Gastiaburu, 1915.

Bartonella bacilliformis Strong, Tyzzer, Brues, Sellards, and Gastiaburu, 1915.

Definition.—*Bartonella* with the characters of the genus.

History.—In 1901 and 1902 Barton found an organism in Oroya fever which Tamayo and Gastiaburu identified as belonging to the paratyphoid group.

In 1905 Barton described bacillary-like bodies in the red cells of persons suffering from malignant fever. In 1909 he noted these bodies in fourteen additional cases, and stated that they were protozoa, and probably the cause of the disease. In the same year Gastiaburu and Rebagliati confirmed these findings and regarded the organism as the cause of Oroya or Carrion's fever. In 1915 Strong, Tyzzer, Brues, Sellards, and Gastiaburu, confirmed and enlarged these discoveries and named the parasite.

Morphology.—In fresh blood-films the parasite appears as a rounded or rod-shaped body, 0·5-1·0 microns in diameter in the former case, and 1·5-2·5 microns in length in the latter. They are very abundant in severe cases, and are endowed with a definite motility which is totally distinct from pedesis. They glide slowly about the cell. Sometimes a dot or bead-like body can be seen at the two poles.

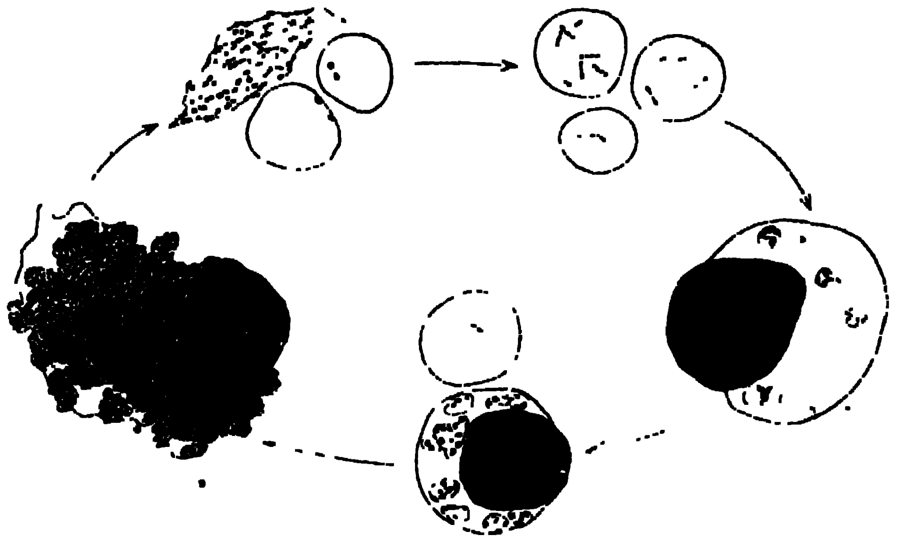


FIG. 165 - LIFE-CYCLE OF *Bartonella baccilliformis* STRONG, TYZZER, BRUES, SELLARDS, AND GASTIABURU, 1915

(Constructed from the illustrations in the Report of the First Expedition of the Harvard School of Tropical Medicine to South America in 1913)

When stained they are seen to be slightly curved, and to be present as single individuals, pairs, or in chains of three to five. V and Y forms are not uncommon, and are considered to represent dividing forms. Cross forms are rare, and due to organisms being superimposed.

The ends of the rods are more intensely coloured than the rest of the organism.

Some forms are rounded, oval, or almost pyriform. As many as ten parasites may be found in a single cell, which they apparently destroy.

Life-Cycle.—They are also to be found in large swollen endothelial cells, free or attached to the vessel wall, in the spleen and the lymph glands. An endothelial cell may be so distended with rounded and rod-shaped parasites as to occlude a vessel. In these cells the parasite, when coloured by Giemsa's stain, appears as rounded bodies, composed of bluish cytoplasm and containing small granules of chromatin, which vary in number from one to many, and it is suggested that the parasite breaks up into a large number of minute elements, each of which possesses a chromatin granule. These elements grow and become rods, which are set free by rupture of the enclosing sphere, and so fill the endothelial cells, from which they escape also by rupture. The rods are looked upon as gametocytes, rather than merozoites, and are considered to be the forms seen in the red cells.

Comparison.—The organism is believed to resemble *Theileria parva.*

Inoculations.—Attempts to transmit the parasite to inoculated animals failed. The animals used were rabbits and monkeys.

Cultivation.—So far the organism has not been cultivated.

Transmission by Insects.—Experiments have been performed with the mosquito *Phalangomyia debilis* Dyar and Knab, but no evidence of the presence of the parasites in the stomach or salivary glands could be obtained.

Pathogenicity.—It is believed to be the causal agent of Oroya fever.

FAMILY PLASMODIDÆ LUHE, 1906.

Synonyms.—*Gymnospondia* Labbé, 1894, *Acytosporidia* Wasielewski, 1896; *Hæmamœbida* Ross, 1899, *Acytosporea* Minchin, 1903.

Definition.—Hæmosporidia with hæmozoin. The trophozoite grows into the schizont, containing hæmozoin, which breaks up into a number of merozoites, which are usually said never to be flagellate. The oökinete encysts and forms a typical oöcyst, which breaks up eventually into sporozoites.

Classification.—The genera of the Plasmodidæ are: *Plasmodium* Marchiafava and Celli, 1885, *Laverania* Grassi and Feletti, 1889, *Hæmocystidium* Castellani and Willey, 1904.

These genera may be distinguished as follows:—

A. Size large. Schizogony binary or at times quaternary, in general circulation *Hæmocystidium.*
B. Size small. Schizogony into more than four merozoites—
  I. Without crescent bodies—*Plasmodium.*
  II. With crescent bodies—*Laverania.*

Genus Plasmodium Marchiafava and Celli, 1885.

Synonyms.—*Oscillaria* Laveran, 1881; *Hæmatomonas* Osler, 1887; *Hæmatophyllum* Metchnikoff, 1887; *Hæmamœba* Grassi and Feletti, 1889; *Laverania* Grassi and Feletti, 1889; *Cytamœba*, Danilewski, 1890; *Proteosoma* Labbé, 1894; *Hæmosporidium* Lewkowicz, 1897; *Cytosporon* Wasielewski, 1901.

Definition.—Plasmodidæ, in which the gametocytes resemble more or less the schizonts by being round in shape. Schizogony in the peripheral blood.

Nomenclature.—Some remarks are perhaps necessary on the nomenclature. Laveran first used the term *Oscillaria* because he saw the flagellate form, which at that time was thought to be a

Polymitus form because of its flagella. Later Laveran repudiated this term, which, indeed, could not be used, because it had already been applied to a plant. He then suggested the term 'hæmatozoön,' but this is objectionable, because the hæmatozoa are a group of parasites, and not a single genus. Metchnikoff suggested the term *Hæmatophyllum malariæ*, which is equally impossible; therefore the earliest distinctive term is 'plasmodium' which was used by Marchiafava and Celli in 1885.

It is not a good term, because a plasmodium is generally considered to be a mass of protoplasm with several nuclei representing, not one single animal, but several.

General Account.—The malarial parasites may be taken as the typical examples of the Plasmodidæ.

The malarial parasite exists in nature outside the human body in certain species of different genera of the family Anophelinæ, a type of mosquito which is somewhat easily identified by its habit of projecting at almost right angles from the surface on which it stands. In the salivary glands of infected insects the malarial parasites are found as fine fusiform bodies, about 10 to 20 μ in length, and 1 to 2 μ in breadth, lying in the cells or in the duct. These fusiform bodies are called sporozoites, and consist of cytoplasm containing a central nucleus composed of chromatin.

The ends of the parasite are pointed, one being sharper than the other. They are capable of movement forwards, and of flexion into loops or curves. It may be that the sporozoites represent male, female, and indifferent parasites, or they may not; the question is still undecided.

When inoculated into man by a mosquito, they penetrate into the red blood cells, and develop into small endo-corpuscular parasites called the trophozoites, which at first are composed of cytoplasm and a nucleus.

This young trophozoite grows, throwing out pseudopodia for the purposes of nutrition, and presently a vacuole appears, converting the small parasite into a ring form, which, according to Schaudinn, is of benefit in enabling it to absorb nutriment quickly.

The vacuole does not keep pace with the growth of the parasite, and finally in the old form disappears. Early in the ring forms there appear granules of a black pigment, which used to be called melanin, but which has by no means the chemical characteristics of true melanin, as will be described under Malaria. This pigment has been named by Sambon 'haemozoin'—a name which appears to us to be peculiarly suitable, and will therefore be used in this work. It is really of an excrementitious nature. The fully-grown trophozoite now ceases to be amœboid, and, becoming rounded off and full of pigment granules, is called the schizont, which has a subcentral nucleus. This nucleus now divides, so that parasites may be seen with two, three, four, five, six, up to twenty-four nuclei. The cytoplasm around these nuclei segments into small bodies called merozoites, each with a nucleus, but an unsegmented portion containing the hæmozoin, and called the residual mass, or ***nucleus de reliquat***, is always left unsegmented.

The blood-corpuscle now breaks up, and the merozoites, residual protoplasm, and pigment are liberated into the blood stream, where the effete matter and some merozoites are taken up by the leucocytes and destroyed.

The merozoite usually tries to enter a red blood cell and to start again as a trophozoite, thus completing a cycle in the blood of the human being who is acting as host. This cycle is called the *cycle of Golgi*, or *schizogony*. Sometimes more than one merozoite will enter a cell, thus giving rise to multiple infection. In such a case they are generally of the same age, but this is not invariable. In the red cell, under these conditions of multiple infection, some observers have thought that the young trophozoites might conjugate; but this, together with the suggestion of further division of the merozoite, we believe to be incorrect, though it must be admitted that forms with a double nucleus can be seen. When such a binucleate form is seen nowadays, it makes the observer think seriously of a possible flagellate origin, and inclines him to support Sambon and Hartmann's classification, but never, as far as we know, has anyone seen a flagellate merozoite in human malaria.

It will be seen that in going through the process of schizogony one sporozoite becomes several merozoites, and that each of these may again become several merozoites, so that the infection grows unless kept in check by phagocytosis, and perhaps chemical action or quinine treatment.

Each parasite means a red cell destroyed and so much toxin liberated into the blood stream. Hence in a certain number of days (eight to twelve, as a rule) the parasites will have increased to such a degree that their collective toxins, acting upon the organs of the body, upset the metabolism and produce an attack of fever. This period of eight to twelve days is the incubation period of the disease.

It is possible that all the sporozoites develop into schizonts, and there is at present no evidence that they develop into male or female forms directly. If they do not do this, then the merozoites must differentiate sexually; for in about a week male and female forms can be seen in the blood stream, and, moreover, very young stages can be observed.

The earliest form of a sexual parasite is like an ordinary merozoite, but it grows very slowly, and it never possesses a vacuole, and as it grows its protoplasm becomes heavily pigmented and granulated in the female, and lighter and clear in the male. The result is to produce a female type of parasite called the macrogametocyte, or a male type of parasite, the microgametocyte. So that there are three types of parasite - the indifferent or schizont, the female, and the male.

The macrogametocyte is characterized by possessing a small, more or less rounded nucleus excentrically placed and poor in chromatin, and a cytoplasm full of granules and pigment.

The microgametocyte is characterized by having a large nucleus extending like a band across the cytoplasm, and much chromatin, a clear protoplasm, and less pigment.

The macrogametocyte and microgametocyte are the means of propagating the parasite in the mosquito, and if they fail to reach the gut of this insect the microgametocytes die off.

The macrogametocytes, on the other hand, are extremely persistent, and can wait in the body for a long time until some chill or accident lowers its resistance, when they become active and develop merozoites by parthenogenesis, thus accounting for the relapses and the recurrences of malaria, even months and years after having left a tropical country. Hence in malaria there is a latent phase which is capable of lasting an unknown time -at least one to three years, perhaps longer; but upon this subject more will be said later, and, indeed, more information is urgently needed.

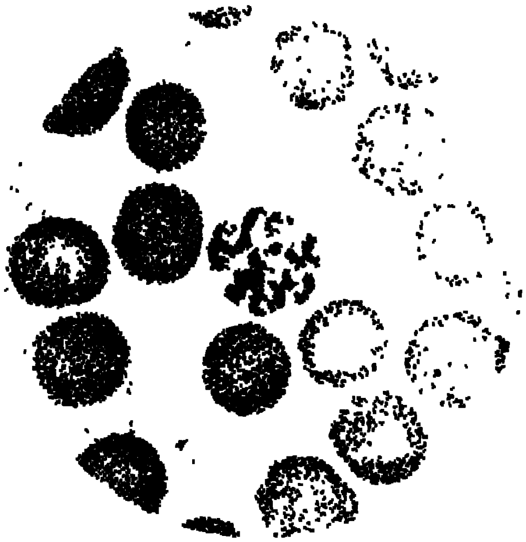


FIG. 166.—SCHIZOGONY IN *Plasmodium vivax* (GRASSI AND FELETTI, 1890). (× 1,000 DIAMETERS)

(By Norman; given us by J. J. Bell.)

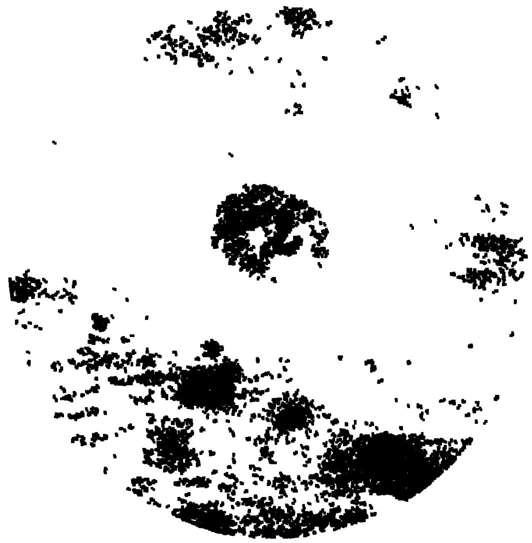


FIG. 167 OÖCYST IN STOMACH OF ANOPHELINE MOSQUITO. (× 1,000 DIAMETERS)

(By Norman, from a preparation by James.)

In developing parthenogenetically, the nucleus of the macrogametocyte divides into two portions, one rich and the other poor in chromatin. The pigment granules gather round the pale nucleus, and with it the surrounding cytoplasm and hæmozoin form a sort of *nucleus de reliquat*. The rest of the protoplasm, rendered clearer by loss of its hæmozoin, contains the nucleus rich in chromatin, which now divides like the nucleus of a schizont, and forms merozoites, which, escaping from the red cell, infect red corpuscles, and start the cycle of schizogony anew.

Etheogenesis is unknown in the malarial parasite.

If a female mosquito (the male does not suck blood) belonging to certain of the genera of the Anophelinæ sucks the blood of a person in whom both macro- and micro-gametocytes are to be found, a new cycle is started in that mosquito. This cycle is sporogony, which is characterized by being a sexual process. Changes now appear in the macro- and micro-gametocyte, which are thought by Schaudinn to be brought about by the alteration in temperature.

The macrogametocyte, escaping from its red cell, undergoes reduction by division of its nucleus once or twice, forming polar bodies. The reduced gametocyte is now called the macrogamete.

Similarly the microgametocyte undergoes changes, for chromidial masses separate from its nucleus and travel to the periphery of the parasite, from which thin threads of protoplasm now project.

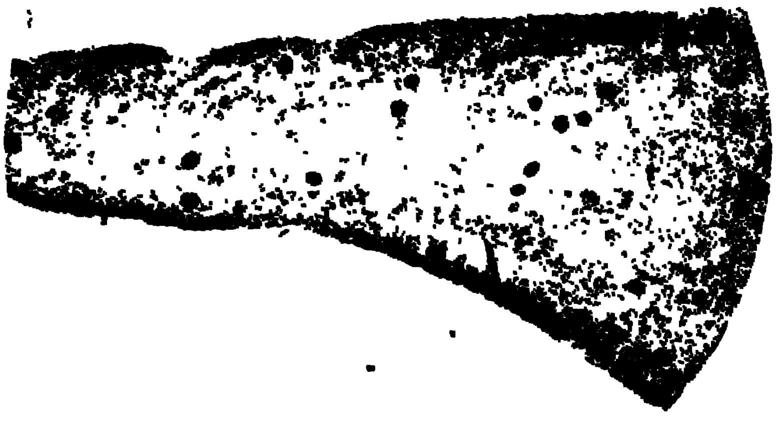


FIG. 168. SPOROCYSTS IN STOMACH OF ANOPHELINE MOSQUITO. (× 1,000 DIAMETERS.)

(By Norman from a preparation by James.)

These threads, which vary from four to six in number, lash about vigorously, moving the whole parasite, which therefore whirls about, and it and its processes, called flagella, were looked upon as a polymitus; hence this stage is often called the polymitus stage.

The threads break off, and are now called microgametes. Each microgamete is composed of a long, tapering thread of protoplasm capable of bending and moving rapidly. Its chromatin is spread along it in dots or bars, and hence the whole structure somewhat resembles a spirochæte, but there is no undulating membrane.

A microgamete now conjugates with a macrogamete, the male and female pronuclei fusing to form a synkaryon, and the resulting zygote is called an oökinete. This zygote elongates, and its anterior extremity, which is more or less clear of hæmozoin, becomes pointed; the nucleus lies in the middle, and the posterior end contains most of the pigment, which may be largely cast off or may be retained.

It now pierces the epithelium of the mosquito's stomach, below which it comes to rest, and forms a thin cyst-wall, and is called the oöcyst. This now grows rapidly, and its nucleus divides into a large number of daughter nuclei, around each of which the protoplasm gathers, forming the sporoblasts, which are somewhat connected together (Fig. 169).

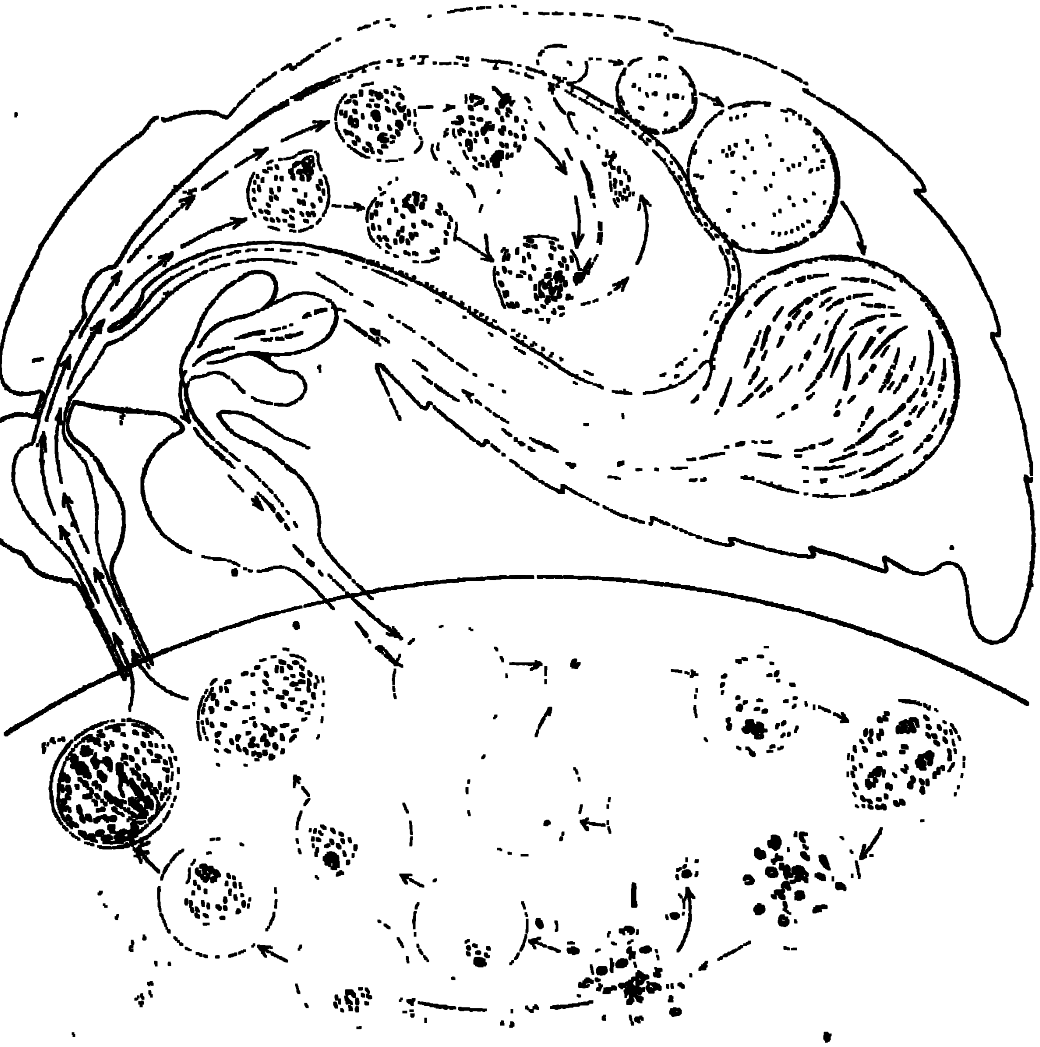


FIG. 169.—DIAGRAM OF THE LIFE-CYCLE OF *Plasmodium vivax* (GRASSI AND FELETTI), IN MAN AND THE ANOPHELINE MOSQUITO.

The nucleus of each sporoblast now divides into several small nuclei. These travel to the periphery, which grows out into a series of small projections, each of which takes a chromatin particle with it. Each of these projections is a sporozoite, so that each sporoblast forms a large number of sporozoites, and leaves a residual mass of pigment and cytoplasm undivided. The cyst, now enormously enlarged, bursts, and the sporozoites escape into the cœlome of the insect, which in this case is a hæmocœle, and therefore they enter the blood, and are carried by it probably all over the insect's body. Certainly they are seen in the thoracic muscles, but finally they find their way to the salivary glands, and so to a new host, or according to Schaudinn to the eggs, and so probably to a new generation of mosquitoes.

Sporogony takes about ten to twelve days, during which the mosquito will have sucked blood three or four times.

Abnormal Forms.—In mosquitoes, whether infected by malarial parasites or by Proteosoma, peculiar bodies, called 'black spores' by Ross, are sometimes found in the stomach wall, which are now known to be protozoal parasites of the genus *Nosema*, which have invaded the oöcysts, and are therefore hyperparasites.

Cultivation. *Plasmodium malariæ*, *P. vivax*, and *Laverania malariæ* were first cultivated by Bass, alone and with John. They grow anaerobically in blood mixed with dextrose at 41° C., but the blood must have no leucocytes if more than one generation is to be cultivated. The whole asexual cycle of *P. vivax* and *L. malariæ* has been completed *in vitro* in the corpuscles of human blood. Forms suggesting parthenogenesis were seen.

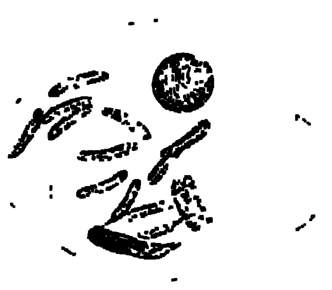


FIG. 170.—AN OÖCYST SHOWING ROSS'S 'BLACK SPORES,' NOW KNOWN TO BE PROTOZOA BELONGING TO THE GENUS NOSEMA

(After Grassi.)

Animal Hosts.—Although species of Plasmodium exist in animals, still there is no evidence that the human parasites live in any other animal than man. Fermi and Lumbau in 1912 have tested this with regard to bats, sparrows, owls, quails, and frogs, with negative results.

Classification.—A number of species, increasing gradually, belong to this genus, among which are two of the malarial parasites, *P. vivax* and *P. malariæ*.

Plasmodium vivax Grassi and Feletti, 1890 (Plate I.).

Synonyms. *Hæmamœba vivax* Grassi and Feletti, 1890; *H. malariæ* var. *magna* Laveran, 1900; *H. malariæ* var. *tertianæ* Laveran, 1901; *Plasmodium malariæ* var. *tertianæ* Celli and Santelice, 1891; *P. malariæ tertianum* Labbé, 1899; *Hæmosporidium tertianum* Lewkowicz, 1887.

Plasmodium vivax is the parasite of tertian malarial fever, and derives its specific name from its energetic amœboid movements, which probably take place for purposes of nutrition.

Its schizogony has been well studied by Golgi and Schaudinn, and its sporogony by Grassi, Bignami, and Bastianelli.

The whole process of the schizogony of *P. vivax* can be summarized as follows:—During the first twenty-four hours after the entry of the sporozoite or merozoite into the red cell the little trophozoite, which at the beginning is about one-third the size of the erythrocyte, grows rapidly, absorbing nutriment from the red cell by its pseudopodia and by the large surface of cytoplasm exposed, owing to the size of the vacuole.

Hence, not merely does it increase in size, but it acts deleteriously upon the enclosing cell, which loses its hæmoglobin, turns pale and degenerates, as is evident by its becoming swollen owing to the absorption of fluid, and by showing, on staining with any modification of Romanowsky, a dotted appearance due to red granules called Schüffner's dots. These dots can be seen in red cells affected by other plasmodia—*e.g.*, *P. canis* in the dog. In growing, it gives rise to a quantity of hæmozoin, which appears as fine, reddish-brown granules, often seen in active movements due to currents in the cytoplasm of the parasite. In about thirty hours it becomes rounded off as the schizont (Fig. 44, p. 294), 8·5 μ in diameter.

From the thirtieth to the forty-eighth hour the fully-grown schizont undergoes sporulation, when it will be noticed that fifteen to twenty merozoites are formed, while the hæmozoin granules are packed together, either into the centre or towards the periphery of the parasite. It will also be noted that the red cell is now considerably swollen and almost colourless.

About the forty-eighth hour the remains of the corpuscle disintegrate, and the merozoites (size 1·5 μ), hæmozoin, etc., escape.

So that *P. vivax* occupies forty-eight hours in the process of schizogony. As curiosities, it may be mentioned that a trophozoite or a schizont may be seen in the same red cell as a gametocyte.

Sporogony.—The development in the mosquito was first worked out in *Anopheles claviger*.

The development of the gametes, and the fertilization of the macrogamete, and the structure of the oökinete, have been carefully described and figured by Schaudinn (*vide* Figs. 45, 46, and 47, p. 294). In about forty hours after the mosquito has been fed, the oöcyst can be found as a round transparent body with strands of yellowish hæmozoin scattered throughout it, lying in the stomach wall beneath the epithelium, and covered over by the musculo-elastic layer of the gut. Its wall is seen to be well defined—*i.e.*, the oökinete has become encysted. By this time the chromatin will have divided into small masses.

On the third day it will have become from one-third to one-fourth larger, and the cyst-wall will be more distinct, and the imperfect segmentation of the protoplasm around the nuclei can be seen. The hæmozoin is seen gathered into little masses lying between the segments of the cytoplasm, which are the sporoblasts. The first stages of the formation of sporozoites may also be observed.

During the fourth day the size increases about a fourth, and the nuclei and their surrounding protoplasm will have formed some twenty to thirty sporoblasts, whose periphery will be marked by a palisade of forming sporozoites.

Between the fourth and fifth day the cysts (50 μ in diameter) full of sporozoites (size 14 μ) will be seen to be projecting into the cœlome.

After the seventh day the oöcyst ruptures, and the sporozoites escape and find their way to the salivary glands, in the cells of which they lie, mainly in those of the mid or poison gland. Thus, about the tenth to the twelfth day after infection the mosquito is ready to spread the disease by its bite, and the cycle of sporogony is complete. It must be remembered that Schaudinn observed infection of the mosquito's egg, but whether the parasite penetrates into the larva, and from that to the pupa, and thus into a second generation, is not known.

Plasmodium malariæ Laveran, 1881 (Plate I.).

Synonyms.—*Hæmamœba malariæ* Grassi and Feletti, 1890; *H. laverani* var. *quartana* Labbé, 1894; *H. malariæ* var. *magna* Laveran, 1900; *H. malariæ* var. *quartanæ* Laveran, 1901; *Plasmodium malariæ* var. *quartanæ* Celli and Sanfelice, 1891; *Hæmosporidium quartanæ* Lewkowicz, 1897; *Plasmodium malariæ quartanum* Labbé, 1899; *P. golgii* Sambon, 1902; *Laverania malariæ* Jannesco, 1905; and *Oscillaria malariæ* Laveran, 1881.

Schizogony.—The young trophozoite, which is smaller than *P. vivax*, forms a compact ring, which lies in an unaltered erythrocyte, and shows, as a rule, but little pseudopodial activity. Very soon hæmozoin appears in the form of dark rodlets.

After the first twenty-four hours the parasite is found to be much larger, and the hæmozoin more abundant. The granules of pigment will be noticed to be gathered at the periphery, and to be very dark in colour, and non motile. The red cell tends, if anything, to become smaller and darker. In about sixty hours the trophozoite will have become the full-grown schizont, which is a large, round, pigmented body surrounded by a rim belonging to the corpuscle. During the next twelve hours its nucleus divides up into six or twelve nuclei, around which the cytoplasm gathers, while the hæmozoin is driven into the centre, and the appearance of a daisy is produced by the central block of hæmozoin and the regular arrangement of the merozoites around it (size 6 μ).

The merozoites (size 1·75 μ) are now set free, and, as a rule, many of them appear to be killed off, and not to be able to affect the red cells. More rarely they go on increasing in number, and recently have been said to cause death in a case (Leishman), but a severe infection is not usual.

The whole schizogony takes place in the peripheral blood, and occupies seventy-two hours.

Sporogony.—Gametocytes are very rarely seen, and only after the disease has lasted a long time, but Vida has recently described all stages of their development as seen in the peripheral blood.

They begin as small forms, with a central nucleus but no vacuole, and soon become pigmented, the fully-grown macrogametocyte being a little larger than a normal corpuscle. Its dark cytoplasm is heavily pigmented, especially at the periphery, at which the nucleus is also placed. The corpuscle forms but a small rim around the parasite.

The microgametocyte shows the usual structure already described, but is less pigmented, and has a clearer cytoplasm. The corpuscle is not enlarged, as in the case of the macrogametocyte, and much more of it is visible around the parasite. The formation of the microgametes has been observed, but the infection of the mosquito is difficult to bring about, though the development in the mosquito has been traced by Bignami and Bastianelli. The oöcyst is characterized by the pigment, which is black, coarse, and gathered into a clump. The cycle of development is the same as in *P. vivax*, but takes about eighteen to twenty-one days to be completed after infection in mosquitoes which were kept at a temperature of about 22° C. This appears to be the degree of heat at which the process takes place best. At the end of that time the completely developed sporozoites can be seen.

Pathogenicity. Causes quartan fever

Plasmodium tenue Stephens, 1914, is an extremely amœboid form, with scanty cytoplasm and much chromatin, found first in blood films from India, but known also in Africa. It may be *Laverania malariæ*. *Plasmodium caucasicum* Marzinowsky, 1916, found on the Black Sea littoral, may also be *Laverania malariæ*.

Plasmodium danilewskyi Grassi and Feletti, 1890.

Synonyms. -*Laverania danilewskyi* Grassi and Feletti, 1890; *Hæmamœba relicta* Grassi and Feletti, 1891; *Cytosporon malariæ avium* Danilewskyi, 1891; *Proteosoma grassii* Labbé, 1894; *Plasmodium relictum* Sergent, 1907.

This parasite was discovered by Grassi in the blood of birds in Italy, and causes death in partridges in Hungary. It affects sparrows in India, and is the form in which Ross first traced the development of a plasmodium in a mosquito. It occurs in Ceylon, and is common in Africa.

The young trophozoite becomes pigmented, and, displacing the nucleus, grows into the schizont, which forms about nine merozoites.

The macrogametocyte has but little chromatin in its nucleus, which is rounded, while the microgametocyte has an elongated, darkly-staining nucleus.

These develop in *Culex fatigans*, *C. nemorosus*, or some other species, when in about twelve to fifteen hours ookinetes are seen, and in about one to two days well-developed oocysts are present in the stomach in the form of round, transparent cysts, with hæmozoin scattered through them.

In three to four days the oöcysts have increased in size, and sporoblasts have appeared, and even sporozoites are forming.

In nine to ten days the oöcyst has become fully developed and bursts, and the sporozoites can first be seen in the muscles of the thorax, and then in the salivary glands, in which they lie principally in the central or poison lobe. The black spores already mentioned can be noted in the stomach, and, according to Stephens and Christophers, in either the thoracic muscles or in the salivary glands.

No traces of parasites have been found in the larvæ or second generation of *Culex*.

PLATE I.

THE MALARIAL PARASITES.

Coloured by Leishman's Stain.

1a—*4a*. PLASMODIUM MALARIÆ.

- *1a*. Young Trophozoite.
- *2a*. Older Trophozoite.
- *3a*. Schizont.
- *4a*. Sporulation.

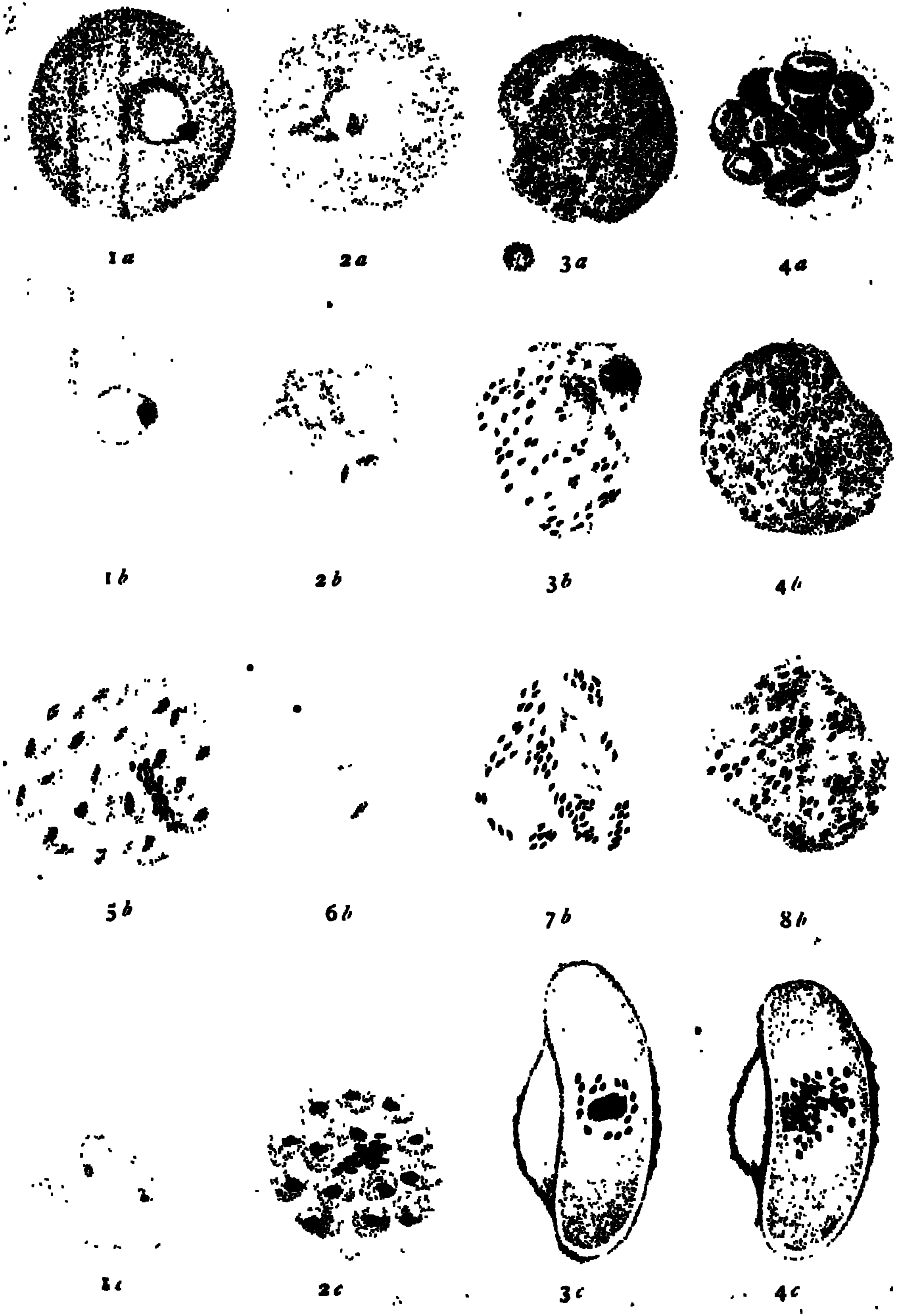
1b—*8b*. PLASMODIUM VIVAX.

- *1b*. Young Trophozoite.
- *2b*. Older Trophozoite, showing Amœboid Movement.
- *3b*. Schizont with single Chromatin Mass.
- *4b*. Schizont with three Chromatin Masses.
- *5b*. Sporulation.
- *6b*. Young Sporont.
- *7b*. Microgametocyte.
- *8b*. Macrogametocyte.

1c—*4c*. LAVERANIA MALARIÆ.

- *1c*. Two Young Trophozoites.
- *2c*. Sporulation.
- *3c*. Macrogametocyte.
- *4c*. Microgametocyte.

PLATE I.



MALARIAL PARASITES.

(Coloured by Leishman's stain.)

Geo Waterston & Sons, Ltd Edin

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Plasmodium kochi Laveran, 1899.

This plasmodium is found in chimpanzees (*Anthropopithecus troglodytes* Gm.), and in monkeys in Africa and in Ceylon; in the latter it causes illness and death. The spleen and bone-marrow are found pigmented. It is said not to be inoculable.

Plasmodium pithoci Halberstaedter and Prowazek, 1907.

Found in the ourang-outang (*Simia satyrus*) and the chimpanzee, in which the trophozoites resemble *P. vivax* and the gametes *P. malariæ*. Schüffner's dots can be seen.

Plasmodium inui Halberstaedter and Prowazek, 1907.

In *Macacus cynomolgus* L. and *M. nemestrinus* L. It is like *P. pitheci*, but the hæmozoin is in the form of fine yellow granules. Merozoites, twelve to sixteen in number. Schüffner's dots absent.

Plasmodium cynomolgi Mayer, 1907.

In *M. cynomolgus* L. Merozoites, eight to thirteen. Schüffner's dots present.

Plasmodium bovis Kolle, 1898.

In cattle in South Africa, in which they produce remittent fever and severe anæmia.

Plasmodium canis Castellani and Chalmers, 1910.

This parasite, which is very common in pariah dogs in Ceylon, was discovered by us in 1908. It resembles *P. vivax*, entering the red cell as a small round merozoite, and growing into a pigmented plasmodium, and finally dividing into a number of merozoites. Schüffner's dots are also present. Fig. 171 shows the schizogony of this parasite, and Fig. 172 the gametocytes. The macrogametocyte has a small rounded nucleus and the microgametocyte an elongated narrowish nucleus extending across the parasite.

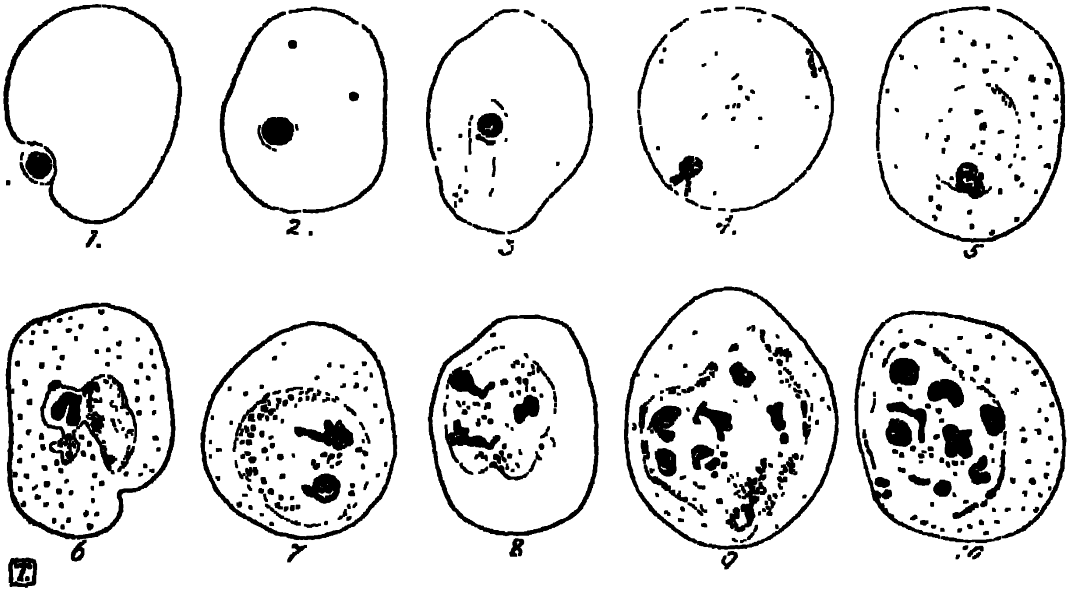

FIG. 171.—*Plasmodium canis* CASTELLANI AND CHALMERS.

1-2, Merozoite entering the corpuscle; 3, young trophozoite (the red cell shows Shüffner's dots); 4-6, trophozoites, enclosing cells showing Shüffner's dots; 7-10, schizonts showing various stages of nuclear division prior to the formation of the merozoites.

Plasmodium equi Castellani and Chalmers, 1913.

Found by us in a horse in Ceylon. It closely resembles *P. canis*.

Plasmodium brasilianum Gonder and Gossler, 1908.

Resembles the human quartan parasite, but found in *Brachyurus calvus* in Brazil.

Plasmodium vassali Laveran, 1905.

Synonym.—*P. vassali* Sambon, 1907.

Found by Vassal in a squirrel—*Sciurus griseimanus*.

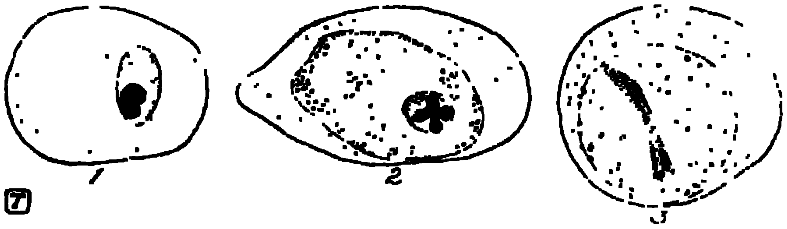

FIG. 172.—*Plasmodium canis* CASTELLANI AND CHALMERS.
1. Young gametocyte; 2. Microgametocyte; 3. Macrogametocyte.

Other Forms.

In Mammals. *Plasmodium murinum* Dionisi, 1898, in *Myotis myotis*, *P. monosoma* Vassal, 1907, in *Vesperugo abramus*.

In Birds.—*P. majoris*, in *Parus major*, *P. vaughani* Novy and MacNeal, 1904, in *Merula migratoria*.

In Lizards. *P. diploglossi* Aragão and Neiva, 1909, in *Diploglossus fasciatus*. *P. tropiduri* Aragão and Neiva, 1909, in *Tropidurus torquatus* Wied in Brazil.

Genus Hæmocystidium Castellani and Willey, 1904.

The characters of this genus resemble those of the genus *Plasmodium*, but the parasites are generally larger, and according to Dobell, the schizogony is very simple, there being as a rule binary and occasionally quaternary division, which takes place in the general circulation. Woodcock, however, considers the forms which Dobell describes as binary fission to be fusion forms of the parasites. Pigment present.

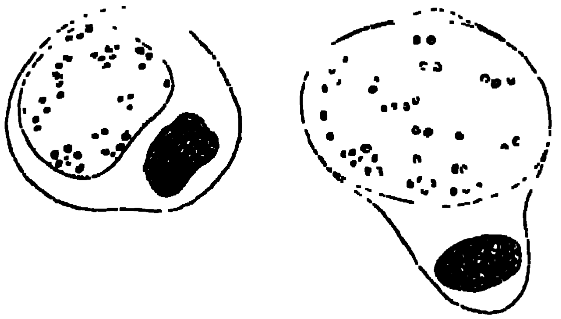

FIG. 173.—*Hæmocystidium simondi* CASTELLANI AND WILLEY.
(After Castellani and Willey.)

Hæmocystidium simondi Castellani and Willey, 1904.

This parasite was found in *Hemidactylus leschenaultii* Gray in Ceylon.

Other species: *H. metschnikovi* Simond in *Chitra indica* Gray in India; *H. mesnili* Bonet in *Naja* sp. (?) in West Africa, *H. roumei* Bonet in *Cinyxis belliana* Gray in West Africa, *H. testudinis* Laveran in *Testudo pardalis* in South Africa; *H. najæ* Wenyon in *Naja haje*, and in *Naja nigricollis* in Khartoum.

Genus Laverania Grassi and Feletti, 1890.

Definition. Plasmodidæ, in which the gametocyte is dissimilar from the schizont, appearing in the form of a crescent. Schizogony in the red blood cells in internal organs.

Laverania malariæ Grassi and Feletti, 1890 (Plate I.).

Synonyms. *Hæmamœba malariæ* Laveran, 1890; *H. præcox* Grassi and Feletti, 1890; *H. laverani* Labbé, 1894; *H. immaculata* Grassi and Feletti, 1891; *Plasmodium malariæ* var. *quotidianæ* Celli and Sanfelice, 1890; *P. præcox* Doflein, 1901; *P. immaculatum* Schaudinn, 1902; *P. falciparum* Blanchard, 1905; *Hæmomonas præcox* Ross, 1899; *Hæmosporidium undecimanæ* Lewkowicz, 1892; *H. sedecimanæ* Lewkowicz, 1892; *H. vigesimotertianæ* Lewkowicz, 1892; *Hæmatozoon falciparum* Welch, 1897.

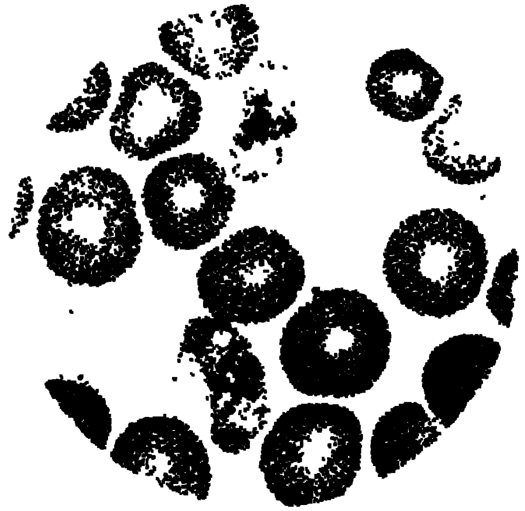

FIG. 174.—MALE CRESCENT OF *Laverania malariæ* (GRASSI AND FELETTI, 1890). (×1,000 DIAMETERS.)

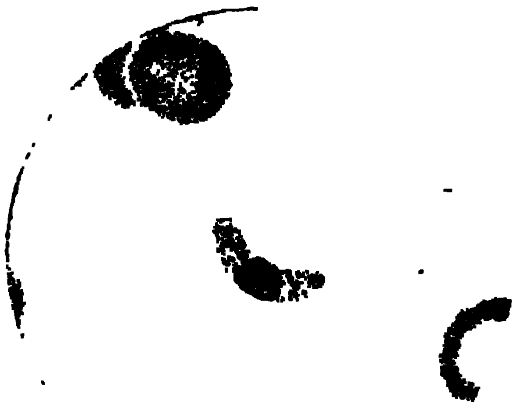

FIG. 175.—FEMALE CRESCENT OF *Laverania malariæ*. (×1,000 DIAMETERS.)

(By Norman, through the kindness of J. J. Bell.)

The young trophozoite begins as a very small parasite, which quickly forms a ring, of which the size is only one-sixth to one-seventh of the diameter of the enclosing red cell. This quickly grows into an oval form, which becomes pigmented, while the enclosing erythrocyte in stained preparations may show the so-called Maurer's dots, the significance of which is not understood.

The fully-grown schizont (size 4·5 μ) is but rarely seen in the peripheral blood, and the segmentation into merozoites (size 0·7 μ) nearly always takes place in the internal organs, when eight to ten or fifteen are formed. When this is in progress there is a great tendency for the red corpuscles to cling together and to the wall of the vessel, and hence to give rise to obstruction of the circulation, which produces the perniciousness of the fevers due to this parasite.

DIFFERENTIAL CHARACTERS OF THE MALARIAL PARASITES.

Character	*P. malariæ.*	*P. vivax.*	*L. malariæ.*
Schizogony ..	Completion in seventy-two hours.	Completion in forty-eight hours.	Completion in forty-eight hours or less.
Young trophozoite	Young trophozoite, smaller than *P. vivax*, larger than *L. malariæ*, movements rather slow; pseudopodia not marked or long	Young trophozoite, large; very actively motile, long pseudopodia.	Young trophozoite, small; actively motile.
Hæmozoin ..	Granules coarse, sluggish; peripherally arranged; dark brown.	Granules fine; movement marked	Granules fine and scanty; often motionless.
Schizont ..	Smaller than red corpuscle	Larger than red corpuscle.	Much smaller than red corpuscle.
Merozoites ..	Six to twelve, regularly arranged in a rosette	Fifteen to twenty regularly arranged	Eight to fifteen, arranged irregularly.
Gametocytes ..	Resemble sporonts, but larger.	Resemble sporonts but larger.	Crescentic in shape.
Erythrocytes ..	Almost normal.	Pale and swollen.	May be small and dark.

Schizogony takes from thirty-six to forty eight hours to be completed.

The gametocytes are characterized by being crescent-shaped and large, with the remains of the red cell stretched round them. The hæmoglobin of the cell is often seen lying in juxtaposition to the parasite, while the remaining portion of the corpuscle is almost colourless.

The macrogametocyte is characterized by its long thin shape.

FAMILY HÆMOPROTEIDÆ Sambon 1906.

Definition. Hæmosporidia with hæmozoin, but with oökinete which does not encyst.

Genus Hæmoproteus Kruse, 1890.

Synonyms. *Halteridium* Labbé, 1894; *Laverania* Laveran, 1899; *Trypanosoma* Schaudinn 1904; *Trypanomorpha* Léger, 1906.

Historical.—These parasites were first described by Grassi and Feletti in the blood of birds in 1890 as *Laverania*, a term altered by Labbé in 1894 to *Halteridium danilewskyi*. In 1904 came Schaudinn's paper showing that they were stages in the life history of trypanosomes, which has been supported by the work of the Sergents, and has been severely criticized by Novy, McNeal, Ross, and Thiroux who believe that Schaudinn made a mistake, and that the flagellates and intracorpuscular parasites are quite distinct. In 1908 a paper by Aragão appeared on *H. columbæ*, which certainly does not support Schaudinn's views; but in 1909 Woodcock's researches, as already mentioned, strongly support that distinguished protozoologist; however, later researches have all tended to indicate that Schaudinn was wrong and that his now celebrated life-cycle for *Hæmoproteus noctuæ* is a mixture of the life-cycles of a hæmoproteus and a trypanosome We, however, at present still give Schaudinn's account, pending confirmation of the recent work on the subject. At all events, the question as to whether Schaudinn was right or wrong cannot, impartially, be said to be settled one way or the other.

Hæmoproteus noctuæ Celli and Sanfelice 1891.

H. noctuæ goes through the cycle of schizogony in *Glaucidium noctuæ* Retz, the little owl, and its sporogony in *Culex pipiens* Linnæus.

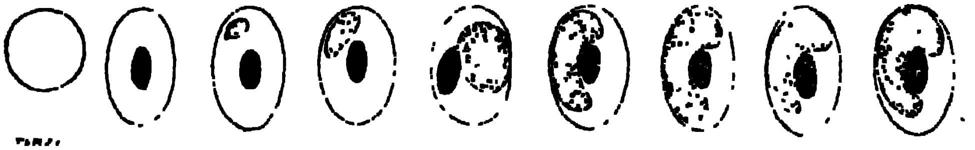

FIG. 176.—*Hæmoproteus mansoni* SAMBON SHOWING THE DEVELOPMENT OF THE GAMETOCYTES.

(After Sambon.)

When this gnat sucks the blood of a little owl infected with hæmoproteus, two halteridial forms in the owl's corpuscles are seen to undergo development in its stomach. These two forms are the microgametocytes and the macrogametocytes.

Microgametocyte.—The microgametocyte appears as a typical halteridium parasite enclosed in an erythrocyte, and possessing pale clear cytoplasm, with coarse hæmozoin granules and a large single nucleus, which is composed of eight groups, each containing trophic and kinetic elements

Macrogametocyte.—The macrogametocyte is a typical halteridium, laden with food granules, lying in a pale disorganized erythrocyte It has a rather small trophonucleus, alongside of which is a small kinetonucleus.

In the Mosquito.—When these gametocytes reach the alimentary canal of *Culex pipiens*, they escape from the erythrocytes, and appear free in the lumen of that canal, and proceed first to reduction and then to zygosis, with the formation of a zygote.

The whole process has been carefully worked out by Macallum in another species of halteridium, and is confirmed by Schaudinn in the present species.

Formation of the Microgametocyte.—The microgametocyte is a clear hyaline body, which, on escaping from the red blood-corpuscles, throws out active flagella, which, after beating about a little, break loose, forming the free microgametes. Schaudinn studied the cytological processes underlying these grosser changes, and found that the trophonuclei were reduced to four chromosomes, while the eight kinetonuclei remain, and, separating from the parent nucleus, form microgametes in the way presently to be described for the development of a male oökinete into a male trypanosome.

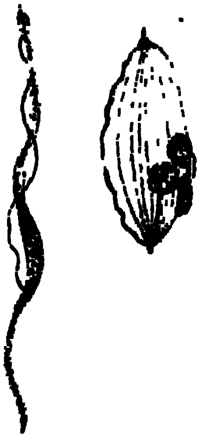

FIG. 177.—*Hæmoproteus noctuæ* CELLI AND SANFELICE.

(After Schaudinn.)

On the left is the microgamete, and on the right a scheme showing the arrangement of the nuclei centrosomes, undulating membrane, and myonemes.

The Microgamete. The microgamete is very thin, and tapering at the posterior extremity where it ends in a tail-like prolongation of the cytoplasm containing a portion of the trophonucleus. The anterior end is acutely conical.

The trophonucleus is elongated into a long thread, extending from the anterior to the posterior end of the body and carrying four chromosomes in the form of dots at regular intervals.

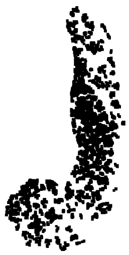

FIG. 178.—*Hæmoproteus noctuæ* CELLI AND SANFELICE: THE OÖKINETE.

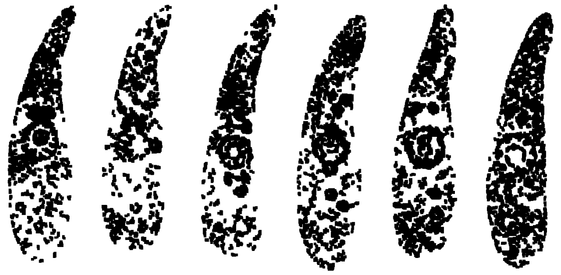

FIG. 179.—*Hæmoproteus noctuæ* CELLI AND SANFELICE: MATURATION OF THE OÖKINETE.

(After Schaudinn.)

The kinetonucleus is situate in the posterior third of the cytoplasm and consists of a rather elongated mass, with eight chromosomes and one intranuclear centrosome.

In addition to this centrosome there are two others—an anterior, situate just at the base of the anterior conical projection, and a posterior, situate just anterior to the tail, being connected with the trophonucleus by a chromatin bar. The undulating membrane runs from the anterior to the posterior centrosome, and is strengthened by eight myonemes.

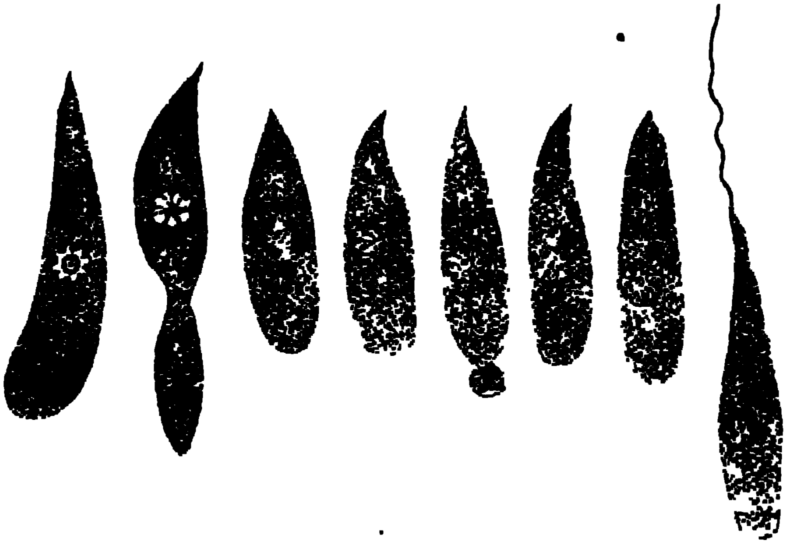

FIG. 180.—*Hæmoproteus noctuæ* CELLI AND SANFELICE.

(After Schaudinn.)

Formation of the indifferent oökinete and its development into the indifferent trypanosome.

Formation of the Macrogamete. The macrogametocyte becomes rounded and ruptures the remains of the erythrocyte, and is set free. The centrosome of the trophonucleus disappears, and the chromatin forms a spiral thread, which separates by longitudinal and transverse divisions into four tetrads. The kinetonucleus first forms a spindle, and then divides, causing the first reduction, which results in four dyads, and then a second division follows, leaving four monads or single chromosomes. The kinetonucleus now returns to its old position outside and close to the trophonucleus, and the macrogamete is fully developed.

Schaudinn was not able to trace out the reduction of the kinetonucleus, but it ultimately consists of four chromosomes and a centrosome, which, Woodcock points out, are not wholly sexual.

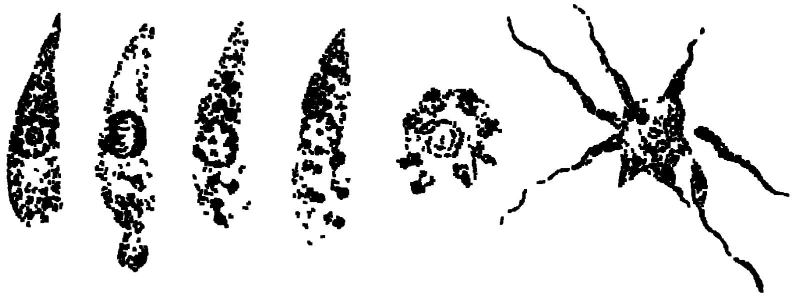

FIG. 181.—*Hæmoproteus noctuæ* CELLI AND SANFELICE.
(After Schaudinn.)
Formation of the male oökinete, and its development into the male trypanosome.

Zygosis.—This consists in the penetration of a microgamete into a receptive cone, which has arisen from the cytoplasm of the macrogamete on the side where the nuclei are situated.

The only parts which enter are the male trophonucleus, which is reduced, and the male kinetonucleus, which is not reduced, but which now undergoes two divisions. The trophonuclei of the male and female elements fuse and form the fusion spindle, at either end of which the kinetonuclei take up positions, and thus the zygote is formed.

Oökinete.—While zygosis is proceeding, and even before the complete formation of the synkaryon, the zygote becomes vermiform and motile, and is therefore called an oökinete. It consists of an anterior, hyaline, changeable end, which is followed by a region of cytoplasm with vacuoles, then by a denser region with the nuclear spindle just described, and finally a rounded posterior end full of granules and hæmozoin. From this posterior end a portion of cytoplasm enclosing granules and hæmozoin, etc., is cut off, thus freeing the oökinete of waste material. The spindle of the synkaryon now consolidates to form eight chromosomes, which will constitute the trophonucleus, while the two kinetonuclei at either end of the spindle, meeting together, form a single kinetonucleus, which takes up a central position inside the trophonucleus, and divides into eight chromosomes, with a centrosome in its centre. The nucleus of the oökinete, therefore, consists of a central centrosome, with eight surrounding chromosomes, around which lie another eight chromosomes, bordering the periphery.

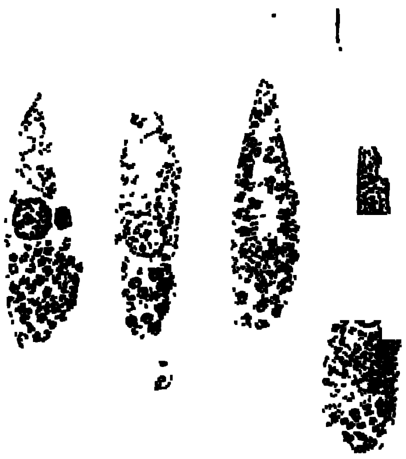

FIG. 182.—*Hæmoproteus noctuæ* CELLI AND SANFELICE: DEVELOPMENT OF THE FEMALE OÖKINETE AND THE FEMALE TRYPANOSOME.

(After Schaudinn.)

But oökinetes are not all alike. On the contrary, Schaudinn describes three kinds:—

1. *Indifferent Oökinete.*—Cytoplasm clear, and staining faintly, with one or two large vacuoles anteriorly, and having some granular material and hæmozoin still left.

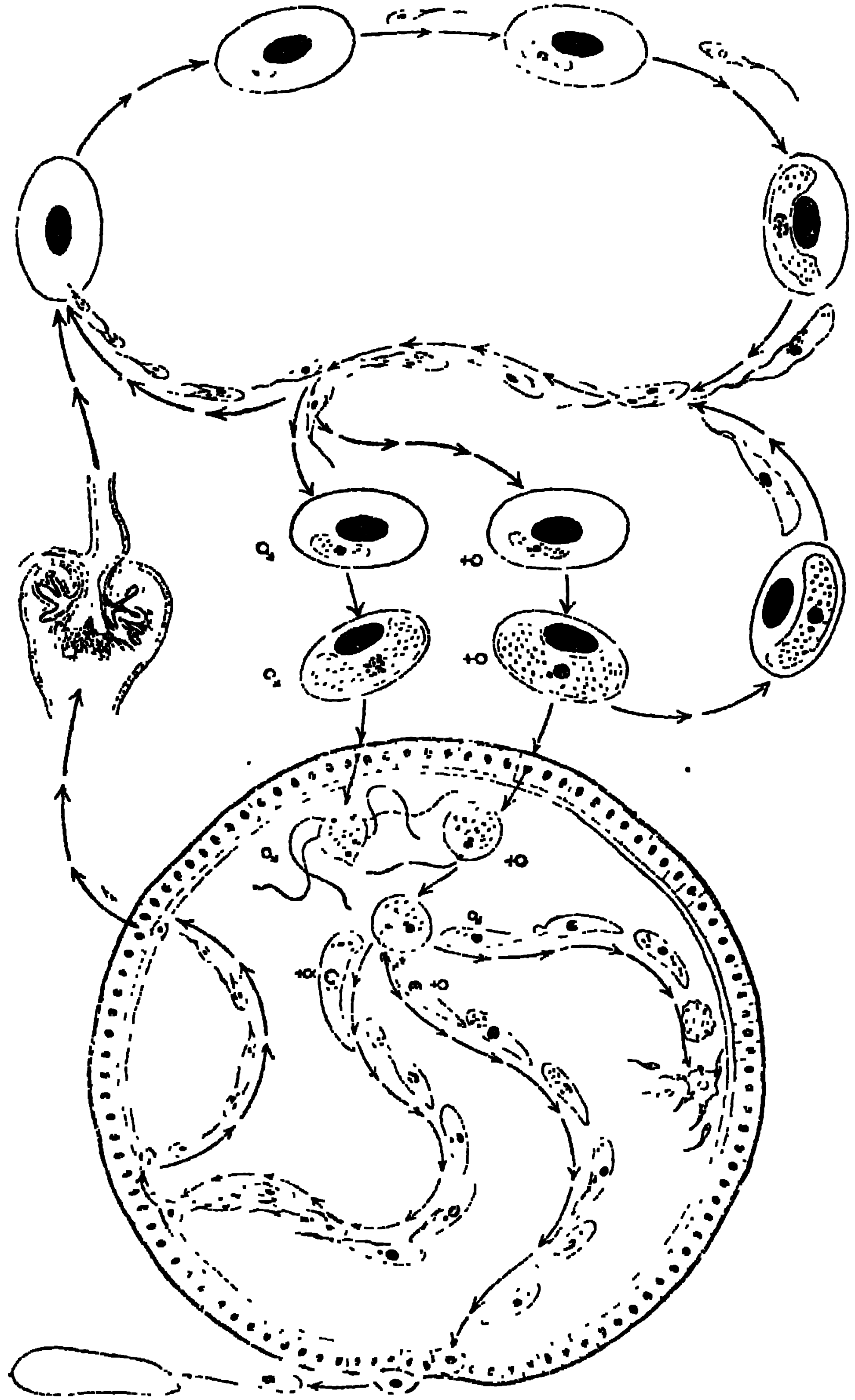

FIG. 183.—DIAGRAM SHOWING THE LIFE-CYCLE OF *Hæmoproteus noctua* CELLI AND SANFELICE.

(After Sambon and Terzi.)

Many authorities consider this life-cycle to be made up of the cycles of a halteridium and a trypanosome, which are believed to be quite distinct.

2. *Male Oökinete.*—Smaller than the indifferent or female forms, with cytoplasm almost hyaline, and much clearer than that of the indifferent form, with granular material completely lacking, nucleus large and rich in chromatin.

3. *Female Oökinete.*—Cytoplasm fairly dense, with plenty of granules, with a nucleus smaller than in the indifferent form.

The Indifferent Oökinete.—The indifferent oökinete starts its development by expelling for a second time a quantity of hæmozoin, while its kinetonucleus unites with the trophonucleus, so that the nucleus now possesses eight compound chromosomes.

The centrosome becomes dumb-bell shaped, and forms an axial spindle, around which the chromosomes are arranged. These now divide, and form a diaster by the different portions passing to either end of the spindle, which is heteropolar, the smaller half being kinetic in function. The nucleus now divides into a larger portion, the trophonucleus, and a smaller, the kinetonucleus. The former enters on a resting stage, while the latter proceeds to the periphery, and forming another axial spindle at right angles to the length of the parasite, divides into two portions by its centrosome forming the axial spindle and the chromosomes the two ends of a diaster. One of these daughter kinetonuclei lying in the ectoplasm is attached to the other, lying in the endoplasm, by means of the axial spindle. The ectoplasmic kinetonucleus forms another spindle, with a longitudinal axis, which grows backwards along a fold of the ectoplasm, expanding it as it goes, to the hinder end of the body. In this way an undulating membrane is formed, which, therefore, contains eight chromosomes—the myonemes—on each side of the folded ectoplasm, while the axial spindle, becoming excentric, forms the flagellum. At the posterior end of the undulating membrane the flagellum joins with the chromosomes, and grows out of the body to form the free flagellum, along which the ectoplasm is drawn for a short distance.

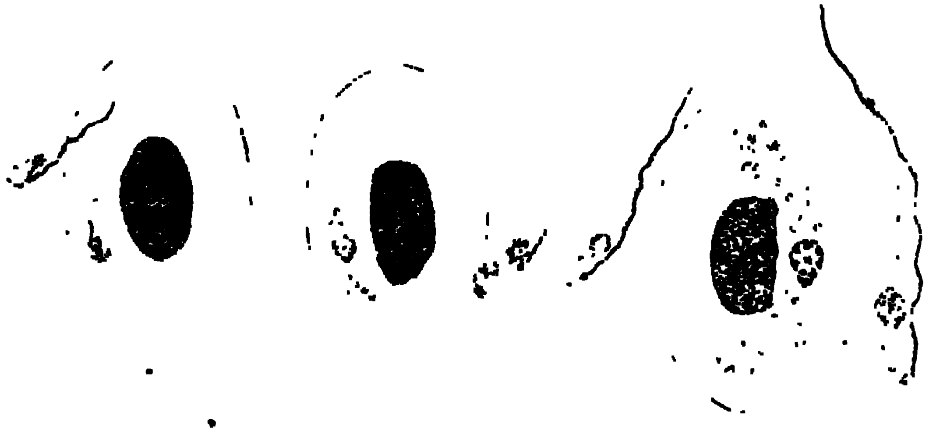

FIG. 184.—*Hæmoproteus noctuæ* CELLI AND SANFELICE.
(After Schaudinn.)

On the left a small trypanosome is seen entering a red corpuscle in the blood of the little owl, and in the corpuscle is seen the first endocellular stage. The second corpuscle shows a more advanced endocellular stage and the act of liberation into the liquor sanguinis. Farther to the right is seen a medium-sized trypanosome. The third corpuscle shows the fully-grown halteridial form, while on the extreme right a fully-grown trypanosome is depicted.

Of the two centrosomes of this spindle, the distal one disappears, while the proximal one forms the blepharoplast at the root of the flagellum.

The endoplasmic daughter kinetonucleus becomes the kinetonucleus of the trypanosome, and thus is formed the indifferent trypanosome, which now multiplies by binary division. After some time it takes on a gregariniform phase, and becomes attracted to an epithelial cell in the stomach of the mosquito by its flagellum, which is reduced to a short rod. While so attached it may multiply by binary division, and may also penetrate in between the cells of the stomach and encyst, losing its flagellum.

After a period of rest the trypanosome can become active again, but after a time it must either (1) pass into the blood of the little owl, (2) become a male or female form, (3) die out.

The Male Oökinete.—The male oökinete forms a heteropolar diaster, but with a subdivision of the elements into male and female instead of into kinetic and trophic.

The larger or female portion disappears, while the smaller or male portion forms eight double nuclei with kinetic and trophic elements, which are distributed throughout the cytoplasm.

The oökinete now becomes rounded, while the eight double nuclei travel to the periphery, which grows out into little elevations, each with a double nucleus. Each little elevation grows into a little male trypanosome in the same manner as in the indifferent form, and breaks off from the 'rest body' (*nucleus de reliquat*) of the parent cell. These male trypanosomes, according to Schaudinn, simply die off.

The Female Oökinete.—In this form the same changes take place as in the male oökinete, but it is the small male nucleus which degenerates, after dividing into a number of forms, while the large female nucleus, which consists of the trophic and kinetic elements, remains, and forms a trypanosome in the same manner as in the indifferent form.

The female trypanosome is slow moving and does not divide, but can become gregariniform and lie quiescent between the epithelial cells for a time. It can also pass into the ovaries and eggs, and lie dormant during the winter.

The female oökinete, however, undergoes parthenogenesis by losing its flagellar apparatus and developing a trophonucleus with a kinetonucleus in contact with it. The kinetonucleus now divides, and undergoes reduction, while the trophonucleus also divides, one portion being lost. The reduced kinetonucleus, which has divided into two, now enters the trophonucleus from opposite sides, and fusing forms the synkaryon of an oökinete, which may become an indifferent, a male, or a female trypanosome.

In the Owl.—The male, female, and indifferent trypanosomes may be injected into the owl during the process of biting by the mosquito, but the majority are of the indifferent type. The male trypanosomes, if they enter, die off. The indifferent trypanosomes divide in the blood until a small size is reached, when they enter the erythrocytes and become a young halteridium by the flagellar apparatus disappearing and the kinetonucleus approaching the trophonucleus.

In twenty-four hours this parasite, which now contains hæmozoin, becomes active, and, re-forming its flagellar apparatus, leaves the blood cell usually at night as a typical *Trypanosoma noctuæ*. After a short period of activity it enters another erythrocyte and grows till the next night, when it again becomes free. This process takes place six times before the trypanosome attains its full size, when it undergoes repeated division until again small, thus completing the cycle of schizogony. The small extracellular forms may be looked upon as the merozoites, and the intracellular forms as trophozoites, and the large extracellular form as a schizont. The sexual forms are developed from the merozoites, i.e., the very young indifferent trypanosomes, which enter the red cells, and become microgametocytes and macrogametocytes, thus completing the cycle of sporogony.

Remarks.—Novy and many others are convinced that Schaudinn is entirely wrong, and that he was dealing with a double infection of a halteridium and a trypanosome, both of which probably develop in entirely different ways. We are also convinced that these parasites are Hæmosporidia.

Hæmoproteus columbæ Celli and Sanfelice, 1891.

Hæmoproteus columbæ is the halteridium of *Columba livia* L. Its life-history is not exactly known at present, but has been studied by Ed. and Et. Sergent and by Aragão. According to the latter observer it would seem to have the usual two life-cycles of schizogony and sporogony joined into one, taking place in *Columba livia* and in *Lynchia maura* or *L. brunea* (*lividicolor*) Oliv.

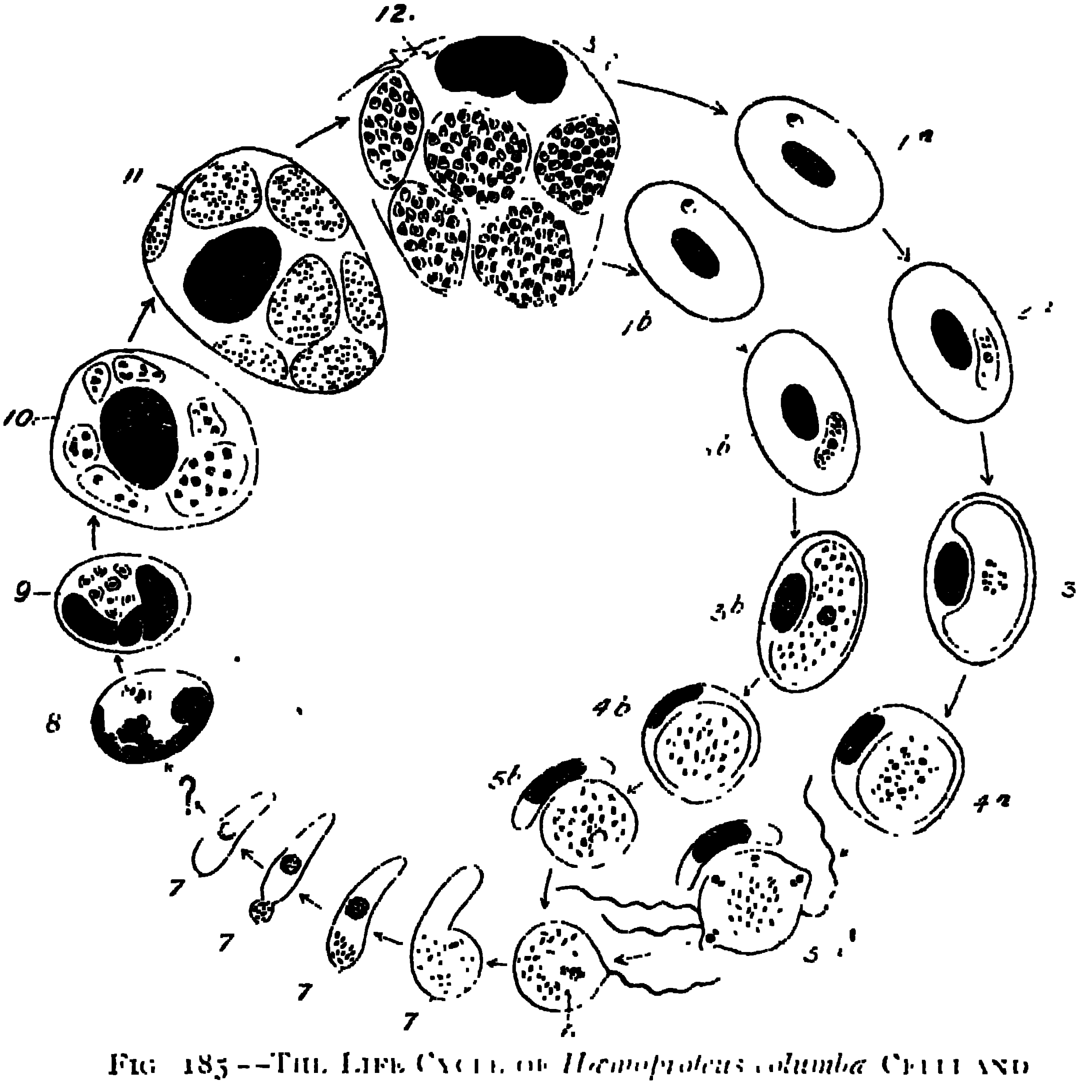

FIG. 185.—THE LIFE CYCLE OF *Hæmoproteus columbæ* CELLI AND SANFELICE.

(According to the researches of Aragão. After Aragão from *Archiv f. Protistenkunde*.)

Starting with the macro- and microgametocytes, which are of the same appearance as in *H. noctuæ*, and which enter the gut of the *Lynchia* along with the blood sucked from the pigeon, the usual processes of reduction, with the formation of microgametes and macrogametes and ookinetes, and the clearance of waste matter from these latter, are gone through. The further changes undergone by the ookinete are at present unknown.

After the *Lynchia* bites a pigeon, a small uninuclear parasite is to be found in a leucocyte, first at the site of the bite and later in the lungs, where the further development takes place. First the small parasite divides into a number of mononuclear forms, which, along with the leucocyte, grow enormously, and form large parasites, at first full of nuclei, and later of mononucleated merozoites, the whole process taking some twenty-six or more days. The minute merozoites now enter the red corpuscles and grow into typical Halteridia. It appears that there are no trypanosome stages, and, indeed, the only form of that nature met with was *Trypanosoma avium* Novy and McNeal.

This is quite a different history from that of Schaudinn for *H. noctuæ*, but it must be observed that it is incomplete, and, therefore, deductions cannot safely be drawn from it.

Other Species.—A large number of species are described by Celli and Sanfelice, Novy and McNeal, and others, which have been found in birds as well as in some reptiles.

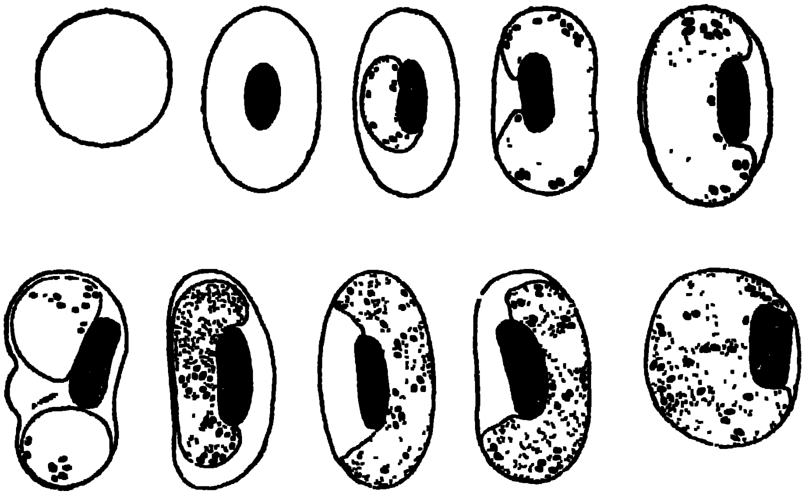

FIG. 186.—*Hæmoproteus columbæ* CELLI AND SANFELICE. (After Sambon.)

Sambon has described, under the name of *Hæmoproteus mansoni* (Fig. 176), a new species found in the red grouse (*Lagopus scoticus*), the gametocytes of which are not closely adherent to the nucleus of the erythrocyte, as is usually the case, and sporogony takes place in a parasitic fly of the grouse (*Ornithomyia lagopodis*), in the stomach of which oökinetes were found.

Anschütz has described a schizogony of *H. oryzivoræ* taking place in the circulating blood of *Padda oryzivora*.

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CHAPTER XXII

NEOSPORIDIA

Neosporidia—Myxosporidia—Actinomyxidia—Sarcosporidia—Haplosporidia—Protozoa incertæ sedis—Chlamydozoa—Filterable viruses—References.

NEOSPORIDIA Schaudinn, 1900.

Definition.—Parasitic plasmodromata, without motile organs, in which spore-formation and trophic growth proceed simultaneously.

Remarks.—The Neosporidia are protozoa in which reproduction and growth go on together. In the Telosporidia the trophozoite grows into the schizont, which divides into spores; in the Neosporidia growth and spore formation go on together; but, as in the case of all attempts at classification, there are exceptions, for the trophozoite may grow into the schizont, and then divide.

It appears as though the Neosporidia were evolved from a sarcodinal ancestor.

They are divided into four orders: (1) Myxosporidia, (2) Actinomyxidia, (3) Sarcosporidia, (4) Haplosporidia; and, in addition, there are a number of parasites belonging evidently to the protozoa, which cannot easily be classified, and are therefore placed in an addendum to the Neosporidia as *Protozoa incertæ sedis*.

ORDER I. MYXOSPORIDIA Butschli, 1881.

Neosporidia with spore-formation commencing early in the amœboid trophozoite. Each spore has one or more polar capsules.

The Myxosporidia are subdivided into:—

Suborder I. Phænocystes Gurley, 1893. **Synonym.**—Myxosporidia (*sensû stricto*). Spores with two to four large, clearly visible polar capsules.

Suborder II. Cryptocystes Gurley, 1893. **Synonym.**—Microsporidia (Balbiani). Spores with one minute polar capsule, which is only rendered visible by treatment with reagents.

SUBORDER I. PHÆNOCYSTES Gurley, 1893.

Phænocystes comprise the true Myxosporidia, being usually found in Teleostean fish, though they may occur in elasmobranchs, amphibia, and reptiles.

In fish they have long been known as psorosperms, being found in the bile-passages, the urinary organs, the muscles, and the nervous system.

The amœboid trophozoite has a differentiation of its cytoplasm into endo- and ecto-plasm, and moves about by pseudopodia. Spore-formation begins early by a concentration of the cytoplasm around one of the nuclei of the trophozoite. This concentrated area is marked off by a capsule, and is the pansporoblast. The nucleus of the pansporoblast divides repeatedly, after which the cytoplasm splits into two masses—the sporoblasts—each of which is covered by a cuticle and contains three nuclei.

The cytoplasm of the sporoblast now divides into three areas around the nuclei. One of these areas is large, and is called the sporoplasm, while the other two are small, and form the polar capsules. Each spore, therefore, contains two polar capsules and one mass of sporoplasm, which represents a single sporozoite. Each polar capsule develops a spirally coiled thread. A spore escapes when the parent trophozoite dies, and then finds its way out of its host by the bile or urine, or through the tissues into the alimentary canal. For further development it must be swallowed by another host, in whose alimentary canal the threads of the polar capsules are extruded, fixing the little spore, which bursts and allows the amœboid sporozoite to escape and go on its travels in search of a suitable tissue. Perhaps *en route* it conjugates with another sporozoite; if so, this is not known. While sporogony is preparing, schizogony may take place by plasmotomy, which is the division of the multinuclear trophozoite into two or more forms.

It will thus be seen that growth, plasmotomy (schizogony), and spore-formation (sporogony) go on simultaneously.

Classification.—*Disporea* Doflein, 1899.—Phænocystes with two spores.

FAMILY.—*Ceratomyxidæ* Doflein, 1901.

Genera.—*Ceratomyxia*, *Leptotheca.*—Parasitic in fish and frogs.

Polysporea Doflein, 1899.—Phænocystes with more than two spores.

FAMILY 1.—*Myxidiidæ* Auerbach, 1910.

Genera.—*Sphærospora*, *Myxidium.*

FAMILY 2.—*Chloromyxidæ* Thélohan.

FAMILY 3.—*Myxobolidæ* Gurley, 1893.

SUBORDER II. CRYPTOCYSTES.

This order is divided by Doflein and Perez into:—

Tribe 1. *Monosporogenea* Perez.—Trophozoite becomes a single pansporoblast (sporont), which produces a single spore.

Tribe 2. *Oligosporogenea* Doflein, 1899.—Trophozoite becomes a single pansporoblast (sporont), which produces four to eight spores.

Tribe 3. *Polysporogenea* Doflein, 1899.—Trophozoite becomes numerous pansporoblasts (sporont), which produce many spores.

TRIBE 1. MONOSPOROGENEA.

This tribe includes *Nosema bombycis* Nägeli, 1857, which is the cause of pébrine, the silkworm disease. *N. apis* Zander, 1909, was shown to be the cause of microsporidiosis in bees in England by Fantham and Porter.

TRIBE 2. OLIGOSPOROGENEA Doflein, 1899.

This includes the genera *Gurleya* Doflein, *Thélohania* Henneguy, and *Pleistophora* Gurley.

TRIBE 3. POLYSPOROGENEA Doflein, 1899.

This includes the genera of *Glugea* Thélohan, and *Myxocystes* Mrazek, of which *Glugea anomala* Moniez is a parasite of the stickleback.

Microsporidium polyedricum Bolle, a doubtful species, is said by Perroncito to occur in man.

ORDER II. ACTINOMYXIDIA Stolc, 1899.

These are parasites in the Tubificidæ of the oligochæte worms, and need not concern us.

ORDER III. SARCOSPORIDIA Bütschli, 1882.

Definition.—Neosporidia in which the young trophozoite is, with rare exceptions, found in the muscle-fibre of warm-blooded animals. Spore-formation commences early, and proceeds during the whole growth of the trophozoite, which may attain a very large size, when it is covered by two coats, the inner of which is prolonged internally through the parasite, dividing it into a series of chambers.

Remarks.– The Sarcosporidia, discovered by Miescher in 1843, are very common parasites, and in the form of *Sarcocystis tenella* may be seen by the practitioner in the tropics in meat sent as food to gaols and hospitals.

Two families are known: (1) *Sarcocystidæ*, (2) *Rhinosporidiidæ*.

1. Sarcocystidæ Poche, 1913.

Definition.—Sarcosporidia found in muscle fibres, and divided into chambers by septa.

Sarcocystis Lankester, 1882.

Synonym.—*Gastrocystis* Chatton, 1910.

Definition.—Sarcocystidæ with outer radially striated and inner homogeneous coat and poles of undifferentiated protoplasm.

Type Species.—*Sarcocystis miescheriana* Kuhn, 1865.

Though a common parasite, its life-history is by no means well known. The youngest form is the trophozoite described by Bertram, which lies in a muscle-fibre, and consists of cytoplasm united by a cuticle, and containing several mononuclear pansporoblasts. The next stage is more advanced, for in this the trophozoite has grown considerably, and now consists of two coats—an outer, radially striated, and an inner, homogeneous, which is prolonged externally into filaments and internally into a series of septa, marking out chambers, each of which contains one pansporoblast. Internal to this coat is a layer of cytoplasm forming the endoplasm of the parasite.

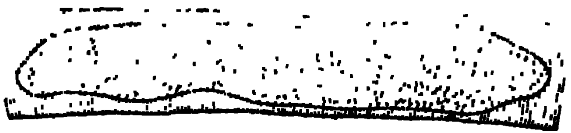

Fig. 187.—*Sarcocystis tenellæ bubali*: Young Form.

The poles of the parasite consist of undifferentiated endoplasm, and form the areas of growth of the young trophozoite. The pansporoblast breaks up into a large number of spores.

The third stage is reached when the parasite has grown so much that it has stretched the muscle-fibre, in which it is lying, into a thin sheath covering it, and therefore now appears to lie between the muscle-fibres. The endoplasmic layer extends all round the interior of the parasite, so that the pansporoblasts are formed from the whole periphery, and therefore the youngest forms are in this position, while, farther in, chambers with the fully-developed pansporoblasts are found, and, still farther in, is the centre of the parasite, filled by a granular substance formed from broken-down and dead spores which have been too long in existence.

As to the spores, a curious point to be noted is that some observers only describe gymnospores, while others only describe chlamydospores. Minchin suggests that this is because parasites in different stages of their life-history have been examined, and he looks upon the gymnospores as merozoites and the chlamydospores as spores, and these views are strongly supported by Korté's description of a form in *Macacus rhesus*.

The merozoites are crescent-shaped, naked spores, from 1 to 21 μ in length, according to the species, consisting of a finely granular protoplasm with a nucleus, some granules, and one or two vacuoles. They are thought to be the means by which the parasite spreads itself in its host, especially as they are motile by gliding, corkscrew, or amœboid movements.

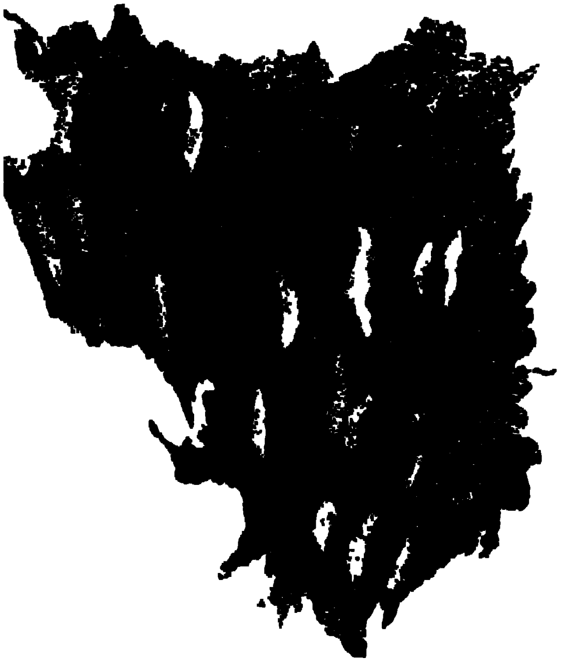

FIG. 188.—*Sarcocystis tenellæ bubali* IN MEAT.

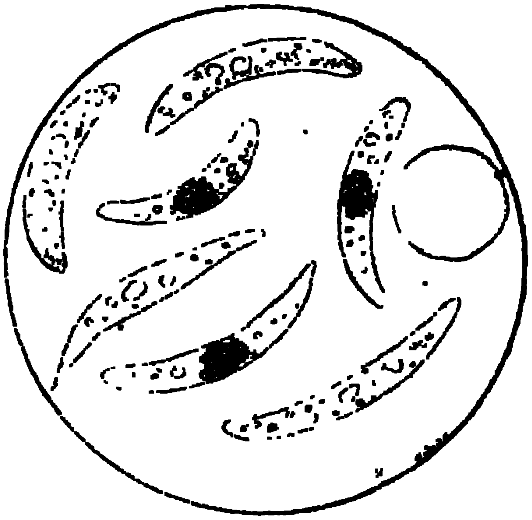

FIG. 189.—SARCOCYSTIS SPORES FOUND IN THE BLOOD OF *Bos indicus* BY CASTELLANI AND STURGESS.

The spores are from 3 to 14 μ long in *Sarcocystis tenella*, with one extremity rounded and the other pointed. They are curved, and surrounded by a thin membrane. The pointed third of the spore is spirally striated, due to fine folds in the outer capsule, while the blunt third contains a nucleus. It is obvious that this resembles the spore of a myxosporidian, and, in fact, Van Eecke says that one, two, or even three filaments issue from a spore. The spores can be seen in the peripheral blood at times.

It is thought that these spores spread the infection to another host, but in what manner is not clear. Perrin has recently suggested that the parasite may be transmitted by the larvæ and imagines of the blow-fly (Calliphora) or the flesh-fly (Sarcophaga).

It is true that Smith has infected (after a long incubation) mice by feeding them on the flesh of infected mice, but that, of course, might simply be by the merozoites, and would in any case not explain how herbivorous animals are infected. Our feeding experiments with a dog were not successful.

Erdmann says that the spore germinates in the intestine of the host, and liberating the toxin—sarcocystin—which may come from the polar capsule, causes the epithelium to be shed, while the little amœba coming out from the spore is able to penetrate the denuded area and to get into the lymph spaces of the intestine, where it lives about a month and then passes on to the muscles.

Crawley considers that the spore bores its way into the intestinal cells where it appears to undergo some form of schizogony. At all events it disappears in twenty-four hours, but later he thought that he had noted sexual differentiation in these spores in the cells, and the formation of a zygote.

Pathogenicity.—*Sarcocystis tenellæ bubali* is very common in the buffalo-meat in Ceylon, and frequently causes inquiries to be made. It appears as white particles, called by the native butchers 'milk nerves,' lying among the muscular fibres of tongue, larynx, diaphragm, and skeletal muscles. This ingestion of infected meat has apparently no deleterious effect on man, but the spores may be the cause of irregular fever.

Classification.—A number of species are recognized:—

1. *Sarcocystis miescheriana* Kühn 1865, found in the pig.

2. *S. bertrami* Doflein, 1901, in the horse.

3. *S. tenellæ* Railliet, 1886, in the sheep. *S. tenellæ bubali*, in the Ceylon buffalo. Vuillemin has described a case of this infection in man.

4. *S. blanchardi* Doflein, 1901, in cattle.

5. *S. lindemanni* Rivolta, 1878. This species has been found in man. They were first described indefinitely by Lindemann in 1868, in the myocardium and on the valves of the heart of a person who had died of dropsy. They were said to be 3 millimetres in length and 1·5 millimetres in breadth, but it is very doubtful what these really were.

Rosenberg in 1892, reports a most doubtful case of a cyst in a papillary muscle in a person who died from pleuritis and endocarditis. Kartulis described them in the muscular system and liver (most doubtful) of a person who died from multiple abscesses in the liver and muscles. The man was a Sudanese. Koch, in 1887, described an undoubted case in Egypt.

Baraban and St. Remy, in 1894, described them in the laryngeal muscles of a man who had been executed. This description is not to be doubted. The parasite is described as being 1·6 millimetres long, and about 0·17 millimetre in width. Vuillemin in Nancy and Darling (1909) in Barbados have recorded cases.

6. *S. hueti* Blanchard, 1885, in the seal.

7. *S. kortei* Castellani and Chalmers, 1909.—This parasite, found by Korté in the thigh muscles of *Macacus rhesus*, is peculiar in that the inner coat was not continued into the cytoplasm of the trophozoite, and the endoplasm contained only gymnospores (merozoites), and no pansporoblasts or alveolar network. The spores contained nothing but a nucleus, no cell membrane or other structure being visible. There were no signs of any reaction on the part of the tissues.

8. *S. aramidis* Splendore, 1907.—Parasite in *Aramidis saracura*, a Brazilian bird.

9. *S. ammodromi* Splendore, 1907.—*Miescheria ammodromi* Splendore, 1907. Mesnil says it is not generic, and perhaps not specific. It is found in a Brazilian bird, *Ammodromus manimbe*.

10. *S. leporum* Crawley, 1914, in American rabbits.

11. *S. setophaga* Crawley, 1914, in American redstarts.

12. *S. muris* Blanchard, in rats.

2. **Rhinosporidiidæ** Poche, 1913.

Definition.—Sarcosporidia found in connective tissue and not divided into chambers by septa.

Rhinosporidium Minchin and Fantham, 1905.

Definition.—Rhinosporidiidæ with well-defined sporoblast.
Type Species.—*Rhinosporidium seeberi* (Wernicke, 1900).

Rhinosporidium seeberi Wernicke, 1900.

Synonym.—*Rhinosporidium kinealyi* Minchin and Fantham, 1905.

Rhinosporidium was discovered in 1896 by Dr. Guillermo Seeber in Buenos Ayres in a nasal polypi in a young man of nineteen years of age. In 1900 he published a description of the parasite, and in the same year Wernicke gave it the name of *Coccidium seeberi*.

Kinealy, in 1903, reported to the Laryngological Society a peculiar case of polypus growing from the septum of the nose of an Indian in Calcutta as a pedunculated vascular growth resembling a raspberry in appearance by having whitish spots on the general red surface. On section, this tumour was found to have peculiar bodies embedded in it.

It was then carefully examined and described by Minchin and Fantham, who came to the conclusion that it was a haplosporidian, and named it *Rhinosporidium kinealyi*.

In 1905 Nair of Madras came across a similar polypus in several people who all came from the small native State of Cochin on the west coast of India. These polypi have been carefully described by Beattie in 1906. Castellani and Chalmers have found it in polypi in Ceylon.

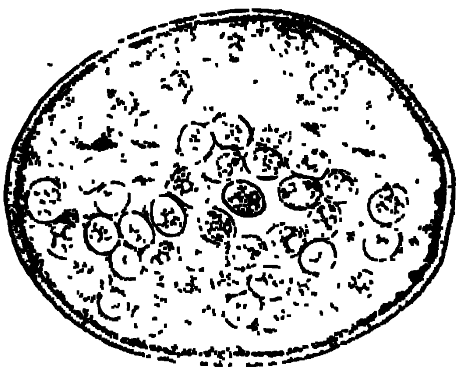

FIG. 190.—*Rhinosporidium seeberi* WERNICKE.
(From a nasal polypus in a case in Ceylon; schematic, and highly magnified.)

Morphology.—On cutting into the polypus it is noticed that there are minute dots visible to the naked eye, and capable of being dissected out. These dots are cysts.

When examined with the microscope, it is seen that the growth is covered by stratified pavement epithelium, which shows signs of proliferation and invasion by polymorphonuclear leucocytes. Under this epithelium there is a stroma formed of delicate fibrous tissue, myxomatous in places, and cellular at other spots. The cysts were found to be oval, round, tubular, branched or irregular bodies, lying below the epithelium principally, but also found in hæmorrhages and in cell collections. The wall of the cyst is generally thin, and has either an opening or a conical elevation at one point. It consists of two layers—a thinner external and thicker internal coat. The smaller cysts, from 10 to 30 μ in diameter, contained undifferentiated protoplasm with a vesicular nucleus containing a nucleolus. The larger cysts had one or more definite chromatic masses. A fully-developed cyst is lined with protoplasm, in which young pansporoblasts are forming, while the centre of the parasite is full of old pansporoblasts, separated from one another by an indefinite framework continuous with the capsule. A young pansporoblast is seen to be a small oval or rounded mass of cytoplasm with a single nucleus. This body grows, and becomes surrounded by a membrane, while its nucleus divides by amitosis into four to sixteen spores, each of which has a very thin wall and a central nucleus. The pansporoblasts and spores are set free by rupture of the cyst, and may be surrounded by polymorphonuclear leucocytes, thus forming minute abscesses, or may be engulfed by mononuclear leucocytes, or may grow into parasites, or escape from the host in the nasal secretion. The method of infection is not known.

The framework inside the cyst separating the pansporoblasts indicates that *Rhinosporidium* belongs to the Sarcosporidia, and not to the Haplosporidia.

Pathogenicity.—The pathology appears to be a proliferation of the submucosa and mucosa of the nose, brought about by the irritation of the parasite (see p. 1578).

ORDER IV. HAPLOSPORIDIA Caullery and Mesnil, 1899.

Synonym.—*Haplosporidiidea* Poche, 1913.

Neosporidia with very simple life-history and undifferentiated cell-plasma, without septum and with spores of simple structure, with one nucleus, and no polar capsules.

The Haplosporidia are characterized by the simplicity of their life-cycle, which begins with a mononuclear or binuclear trophozoite, which may encyst, and in any case grows larger and larger, while its nucleus divides into several nuclei, so that a multinucleated mass or schizont is formed. This escapes from its cyst and divides up into merozoites, either directly or after plasmotomy, each of which becomes a trophozoite, thus completing schizogony. Sporogony is unknown.

They are parasites of fishes and invertebrates.

Classification.—Family 1. Haplosporidiæ Caullery and Mesnil.—Spores with double envelope and opening.

Genus 1. *Haplosporidium.*—Spores closed by a valve. In annelids.
Genus 2. *Urosporidium.*—Spores open. In annelids.

Family 2. Bertramiidæ Spore envelope without opening.
Genus 1. *Bertramia.*- Stomach of fish.
Genus 2. *Ichthyosporidium.* In tumours of fish (Figs. 191-196).

Family 3. Cœlosporidiidæ.- Spores nude.
Genus 1. *Polagarynum.*
Genus 2. *Blastulidium.*

Protozoa Incertæ Sedis.

Cytoryctes variolæ Guarnieri, 1892.

Synonym.—*Strombodes jeuneri* Sjöbrung, 1902.

In 1892 Guarnieri described peculiar parasitic bodies in lesions of smallpox, and in those produced by vaccination of the cornea of rabbits, etc. Pfeiffer, in 1893, confirmed these findings, as did Jackson Clarke in 1894, and Wasielewski in 1897. Councilman, Magrath, and Calkins, in 1903, published the full account of the life-history of the parasite, and their findings have been confirmed—in part, at least—by De Korté in 1905.

In its youngest form *Cytoryctes variolæ* is seen in the cells of the skin as a minute spherical homogeneous body, 0·7 μ in size. No differentiation into nucleus and cytoplasm is possible, as the organism appears to be all nucleus. The parasite grows to 3 μ, and then shows a vacuolization in the centre, with sometimes a central dot. The periphery next shows minute unstained dots, which, when they become larger, take on the green of a Borrel's stain. The red staining material is called by Calkins protogonoplasm.

The organism can now change its shape and throw out pseudopodia, and lives in a vacuole near the nucleus; there is no ectoplasm or endoplasm, no vacuoles, but only chromatin granules of protogonoplasm. Volpino has described minute motile granules in the epithelial cells, which he considers to be the true parasites.

Auto-Infection.—In a large parasite to 14 μ) the protogonoplasm is distributed through the body in minute spherical granules lying in a minute vesicle, forming granules from 0·7 to 1 μ in diameter, which are liberated by disintegration of the framework of host cell, while the rest of the cytoplasm form a *nucleus de reliquat*.

Sexual Development.—The homogeneous granules or gemmules may start the cycle of cytoplasmic organisms again, or may become germ-cells in the nucleus. The gemmules reach the nucleus, but they now stain uniformly and become minute, clearly-defined, homogeneous bodies—female gametocytes. Sometimes they fail to reach the nucleus and remain in the cytoplasm, in which they can only partially develop. Within the nucleus Calkins thinks they form male and female gametocytes, homogeneous granules, or the gemmules become spherical, with central red masses, and later red masses at the periphery—the male gametes. No conjugation has been observed.

The zygote is an amœboid body lying in the nucleus, and staining deeply. This zygote becomes a pansporoblast and the mother-cell of the sporoblasts. The spore is very minute, and contains a vacuole; it migrates, and may travel into the nucleus and form secondary sporoblasts.

Cytoryctes (Doubtful Species).

This organism can be found as corroid bodies in the smears taken from the heart muscle of animals suffering from foot and mouth disease.

Neuroryctes hydrophobiæ Calkins, 1907. •

Neuroryctes hydrophobiæ, better known as the Negri bodies, because they were discovered by Negri in 1903 as round or oval bodies, 1 to 23 μ in length, in the nerve-cell of the brain, especially the *Cornu ammonis*, of animals suffering from hydrophobia, are now generally accepted as the cause of the disease. Hydrophobia is so common in India and Ceylon that a knowledge of its parasite is necessary to the practitioner in that part of the tropics.

Some authorities consider these bodies to be cell-structures, but in our opinion there cannot be any doubt that they are parasites, especially after the further investigation of Negri, amply confirmed by Williams, Lowden, and Calkins, who named it *Neuroryctes hydrophobiæ* Calkins, 1907. Prowazek believes them to be Chlamydozoa. When stained by Giemsa the protoplasm takes on a bluish tinge like the malarial organism, while there is a central

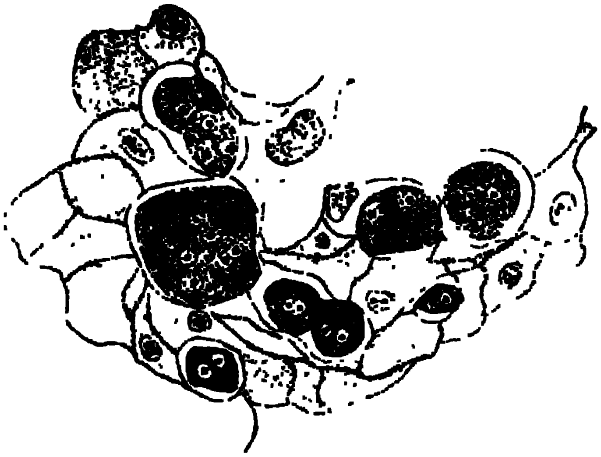

FIG. 191.—A SERIES OF SMALL ICHTHYOSPORIDIA ENCLOSED IN CONNECTIVE TISSUE.

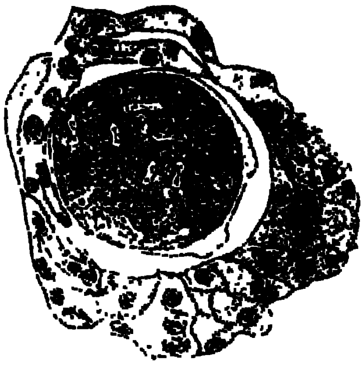

FIG. 192.—A MEDIUM-SIZED ICHTHYOSPORIDIUM IN A NEST OF CONNECTIVE TISSUE.

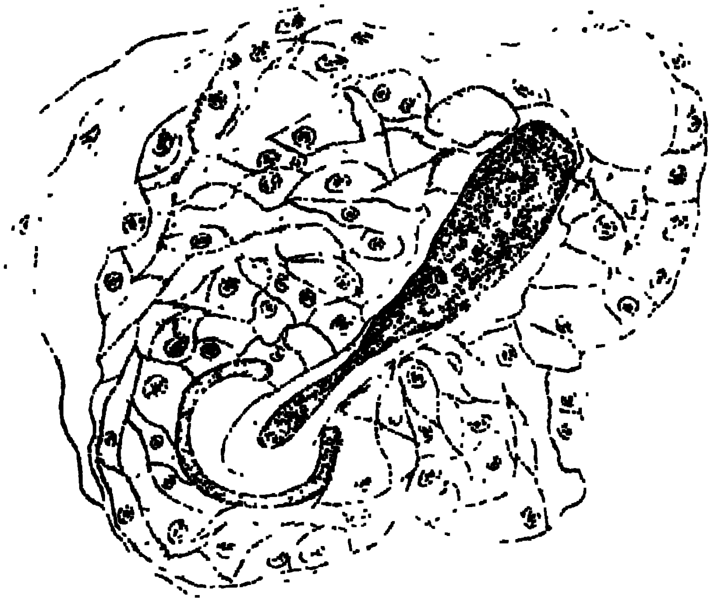

FIG. 193.—ESCAPE OF THE ICHTHYOSPORIDIUM FROM ITS CYST.

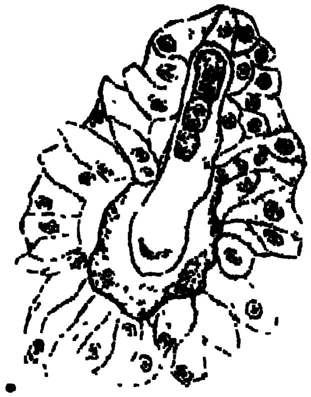

FIG. 194.—BREAKING-UP OF AN ICHTHYOSPORIDIUM INTO REPRODUCTIVE BODIES.

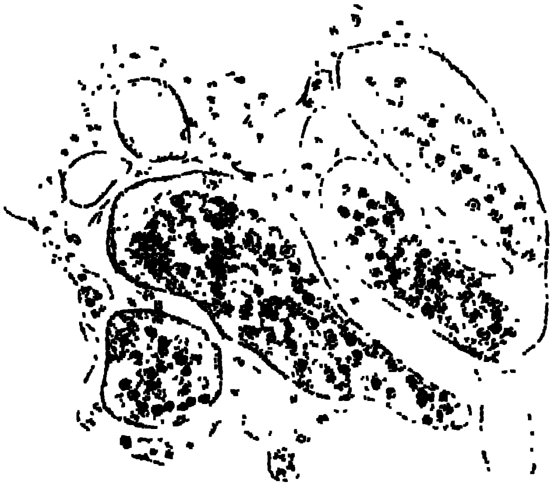

FIG. 195.—LARGE ICHTHYOSPORIDIA, ONE OF WHICH (ON THE RIGHT) IS UNDERGOING PLASMOTOMY.

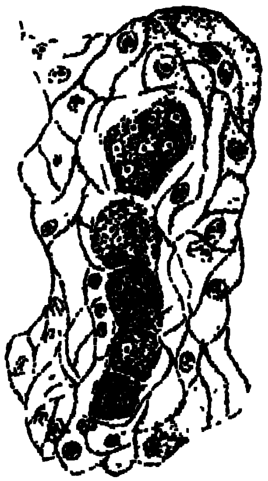

FIG. 196.—YOUNG FORMS DEVELOPED FROM THE BREAKING-UP OF A LARGE PARASITE.

(From drawings by Miss Robertson.)

body like a nucleus, composed of a periphery of chromatin, and containing a central chromatic particle staining red. Negri, Williams, and Lowden give drawings indicating the rapid division and growth of the organism, which apparently as it grows divides, until finally large forms result whose chromatin breaks up into minute masses.

They consider that the parasite reaches the nervous system by spreading along the nerves, which it does more quickly than travelling by the blood

Cyclasterella scarlatinalis Mallory (**Doubtful Species**).

In 1904 Mallory described round and elongated bodies, sharply stained with methylene blue, 2 to 7 μ in size, lying in the epithelium of the epidermis, together with radiate bodies, composed of a central spherical body with ten to eighteen segments radiating away from it, in epithelial cells and lymph-spaces of the epidermis of people suffering from scarlet fever.

This discovery has since been confirmed by Field and Duval, both during life and in post-mortems.

Further research is needed before the nature of these bodies can be definitely settled.

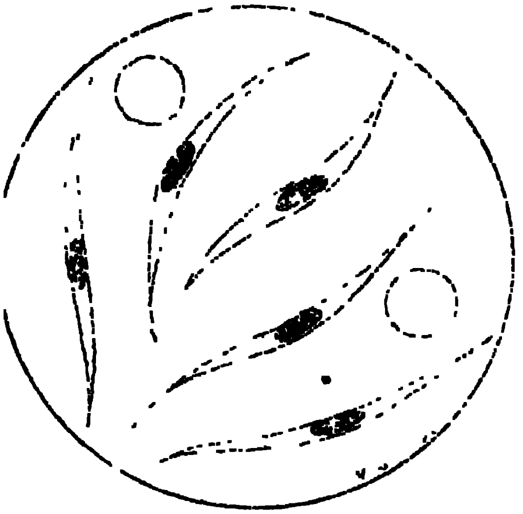

Fig. 197.—*Sergentella hominis* Brumpt.

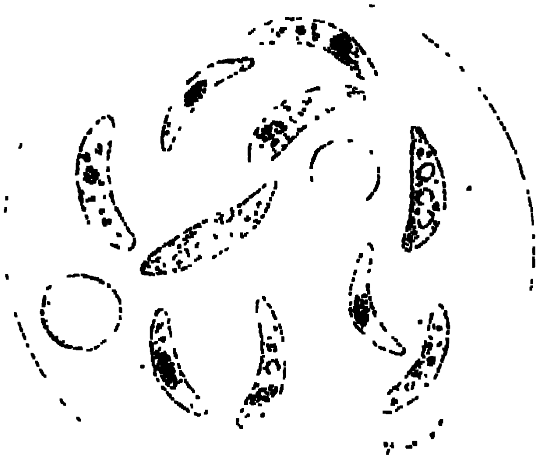

Fig. 198.—Sarcocystis Spores found in the Blood of Man by Castellani and Willey.

Coccidioides immitis Rixford and Gilchrist, 1897 (**A Fungus**).

Synonyms.—*C. pyogenes* Rixford and Gilchrist, 1897; *Coccidium posades* Caxton (?), 1898.

These parasites were first seen by Wernicke and Possadas in Buenos Ayres, and later in the United States by Rixford and Gilchrist, Montgomery, Moffit, and Ophuls, where they cause an infection producing nodules in the skin, liver, kidney, genitalia, and lymphatic glands.

This so-called protozoon is a fungus (see p. 985)

The Bodies of Ureteritis Cystica (**Doubtful**).

In this disease the kidney is hydronephritic and the ureter and bladder are cystic.

The cysts contain large and small oval and irregular cells with bright globules, variously interpreted as Coccidia, Myxosporidia, and cell inclusions.

Sergentella hominis Brumpt, 1910.

Et. and Ed. Sergent in 1903 reported a vermiform body, 40 μ long by 1 to 1·5 μ broad, pointed at each end, with a nucleus in the middle, in the blood of a person suffering from night-sweats and nausea.

Bodies found by Sambon in Pseudochirus peregrinus.

Sambon has found bodies in a lemur which may have some relationship to the spores of Sarcocystis, but this is doubtful.

Bodies described in Man by Castellani and Willey.

These bodies were found and described in 1905 in two patients suffering from irregular fever. They generally have a crescentic shape, 10 to 30 μ in length, and 1.5 to 4 μ in breadth. They often present vacuoles, and a nucleus may be seen in some specimens, but not in all. The whole body stains bluish, while here and there granules of chromatin can be seen. They cannot be compared with malarial crescents, as they never contain pigment. These bodies may be spores of Sarcocystis.

Protozoal Bodies found in Dysentery.

In 1914 Castellani described a peculiar protozoal organism (*Entoplasma Castellanii* Paul 1914) which he found in three cases of dysenteric colitis, in which amœbæ and dysenteric bacilli were absent. One of the cases had been infected in Burma, and the other two probably in Ceylon.

In fresh preparations the organisms appeared as large pear-shaped or flask-shaped bodies, 60-80 microns in diameter, actively motile, and showing only slight changes of shape while moving, and no pseudopodia.

The anterior portion at its upper part was shaken by very rapid vibratile movements, as though produced by a flagellum. No such organella could be seen in fresh or stained preparations by Castellani or any other observer. The cytoplasm was very vacuolated. In stained preparations a group of granular bodies could be seen and were thought by Mesnil to be a diffuse nucleus.

FIG. 199. —*Entoplasma Castellanii* PAUL, 1914.

Chlamydozoa Prowazek, 1907.

Definition.—The Chlamydozoa are a collective group of minute parasites, which either live extracellularly, when they are capable of passing through the usual filters, or intracellularly, when they excite a reaction upon the part of the enclosing cell which produces a substance which encloses them as it were with a mantle, thus forming a cell inclusion.

Remarks.—This collective group was formed by Prowazek to embrace a number of minute parasitic forms which become enclosed in a cellular product as with a mantle. The general tendency is to range these forms among the Protozoa. The minute granules are the parasites, and the surrounding substance is either plastin or chromatin from the nucleus, or a fatty substance. The name Chlamydozoa is derived from the Greek ζῷον, an animal, and χλαμύς, a mantle. At the present time doubt is expressed as to causal action of the Chlamydozoa as well as to their parasitic nature.

History.—In 1907 Prowazek and Halberstaedter, on examining trachoma smears stained by Giemsa's method, found dark blue granular inclusions in the protoplasm of the epithelial cells. These granules were at first round or oval, and increased in size, at the same time becoming less dark, while minute red dots appeared, which increased rapidly in numbers, while the blue masses gradually disappeared. The granules formed *cell inclusions*, and the blue masses were considered to be a reaction product on the part of the cell, and were thought to be composed of plastin, while the minute red dots were considered to be the virus. The reason why they considered the blue granules to be distinct from the red points was because the blue gradually disappeared, while the red points, or *elementary bodies*, could be seen extracellularly situated. They inoculated anthropoid apes successfully with trachoma, and found the same bodies in this infection. These researches were confirmed by Greef in the same year, and were extended in 1908 by Stargardt and Schmeichler in 1909, who described a conjunctivitis neonatorum non-gonorrhoica with typical Chlamydozoa. In 1909 Heymann found the same bodies in four cases of gonorrhœal conjunctivitis in newly-born infants. This discovery was of the greatest importance, because since the days of Kroner it had been known that the conjunctivitis of the new-born was not always due to the gonococcus. Linder, in 1909, and Wolfrum, in 1910, showed that there were two forms of blennorrhœa--viz., a conjunctivitis neonatorum caused by the gonococcus, and a second caused by Chlamydozoa, this latter disease being termed by Linder 'inclusion-blennorrhœa' in contradistinction to gonoblennorrhœa. Linder maintains that the same virus produced trachoma, inclusion-blennorrhœa, and that this virus can be found in the male and female genital passages, and he bases his opinion on the facts that he has been able to produce trachoma in monkeys inoculated from a case of non-gonorrhœal urethritis in a man, from two such cases in women, and from several cases of inclusion-blennorrhœa in infants. Further investigations have shown that inclusion-blennorrhœa is histologically similar to trachoma.

Later, Leber and Prowazek in 1911 found a similar organism, *Lyozoon atrophicans* in epitheliosis desquamativa, and in the same year Uhlenhuth found inclusions in swine pest, and Botteri in spring catarrh.

In the meanwhile Halberstaedter and Prowazek had in their first paper grouped with these cell inclusions the forms described in smallpox, hydrophobia, molluscum contagiosum, epithelioma contagiosum, and Lipschütz grouped the causes of dermotropismus, or human dermatoses, under the subhead Strongyloplasmata. Finally the whole subject was gathered together and reviewed by Prowazek in 1911 in his 'Handbuch der Pathogenen Protozoen.' Somewhat similar bodies have been seen by Castellani in sprue in cells from the oral mucosa, although most of these inclusions are non-granular, and he doubts their parasitic nature. He has observed somewhat similar bodies in conjunctivitis and in urethritis of a non-gonorrhœal nature.

Morphology.—On examining the cells from a case of urethral discharge of non-gonorrhœal origin, or the cells from the discharge in certain forms of conjunctivitis, they can be seen to contain peculiar masses of granules which are grouped into oval or roundish bodies, measuring 2 to 6 μ in transverse or maximum diameter. The individual granules measure 0·5 to 1 μ in diameter, and stain a purplish-red colour with Giemsa or Leishman's preparations. These granules appear to be embedded in a pale bluish matrix.

Life-History.—The smallest form or *elementary body* is merely a minute speck of chromatin, apparently without any cytoplasm, which lives extracellularly, but may enter a cell. This entry into the cell is not a process of phagocytosis, as may be shown by the absence of the usual vacuole, and by the fact that they do not show the usual yellow coloration when stained by neutral red. Inside the cell the elementary body grows in size, and becomes the *initial body*, which becomes surrounded by the mantle, and thus forms the *cell inclusion*. This body now breaks up into a number of small bodies called *initial corpuscles*, which divide by simple division—*i.e.*, by the formation of dumb-bell forms, the two ends of which simply move apart until the connecting thread is broken. The result of the division of the initial corpuscles is the *elementary body*. In this way the life-cycle is completed.

Comparison.—It will thus be seen that the Chlamydozoa are the granules inside the body of the *Cytoryctes variolæ* or the *Neuroryctes hydrophobiæ*, and that the whole organism of these two forms corresponds to the mantle and parasite of the chlamydozoon.

Pathogenicity.—They are believed to be the cause of smallpox, vaccinia, trachoma, Samoan epitheliosis, hydrophobia, scarlet fever, etc.

Classification.—The Chlamydozoa are classified into:—

A. *Chlamydozoa vera.*

Chlamydozoa, which commences as elementary bodies from cell inclusions.

1. Cytoryctes group—cause destruction of the cell.
2. Cytooikon group—cause proliferation of the cell.
3. Gelbsucht group—cause gelbsucht in the Lepidoptera.

B. *Chlamydozoa strongyloplasmata.*

Chlamydozoa, which always remain as elementary bodies—*e.g.*, the forms in the peripneumonia of cattle and the diphtheria in birds.

Only the Cytoryctes and Cytooikon groups concern us.

The Cytoryctes Group.

It is important to distinguish between the Chlamydozoon of such a disease as smallpox and the parasite *Cytoryctes variolæ*. The Chlamydozoon is one of the chromatic particles of *C. variolæ*, the protoplasm of which forms the mantle. The Cytoryctes group includes the parasites of:—

1. Vaccinia.
2. Variola.
3. Scarlet fever.
4. Hydrophobia.

The Cytooikon Group.

The Cytooikon group includes:—

1 *Lyozoon atrophicans* Leber and Prowazek.
2. Trachoma bodies.

The former group have been described above, and the latter group will be dealt with in the chapter dealing with the diseases of the special senses.

The Filterable Viruses.

By the term 'filterable virus' is meant micro-organisms so small that they will pass through the pores of filters which are too small to allow the passage of bacteria. The term 'ultramicroscopic' is also used for filterable viruses, but is not free from objection.

History.—In 1892 Iwanowski demonstrated the filterability of the mosaic disease of the tobacco plant, and in 1898 Löffler and Frosch discovered that the virus of foot and mouth disease would pass through the pores of the finest porcelain filter. Shortly afterwards Beijerinck confirmed Iwanowski's observations, and since then numerous observations have been made.

IN MAN.—*Yellow fever* virus by Reed and Carroll in 1901, destroyed it heated to 53° C. for ten minutes; *Molluscum contagiosum*, by Julius Véry in 1905; *Dengue fever* by Ashburn and Craig in 1907; *Three days' fever* by Doerr in 1908; *Poliomyelitis* by Lentz, Landsteiner, Levaditi, Flexner, and Lewis in 1909; *Typhus* by Nicolle in 1910; *Measles* by Goldberger and Anderson in 1911, as well as *Trachoma*, *Scarlatina*, *Verruca vulgaris*, and, according to Nicolle, *Influenza*.

ANIMALS AND MAN.—*Foot and Mouth Disease* by Löffler and Frosch in 1898; *Vaccinia* by Siegel in 1905, *Variola* and *Rabies*.

Besides these filterable viruses others have been found in diseases of birds and one in plants.

Cultivation.—The virus of pleuro-pneumonia of cattle, of fowl pest, fowl diphtheria, epithelioma contagiosum, and of Novy's rat disease have been cultivated. The organism of pleuro-pneumonia is a very small spirochæte, but the organisms of the other disease are only evident by the fact of their infectivity in subcultures carried beyond any reasonable limit of dilution from the original.

Immunity.—In nearly every case the immunity produced by a filterable virus is complete and of long duration.

Secondary Infections.—Secondary infections with bacteria are common, and it is thought that many of the so-called typical symptoms of the disease may be due to the secondary agent.

Methods of Infection.—The methods of infection are various: (1) By blood-sucking insects—*e.g.*, *Stegomyia calopus* and yellow fever, etc.; (2) by entry through an abrasion—*e.g.*, *Molluscum contagiosum ;* (3) by contact—*e.g.*, fowl pest; (4) by unknown methods —*e.g.*, Novy's rat disease.

Nature.—The nature of the viruses is unknown; some, especially those spread by blood-sucking agents, are probably protozoal, but others may be bacterial.

Classification.—The filterable viruses may be divided into—

1. Filterable viruses associated with no known organism.
2. Filterable viruses associated with some known organism.

1. *Filterable Viruses associated with No Known Organism.*

Under this heading come the viruses of several diseases of importance in tropical medicine—*e.g.*, the virus of yellow fever, of dengue fever, of pappataci fever, of typhus fever.

Yellow Fever.—The virus is found in the blood only during the first three days of the fever. It can pass through Berkefeld and Chamberland B filters, and can be destroyed by heating to 55° C. for ten minutes, or by a temperature of 24° to 30° C. for forty-eight hours. It is conveyed by *Stegomyia calopus* after an interval of twelve days from the time of the infective feed.

Dengue Fever.—The virus is in the blood during the fever, and can be filtered through Berkefeld filters impermeable to *Micrococcus melitensis*. It is spread by *Culex fatigans*.

Pappataci Fever. The virus exists in the blood during the first day of the fever, and can be filtered through Berkefeld filters, and is spread by *Phlebotomus papatasii* after an interval of seven days from the date of the infective feed.

Typhus Fever.—The virus exists in the blood, and can be filtered through *the coarser* Berkefeld filters. It is destroyed by a temperature of 52° to 55° C.; it is spread by *Pediculus vestimentorum* L.

Verruga Peruviana.—The experiments of Strong, Tyzzer, Brues, Sellards, and Gastiaburu tend to show that the virus of this disease is a filterable virus, and distinct from that of Oroya fever. It appears to be similar in many respects to the virus of smallpox. It can be inoculated successfully into monkeys, but only a modified form of the disease appears, the lesions regressing in four to five weeks (analogy with inoculated smallpox). It has also been transmitted to rabbits and dogs. It has not yet been demonstrated that *Phlebotomus verrucarium* or any other insect does transmit the disease, but it is believed that some arthropod is the carrier.

2. *Filterable Viruses associated with Some Known Organism.*

Borrel has clearly shown that a minute flagellated organism (*Micromonas mesnili*) exists in the filtrates of sheep-pox, and it is quite possible that all filtrates contain these minute organisms, and, further, there is reason to suppose that certain larger organisms possess these minute forms in some stage of their life-cycle—*e.g.*, the organisms of trachoma, variola, and vaccinia.

Bradford, Bashford and Wilson have described minute bodies which they state to have cultivated, using Noguchi's method, from cases of acute infective polyneuritis, influenza, trench fever, typhus, and other conditions.

Trachoma.—The virus passes through the Berkefeld filters, and can be successfully inoculated into monkeys.

Variola and Vaccinia.—The virus passes through Berkefeld and *the coarser* Chamberland filters, and is destroyed by heating to 57° to 58° C. in fifteen minutes, or by almost any disinfectant, by saponin, vicin, bile, taurocholic acid, and sodium oleate.

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CHAPTER XXIII

HETEROKARYOTA

Preliminary—Heterokaryota—Ciliata—Balantidium—Nyctotherus—References.

DIVISION B. HETEROKARYOTA Hickson, 1903.

PHYLUM V. CILIATA Perty, 1852.

The Ciliata are free-living or parasitic Heterokaryota, found principally in water, where they exist upon small animal and vegetal organisms and the débris of decomposing plants and animals. Some of them can live in the alimentary canal of man and animals, obtaining their food from its contents, and increasing to such numbers as to cause irritation of the intestine.

Their movement is by cilia, but always with one end, the anterior, in front. They turn round when desiring to progress in a different direction. This anterior end may be similar morphologically to the posterior, or may be characterized by being more pointed, by having a mouth, or by peculiar sensory cilia (Hypotricha), or by a peristome of long cilia (Heterotricha). The body, which may be spherical or flattened, is divided into an ectoplasm (the cortex) and endoplasm (the medulla). The ectoplasm may simply be a clear outer layer of the protoplasm, or it may be differentiated into three layers. The first is very thick and very tough; the next, called the alveolar sheath, is marked by vertical parallel lines, which are the contractile myoneme threads; while the innermost layer next to the endoplasm consists of clear transparent ectoplasm.

The semifluid endoplasm is in constant rotatory motion, containing food vacuoles, contractile vacuoles, nuclei, pigment granules, colourless granules, crystalline bodies, and smaller particles. The cytostome or mouth is present in all except the parasitic Opalinæ. It is a slit in the cortex at the anterior end of the body, which can be opened for the reception of food, but is usually kept closed. It may be on the surface or may be carried inwards by a funnel-shaped depression in the ectoplasm called the vestibule, which may be lined by cilia specialized for the capture of food.

A cytopyge, or cell anus, occurs in *Nyctotherus*, but as a rule no definite opening appears, and the undigested food is simply pushed through the cortex.

Two wholly distinct nuclei exist in the Heterokaryota, a mega- or macro-nucleus and a micronucleus. They are not merely different in size, form, structure, and appearance, but also in function; for the macronucleus is somatic and trophic in its function, while the micronucleus is purely sexual. They are not comparable to the tropho- and kineto-nuclei of the trypanosomes.

The macronucleus is generally well marked, but breaks down into granules before or after conjugation. It consists of an achromatic portion, with a chromatic portion in the form of a close-meshed network of fibrils, but whether there is a definite surrounding membrane or not is doubtful.

The micronucleus, when at rest, is a minute irregular granule of chromatin lying in the centre of a perfectly clear achromatic area. Probably there is only one in each animal, and the appearance of two or more is due to reproductive phases which are just finishing.

The Ciliata are characterized by the presence of protoplasmic processes projecting all over the body. These are fine, short whips, called cilia, which in places are transformed into thick processes called cirri or flat membranes in certain species. The cilia are processes of the pellicle, but they appear to be supported by a thread of specialized ectoplasm. The short, fine cilia are for motion, and the long, motionless cirri for the purpose of entangling food-particles. The membranes are supposed to be formed of fused cilia. Trichocysts exist in the Holotricha, and an excretory organ has recently been described by Metcalfe in certain species of Opalina, parasitic in frogs, while other Ciliata have a contractile vacuole.

Reproduction may take place asexually by (1) transverse or longitudinal division; (2) gemmation, simple or multiple, (3) encystment and spore-formation, or sexually by conjugation.

1. **Fission.**- There is no morphological distinction between longitudinal and transverse fission, in which the following changes take place: (1) A second mouth is formed; then comes (2) enlargement and division of the micronucleus, followed by (3) enlargement and division of the macronucleus; and, finally, (4) division of the cytoplasm.

2. **Encystment and Spore-Formation.**- The animal encysts and breaks up into a number of small individuals.

3. **Conjugation.**- Conjugation has been best described by Calkins and Caullery in *Paramæcium aurelia*. Two conjugating cells about the same size are placed so that the mouths are directly opposed The micronucleus swells, its chromatin becomes granular, elongated, crescentic, fusiform, and finally forms two nuclei, each of which at once divides into two. Of these, two degenerate, while the other two divide to form a migratory, or male, and a stationary, or female, pronucleus. The male interchange and fuse with the opposite female nuclei, and then the organisms separate. The macronucleus fragments and disappears, and the synkaryon breaks up into eight micronuclei.

Four of these swell, and are changed into macronuclei; so that four micro- and four macro-nuclei are in the same cell, which divides into two very small cells with two macro- and micro-nuclei each. These cells grow to nearly full size, and then divide, giving rise to the typical protozoon, with one macronucleus and one micronucleus.

Parasitism.—A great many species of the Ciliata are parasitic in the intestine or bladder of other animals, and some are epizoic.

The latter will often be met with as *Vorticellæ*, living on *Anopheles* and *Culex* larvæ. The former are found largely in the Orthoptera, the Amphibia, and in herbivorous mammals—*e.g.*, horse and cow.

In man a few have been recorded: *Chilodon dentatus* Dujardin, 1842; *C. uncinatus*, *Colpoda cucullus* Schutz, 1889; *Balantidium coli* Malmsten, 1857; *B. minutum* Jakobi and Schaudinn, 1898; *Nyctotherus faba* Jakobi and Schaudinn, 1898; *N. giganteus* Krause, 1906; *N. africanus* Castellani, 1905.

Parasitism does not appear to affect the structure of the animal, unless the loss of the cytostome in Opalina, parasitic in frogs, is considered to be due to this cause.

Pathogenicity.—The ciliate parasites, as a rule, appear to cause but little effect, unless they are present in large numbers, when diarrhœa, often severe and long-persisting, may result.

Classification.—The Ciliata are classified into four orders:—

Order I. Holotricha Stein, 1859.—Mobile Ciliata without special oral cirri (*Chilodon*, *Colpoda*).

Order II. Heterotricha Stein, 1859.—Mobile Ciliata with special oral cirri (*Balantidium*, *Nyctotherus*).

Order III. Hypotricha Stein, 1859.—Mobile Ciliata with well-developed dorsal and ventral surfaces. Not known to be parasitic in man.

Order IV. Peritricha Stein, 1859.—Fixed Ciliata. Not known to be parasitic in man.

ORDER I. HOLOTRICHA Stein, 1859.

Definition.—The Holotricha are free-moving Ciliata, in which all the cilia are of approximately equal length and thickness, and never possessing cirri.

Remarks.—It is divided into two suborders:—

Suborder 1, *Gymnostomata*.—Mouth closed when ingesting food.

Suborder 2, *Hymenostomata*.—Mouth always open, and provided with an undulating membrane.

SUBORDER GYMNOSTOMATA Butschli 1889

Family Chlamydodontidæ Stein.—In this family there is a genus *Chilodon* Ehrenberg, 1833, which includes oval, strongly dorso-ventrally compressed Chlamydodontidæ, commonly found in infusions, of which one species, *C. dentatus* Dujardin, 1842, was found in great abundance by Guiart in the motions of a woman suffering from severe dysentery in Paris. Manson and Sambon have described a case of chance-parasitism due to another species, *C. uncinatus* Blochmann, in a patient from tropical South Africa.

They noted that the parasites were only found in the mucus, never in the fæcal masses. They were present in very large numbers, and were found to be all gametes, some of which were conjugating. It appears probable that Guiart's parasites may really have been *C. uncinatus*, and not *C. dentatus*.

SUBORDER HYMENOSTOMATA Hickson, 1903.

FAMILY CHILIFERIDÆ Bütschli.—The genus *Colpoda* Müller, 1773, includes the kidney-shaped Chilifera, with rows of cilia twisted from left to right, commonly found in hay infusions, of which one species, *Colpoda cucullus* Schutz, 1899, commonly found in the water of marshes, was noticed in a brickmaker attacked with dysentery in Berlin. *Uronema caudatum* Dujardin, 1841, has been found in the motions of cases of diarrhœa in man.

ORDER II. HETEROTRICHA Stein, 1859.

The Heterotricha are free-moving Ciliata, with strong cirri or membranellæ, forming an adoral ring enclosing a space, the peristome, at one part of which the mouth opens. The order is divided into Polytricha, Oligotricha.

Polytricha Hickson, 1903.—Heterotricha in which the surface of the body is covered with rows of short cilia.

FAMILIES.—*Plagiostominidæ* Claparède and Lachmann, *Bursarinidæ* Bütschli, *Stentorinidæ* Stein, *Gyrocorynæ* Stein.

y BURSARIDÆ Kent, 1880.

Synonym.—*Bursarinidæ* Butschli.
This family includes the genus *Balantidium*.

Genus Balantidium Claparède and Lachmann, 1858.

Definition.—*Bursarinidæ* with a large peristome and a well-marked anal aperture.

Remarks.—Balantidium is common in the rectum of pigs, and is sometimes found in the intestines of man. Cyst 80-100 μ in diameter.

Balantidium coli Malmsten, 1857.

Synonyms.—*Paramæcium coli* Malmsten, 1857; *Plagiostoma coli* Claparède and Lachmann, 1858; *Leucophrys coli* Stein, 1860; *Balantidium coli* Stein, 1867; *Holophrya coli* Leuckart, 1863.

Balantidium coli is constantly found in pigs, and has been found in the colon and the dejecta of man in cases of cholera and diarrhœa.

In shape it is oval, slightly pointed anteriorly, but this depends upon whether the peristome is funnel-shaped or contracted. It is covered with cilia arranged in parallel rows, which give it a striated appearance.

It is 0·06 to 0·1 millimetre in length by 0·05 to 0·07 millimetre in breadth, and possesses a bean- or kidney-shaped macronucleus, and a globular micronucleus situated near it. It develops asexually by transverse division or by conjugation. It can encyst, and in this condition pass from pigs to man. *B. coli* lives in the rectum of pigs, and is transferred by its cysts to man.

It was discovered by Malmsten in a man who had had cholera, and was suffering from diarrhœa and ulcer of the rectum The ulcer had nothing to do with the disease, as it healed, while the diarrhœa was probably due to the parasites.

Casagrandi and Barbagallo produced catarrhal enterocolitis in young cats by means of this parasite.

Strong has investigated, in a masterly manner, the enterocolitis produced by *B. coli* in the Philippine Islands.

Balantidium minutum Schaudinn, 1899.

The body is shortly oval, with a pointed anterior extremity. Length, 20 to 32 μ; breadth, 14 to 20 μ.

The peristome extends into the centre of the body, and has the right lateral border fringed with cilia, and the left lateral border terminates in a hyaline membrane which can pass over to the right side, and has a row of cirri. The cysts are oval.

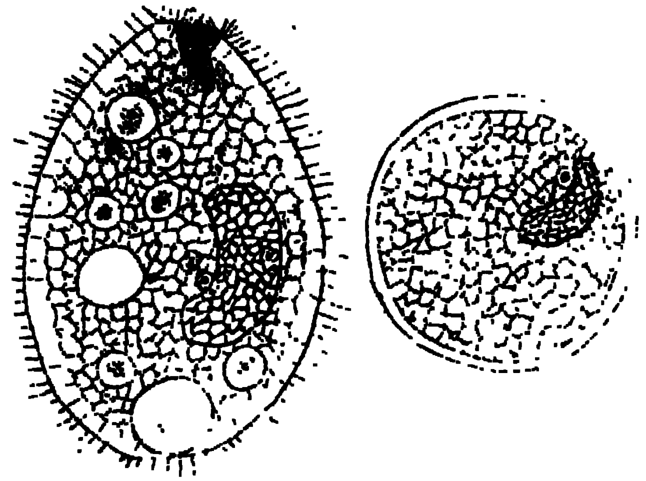

Fig. 200.—*Balantidium coli* Malmsten.

(After Hartmann. From the *Archiv für Schiffs- u. Tropenhygiene.*)

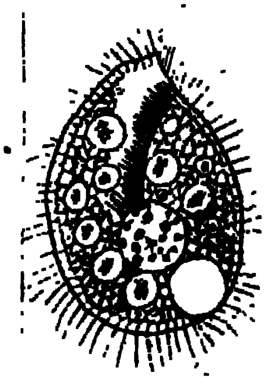

Fig. 201.—*Balantidium minutum* Schaudinn.

(After Hartmann. From the *Archiv für Schiffs- u. Tropenhygiene.*)

This parasite (along with *Nyctotherus faba*) was found by Schaudinn in a German who had often stayed in North America. The symptoms were constipation alternating with diarrhœa associated with abdominal pain.

Balantidium minutum var. **italicum** Sangiorgi and Ugdulena, 1917.

This parasite, which was found by Sangiorgi and Ugdulena in human fæces, differs from *B. minutum* in that the nucleus is excentric, and in the peculiar orientation of the micronucleus.

Genus Nyctotherus Leidy, 1849.

Definition.—Body bean- or kidney-shaped, with a large peristome on the concave side extending from the anterior end up to the middle of the body, from where a curved cytopharynx or œsophagus extends inwards. The macronucleus is large, and situated almost in the centre.

Remarks.—The species are mostly parasitic in the intestine of Amphibia, Insecta, and Myriapoda.

Species known in man: *Nyctotherus faba* Schaudinn, 1899; *N. giganteus* Krause, 1906; *N. africanus* Castellani, 1905.

Nyctotherus faba Schaudinn, 1899.

N. faba is flattened dorso-ventrally, and is 26 to 28 μ in length, and 16 to 18 μ in breadth, and 12 μ in thickness. The cilia on the peristome are of two kinds, those on the right side, of the size of the body, being true cilia, and those on the left side being cirri.

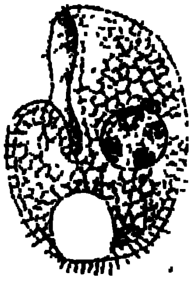

Fig. 202.—*Nyctotherus faba* Schaudinn.

(After Hartmann. From the *Archiv für Schiffs- u. Tropenhygiene.*)

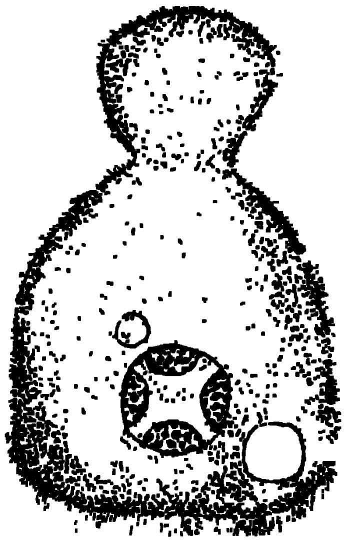

Fig. 203.—*Nyctotherus africanus* Castellani

The contractile vacuole is large, and situated posteriorly. The macro-nucleus is in the centre, and is peculiar in having four or five large collections of chromatin at its periphery. The micronucleus lies close by. The cysts are oval.

This species was discovered by Schaudinn in the same patient as *Balantidium minutum*.

Nyctotherus giganteus P. Krause, 1906.

Synonym.—*Balantidium giganteum* P. Krause, 1906.

This organism, along with *Trichomonas intestinalis*, was found by Krause in the dejecta of persons suffering from typhoid in Breslau.

It is shaped like a truncated cone, with the anterior end narrowed, and the posterior broad. Length, 90 to 400 μ; breadth, 60 to 150 μ. Surface covered with cilia. The peristome is situated laterally, and from it a cytopharynx leads inwards.

The macronucleus is large and bean-shaped, while the micronucleus is small and round. One or two vacuoles can be seen. The cytopyge is situated posteriorly.

In the fæces the parasite becomes rounded off and encysted, and then divides into four.

Nyctotherus africanus Castellani, 1905.

Found by Castellani in a Baganda native. *N. africanus* is hourglass shaped, with the anterior portion much less developed than the posterior. Length, 40 to 50 μ; breadth, 30 to 40 μ. The surface is covered with very minute cilia, which are generally more evident on the posterior portion, being almost invisible on the anterior.

The peristome is short. The cytoplasm is finely granular throughout. The nucleus is situate far posteriorly, near the contractile vacuole. The micronucleus is very small, and situated close to the macronucleus. No food vacuoles are to be seen.

Neither division, conjugation, nor encystment are known.

The patient, who had diarrhœa alternately with long periods of constipation, was suffering from sleeping sickness.

The cæcum contained many parasites, as did other parts of the bowel. The mucosa of the cæcum, colon, and rectum were slightly congested, but not ulcerated. Castellani originally considered this parasite to belong to the genus *Nyctotherus*, but more complete investigations will probably show that it constitutes a new genus.

SUBORDER HYMENOSTOMATA Butschli, 1889.

Genus Uronema Dujardin 1841.

Definition. Hymenostomata ovate or elongate with one or more caudal setæ.

Type Species. - *Uronema marinum* Dujardin, 1841

Uronema caudatum.

Found in a case of diarrhœa.

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CHAPTER XXIV

TREMATODA

Metazoan parasites—Platyhelmia—Trematoda—Classification—Malacotylea—Digenea—Prosostomata—Paramphistomoidea—Fascioloidea—Schistosomidae—References.

SUBKINGDOM II. METAZOA.

Definition.—Metazoa are free-living or parasitic, multicellular animals, characterized by a physiological division of labour among their cells.

Remarks. Tropical medicine is only concerned with parasitic Metazoa, and chiefly with those which affect man. Parasitic Metazoa may be ectoparasites—as, for example, many species of the Insecta—or endoparasites—as, for example, many worms. The ectoparasites can cause disease by introducing toxins, protozoa, or bacteria into the tissues, and in this way they are of the utmost importance as the spreaders of disease, for, as is generally recognized, a disease is very often limited by the special œcological conditions of the animal which spreads its germ. Many of the ectoparasites, such as mosquitoes, are temporary, or, like ticks, periodic; while others, like lice, are permanent parasites.

With regard to the endoparasites, their ill effects on the host depend upon many factors which have been recently studied in considerable detail.

The effects of metazoan parasites on their hosts depend upon the species of the parasites, their condition, the number present, their presence in certain organs, bacterial infection, their migration in the body, the loss to the host in feeding them, the damage caused by their toxins and the condition of the host.

1. The Species of Parasite.—*Filaria* may exist in a host without apparent ill effect, but *Ankylostoma* will produce anaemia, œdema, and perhaps death.

2. The Condition of the Parasite. The dead eggs of *Filaria* are believed to block the lymph channels, and give rise to swelling and rupture of these vessels, thus bringing about lymphangitis and elephantiasis, while the living larvæ apparently do no harm.

3. The Number of Parasites.—A few Ascarides may cause no symptoms, while a large number may lead to serious disease.

4. The Organ Affected.—Ascarides in the alimentary canal are not nearly so virulent as in the liver, while *Paragonimus ringeri* in the lungs will cause a disease somewhat resembling phthisis.

Ascarides may cause serious mischief in the pancreas, as observed by Chalmers; and may cause appendicitis, as noted by Blanchard, Metchnikoff, Castellani, and others.

5. Bacterial Infection caused by the Parasite.—*Trichuris trichiura* may be a harmless parasite in itself, but it is quite capable of introducing bacteria into the mucosa of the vermiform appendix and causing appendicitis, for, as is well known, it burrows in the mucosa. The fever so often found in patients suffering from ankylostomiasis is probably caused by intestinal bacteria entering the small wound produced by the ancylostome.

This method of producing ill effects upon the host appears to us to be of the greatest importance in the tropics, and is, we fear, often overlooked.

6. Migration of the Parasite in the Body.—The larvæ of *Ancylostoma* as they enter the skin cause a dermatitis known as Cooly itch, sore feet, ground itch, etc., which may be primarily due to the irritation of the worm, or secondarily to bacteria introduced into the skin by its agency. The wanderings of the larvæ of *Trichinella spiralis* through the muscles cause the severe symptoms of trichiniasis.

Sambon has pointed out that much that is obscure in the pathogenesis of various forms of helminthiasis might be elucidated by a better knowledge of the migrations of the entozoa in their immature stages from the time they attack the host to that of their settlement in their selective anatomical habitat. He believes that many forms do not go directly to the part in which they are usually found, but may take a very different route from that generally accepted, and may even live for a length of time in other structures before reaching such organs as the alimentary canal or nasal fossæ, which are only sought in order to enable the young to escape from the host. During these wanderings mechanical injury may be caused to the host, and pathogenic micro-organisms may be carried from one part of the body to another.

7. The Absorption of Food.—Leuckart estimates that a *Dibothriocephalus latus* gives off in a year proglottides to the weight of 140 grammes; *Tænia saginata*, 550 grammes; and *Ascaris lumbricoides*, 42 grammes of eggs in the same period.

If the number of these parasites is great, the drain on the host must be considerable, especially in children who need food for growth.

8. Toxins.—This subject has already been dealt with (p. 205).

9. The Condition of the Host.—The condition of the host is also a factor in the diseases produced by these parasites, for though Ascarides may be harmless in a healthy intestine, they may perforate a typhoid or dysenteric ulcer, or a traumatic lesion of the bowel, and cause fatal peritonitis.

With regard to the question as to whether parasites ever benefit human beings, reference can be made to the belief that the development of the *Bacillus tuberculosis* Koch is delayed by the presence of entozoa in the bowels, a view which, with our Eastern experience, we are unable to support.

The old idea that worms were good for children has died out long ago, and we know of no cases of mutualism, or benefit to parasite and host, in the animal parasites of man.

True parasitism is found in those cases in which the parasite benefits and the host is injured. Chance parasites are animals which accidentally and temporarily become parasites.

The life-history of a parasite may be simple, being carried out in one host, or it may be complex, with one or more hosts for its larval stages and another for its adult condition.

Generally these hosts bear a direct relationship to one another, the intermediary host often being herbivorous, and thus becoming infected through eating fæcally contaminated food, and the definitive host being carnivorous or omnivorous, becoming infected through eating the herbivorous host of the larva.

Some parasites, particularly the Microfilariæ in the blood, show a remarkable periodicity in their habits, which appears to be associated with the means of escape from the definitive host by some intermediary host, such as a mosquito or a tick, whose habits agree with the periodicity of the parasite. Such correlations are very numerous in Nature—as, for example, the opening, or emitting of strong odours, by certain flowers at definite times of the day or night, which accords with the habits of insects which help on their fertilization.

Tropical countries are the home *par excellence* for parasites, as the means of infection by bad sanitation, biting flies, etc., are easily available. It is therefore obvious that, as there may be many methods of infection by the mouth, the skin, and the nose, prevention is not an easy matter. It depends upon two factors—personal and public hygiene. The question of personal hygiene is the more important and more easily applied, as only one person is concerned, while that of public hygiene is more expensive and not so easy to apply, as many people have to act in unison in order to produce any effect.

Personal hygiene includes such matters as personal and domestic cleanliness; protection of the skin against infection, by the use of mosquito curtains and boots; avoidance of infection from domestic pets, such as dogs and cats, by not too close association with them; the protection of articles of food against flies and vermin; and the careful cooking of food and filtering of water.

With regard to public rules, the first is the proper disposal of waste, particularly of fæcal matter; careful cattle and meat inspection in well-kept slaughter-houses; and the destruction of ownerless dogs by means of a lethal chamber, in which they are killed by gas.

Classification.—The metazoan parasites of man can be arranged into phyla as follows:—

Phylum I. Platyhelmia.
Phylum II. Nemathelmia.
Phylum III. Annulata.
Phylum IV. Arthropoda.

PHYLUM I. PLATYHELMIA Vogt, 1851.

Synonyms.—*Platodes* Leuckart, 1854; *Platyhelminthes* Gegenbaur, 1859; *Platyhelminthes* Minot, 1877.

Definition.—Platyhelmia are bilaterally symmetrical Metazoa, with dorso-ventrally flattened bodies, and without a true cœlom.

Morphology.—The Platyhelmia are flat-worms, with an oval or tape-like body, which is either covered by a ciliated epithelium, as in the free-living Turbellaria, or with a cuticle under which the surface epithelium has sunk into the parenchyma, forming the so-called subcuticular layer in the parasitic Trematoda and Cestoda. A well-developed musculo-dermal layer is present, but there is no cœlom.

The mouth is generally situated at the anterior end, when present, but it may be moved to the inferior surface, and opens, via a pharynx, into a forked or branched gut, which has no anal aperture. The alimentary canal may, however, be wanting (Cestoda). The excretory system begins in the so-called flame cells—*i.e.*, cells provided with a leash of cilia from which fine channels run, uniting together to form larger channels These ultimately empty into a pair of laterally placed canals, opening to the exterior separately or together, often through an excretory vesicle.

The nervous system consists of a large, bi-lobed, cerebral ganglion, with nerves running forwards and backwards.

The Platyhelmia are mostly hermaphrodite, but may rarely be unisexual; the ova are produced in the ovary, near which they are fertilized, and then, after obtaining food-yolk from the yolk reservoir, which has received it via the vitelline ducts from the yolk glands, they acquire a shell in a shell gland, and then enter a uterus, through which they slowly pass to the exterior.

The male organs consist of testes, vasa deferentia, vesicula seminalis, and a cirrus pouch, with a cirrus and a so-called prostate gland.

Classification.—The Platyhelmia are classified into:

Class I. Turbellaria. Free-living flat worms, covered with cilia.

Class II. Trematoda.—Parasitic flat-worms with an alimentary canal; cuticle non-ciliate.

Class III. Cestoidea.—Parasitic flat-worms without an alimentary canal; cuticle non-ciliate.

Class I. does not enter into the subject under discussion.

CLASS II. TREMATODA Rudolphi, 1808.

Synonyms.—Sucking Worms.

Definition.—The Trematoda are parasitic Platyhelmia, which retain the mouth and alimentary canal, but in which the epidermis not merely loses its cilia during development, but is sunk into the mesoblast after secreting the chitinous cuticle. Suckers are developed in the region of the mouth, and also on the ventral surface.

Remarks.—The knowledge of the Trematoda began in 1379, when

FIG. 204.—*Fasciola hepatica* (× 250.)

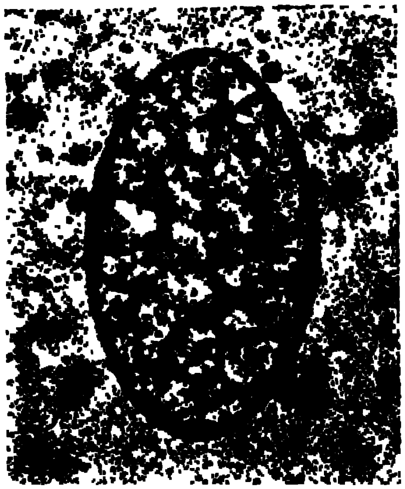

FIG. 205.—*Fasciolopsis buski.* (× 240.)

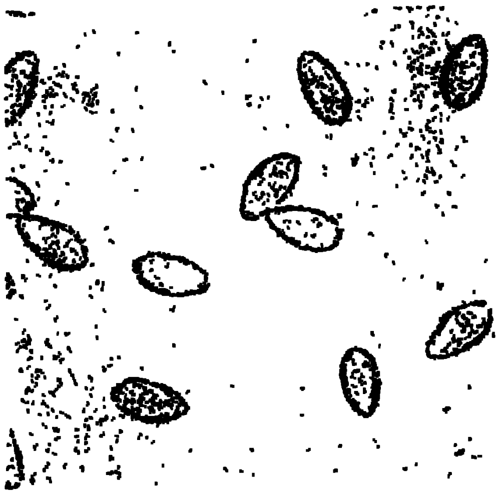

FIG. 206.—*Opisthorchis sinensis* (× 250.)

FIG. 207.—*Schistosoma japonicum.* (× 250.)

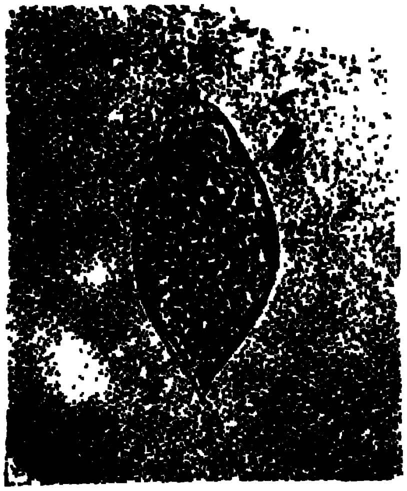

FIG. 208.—*Schistosoma hæmatobium.* (× 350.)

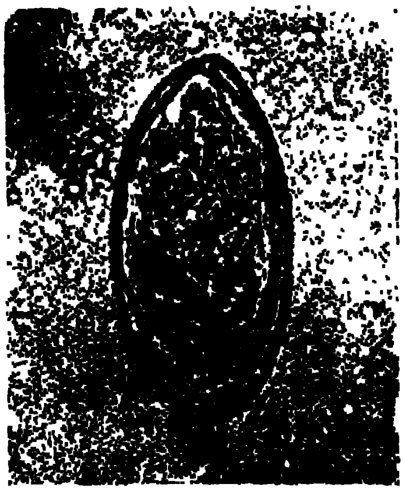

FIG. 209.—*Schistosoma mansoni.* (× 350.)

FIGS. 204-209.—EGGS OF VARIOUS TREMATODES FOUND IN HUMAN FÆCES.

(From photomicrographs by J. J. Bell.)

Jehan de Brie discovered the liver-fluke in the sheep, which was subsequently described by Gabucinus in 1547; but it was not till the time of O. F. Müller, in 1777, that any accurate idea of their form was obtained. Zeder in 1800 made the first attempt to classify parasitic worms, calling the Trematodes 'sucking-worms'; while in 1808 Rudolphi invented the name of the class, deriving it from the Greek τρηματώδης which means, 'pierced by holes.' After this date come many observers, among whom may be mentioned Laurer (whose canal still bears his name) in 1830, van Beneden in 1858, and Leuckart in 1867 (who divided them into Distomea and Polystomea), and Thomas in 1883, who worked out the development of *Fasciola hepatica*. In 1892 Monticelli revived an older classification of the group by Burmeister into three orders.

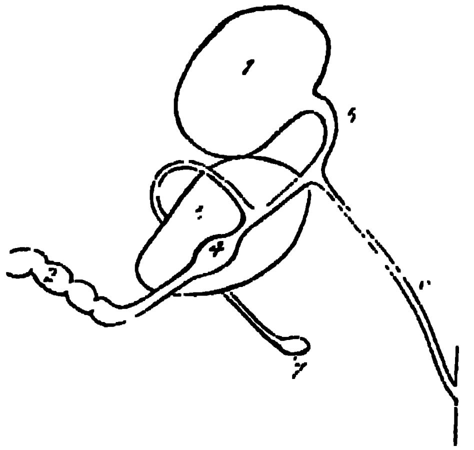

FIG. 210. DIAGRAM OF A TYPE OF THE FEMALE GENERATIVE APPARATUS OF A TREMATODE.

(After Stiles.)

1, Ovary, 2, uterus, 3, shell gland, 4, ootype, 5, ovarian duct, 6, Laurer's canal, 7, vitellarian duct.

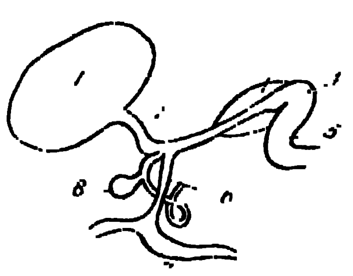

FIG. 211. DIAGRAM OF ANOTHER TYPE OF THE FEMALE GENERATIVE APPARATUS OF A TREMATODE.

1, Ovary, 2, ovarian duct, 3, shell gland, 4, ootype, 5, uterus, 6, Laurer's canal, 7, vitellarian duct, 8, receptaculum seminis.

In 1899 Looss completely revolutionized the whole classification. His work has since been extended by Leiper, Odhner, Lühe, and others. Of recent years our knowledge of the life history of these parasites has been extended in a remarkable manner by Leiper and numerous Japanese observers.

Morphology.—In shape the Trematoda are generally leaf-like or tongue-shaped, and but rarely cylindrical. They are provided with a cuticle, which may have spine-like scales, and with one or two suckers, oral and ventral (often called the 'acetabulum'), which are capable of fixing the parasites by the action of their equatorial, meridional, and radial muscular fibres to the lining of the alimentary canal, or such other organ as they may inhabit.

The mouth lies in the oral sucker, and leads to a pharynx. The œsophagus may be short or long, with or without a sphincter muscle, and is often provided with unicellular salivary glands. The intestinal tubules, which may be branched or simple, end blindly, there being no anal aperture. The food is composed of epithelial cells and blood.

The excretory system is well developed, commencing in special cells provided with cilia (flame cells), which communicate with excretory capillaries. These open into canals, which anastomose freely, and then join the gathering tubes, which open into an excretory vesicle. This vesicle, which may be long or short, pear-shaped or Y-shaped, generally opens posteriorly, but may open dorsally above the acetabulum.

The sexes are but rarely separate, hermaphroditism being usual. The male organs consist of testes, which may be simple or branched, and are, as a rule, situated posteriorly. The vas deferens leads forwards sometimes through a vesicula seminalis to the genital opening, below which a cirrus enclosed in a muscular pouch provided with glands, called the 'prostate,' may be found.

The female organs consist of an ovary, which may be branched and is usually situated in front of the testes, and an ovarian duct, which joins with the vitellarian duct from the yolk glands, making a tube, called the 'oötype,' surrounded by the shell gland, in which the egg is formed (Fig. 210).

A curious little canal, Laurer's canal, joins by its inner aperture the oötype near the uterine tube, while its outer aperture is found on the dorsal surface. The homology of this little canal is not quite clear; it may be a vagina. Sometimes a receptaculum seminis is present The ootype opens into the uterine tube, which is usually much coiled, and has its anterior portion thickened, to form the metatrema or vulva, which opens into the genital orifice (Fig. 211).

The genital pore varies in position, being situated in the mid-line in front of or behind the ventral sucker as a rule. Rarely it opens rather laterally and has a muscular depression of its own.

Life-History. -The full life-history of a number of forms has been worked out by Leuckart and Thomas for *Fasciola hepatica*, under which heading details will be given, by Looss for various amphistomes, by Leiper for the genus Schistosoma, and by numerous Japanese observers for other forms.

Typically there is an alternation of generations where one sexual generation is followed by two asexual generations. Two hosts are required for the whole life-cycle.

Leiper has given the following scheme for the development of a digenetic trematode: –

1. Definitive host	.. ..	Egg.
2. First transition	.. ..	Miracidium.
3. Intermediate host	Sporocyst Sporocyst and daughter cysts Sporocyst and Rediæ Sporocyst, Rediæ, and daughter Rediæ	*Cercariæ*.
4. Second transition	..	Free-swimming or encysted *Cercariæ*.
5. Definitive host	.. ..	Adults.

Luhe has provided the following classification of Cercariæ (slightly modified for convenience of reference):

A. Body without internal differentiation. With cuticular ala—*Lophocercariæ*.

B. Body with internal differentiation. Tails may or may not be forked: -
  I. Acetabulum absent- *Monostomes*.
  II. Acetabulum present -
    (*a*) Posteriorly situate- -*Amphistomes*.
    (*b*) Ventrally situate:—
      1. Mouth central—*Gasterostomes*.
      2. Mouth terminal—*Distomes*.

The *Distome cercariæ* may be identified as follows:—

- A. Tails absent—*Cercariæ.*
- B. Tails present:—
  - I. Tails stumpy—*Monocercous.*
  - II. Tails well developed:—
    - (*a*) Tails joined, forming colony - *Rattenkönig cercariæ.*
    - (*b*) Tails not so joined:
      - 1. Tails set with spines -*Trichocercous.*
      - 2. Tails not set with spines:—
        - (A) Tails forked at end -*Furcocercous.*
        - (B) Tails not so forked:—
          - (C) Base of tail forms space into which body can be drawn -*Cystocercous.*
          - (D) Base of tail forms no such space:—
            - (E) Tail as wide or wider than body—*Rhopalocercous.*
            - (F) Tail narrower than body—*Leptocercous.*

The *Leptocercous cercariæ* may be further differentiated as follows:—

- A. Body armed anteriorly:—
  - I. With collar and crown of thorns -*Echinostomes.*
  - II. With a stylet -*Xiphidiocercariæ.*
- B. Body unarmed anteriorly -*Gymnocephalous cercariæ.*

Habitat.—These parasites are found in all classes of the vertebrates, and may occur in any of the organs, but the most common in man are those of the liver, the intestinal tract, the lungs, and the urinary bladder. It is important to remember that the adult parasites may live in domestic animals, especially in cats, that they may affect pigs and cattle, that development takes place in snails, and that the cercaria are free-swimming, but encystment on grass, water-weeds, etc., must be borne in mind.

Pathogenicity.—Apparently the smaller forms can live in human beings without being suspected, but irritation of the bladder, liver, intestine, and lungs may result either as the effect of the eggs or of the parasite.

Diagnosis.—The systematic examination by the microscope of the fæces after centrifuging, especially in cases of diarrhœa, and of the urine and sputum, is the only certain method of diagnosis.

Treatment.—The treatment of infections by these animals is little studied, but Christopherson has lately recommended Tartar Emetic (*vide* Chapter LXXIX., and more especially Chapter LXXXII.). One may try to kill or expel the intestinal forms by chloroform mixed with eucalyptol or Chenopodium followed by purgation, as described in Chapter LXXV. (Ankylostomiasis), or by extract of male fern all in the same chapter (Tæniasis).

Prophylaxis.—We do not know enough about the life-cycles to lay down general rules about prophylaxis, but it will be obvious that the cat, the dog, the pig, and cattle are indirect sources of infection, while bathing, wading and drinking water as well as green vegetables, particularly those not cooked, must be regarded as definite sources of infection, and so must that delicacy the edible snail, which may not be properly cooked.

Classification.—The classification of the Trematoda is as follows:—

SUBCLASS I. HETEROCOTYLEA Monticelli.

Synonyms.—*Polystomea* Leuckart, *Pectobothrii* Burmeister, and *Monogenea* van Beneden.

These Trematodes are generally ectoparasitic, but may be endoparasitic in amphibia and tortoises.

SUBCLASS II. ASPIDOCOTYLEA Monticelli.

Synonym.—*Aspidobothrii* Burmeister.

These are lowly organized endoparasitic trematodes, with one large sucker occupying the whole ventral surface, found in tortoises, marine fish, and shellfish.

SUBCLASS III. MALACOCOTYLEA Monticelli.

Synonyms.—*Distomea* Leuckart, *Malacobothrii* Burmeister, and *Digenea* van Beneden, 1858.

Definition.—Typical endoparasitic trematodes with never more than two sucking-discs, oral and ventral, and a Laurer's canal.

Remarks.—The Malacocotylea include all the human trematode parasites.

Classification.—The Malacocotylea may be divided into orders as follows:

A. Development without alternation of generations—Order 1. *Monogenea* van Beneden, 1858.
B. Development with alternation of generations—Order 2. *Digenea* van Beneden, 1858.

We are only concerned with Order 2.

ORDER DIGENEA van Beneden, 1858.

Definition.—Malacocotylea with a single median anterior sucker, a vagina, and few eggs which develop by alternation of generations.

Classification.—This order is divided into several suborders, of which *Prostomata* concerns us.

Mouth surrounded by the anterior sucker—Suborder *Prostomata* Odhner, 1905.

SUBORDER PROSTOMATA Odhner, 1905.

Definition.—Digenea, in which the mouth is surrounded by the anterior sucker.

Classification.—The Prostomata are divided into superfamilies in the following manner:—

A. Acetabulum or posterior sucker caudoterminal, subterminal, or ventroterminal, and behind the genitalia or at the most embraced by the vitellaria —Super-family 1, *Paramphistomoidea* Stiles and Goldberger, 1910.

B. Acetabulum or posterior sucker ventral and separated from the posterior extremity by, at least, a part of the genitalia —Super-family 2, *Fascioloidea* Stiles and Goldberger, 1910.

SUPER-FAMILY PARAMPHISTOMOIDEA Stiles and Goldberger, 1910.

Synonym.—*Amphistomata* Rudolphi, 1801.

Definition.—Prostomata with acetabulum, caudoterminal or subterminal, or ventral close to the caudal end. Oral sucker and œsophagus present. Cæca two in number. Hermaphrodites with genital pore ventro-median, præ-equatorial, prætesticular, and præovarial, and with one or two præ-ovarial testes. Vitellaria paired.

Type Family.—*Paramphistomidæ* Fischoeder, 1901, restricted.

Classification.—*Paramphistomidæ* Fischoeder, 1901 restricted; *Gastrodiscidæ* Stiles and Goldberger, 1910; *Gastrothylacidæ* Stiles and Goldberger, 1910. The last-named family does not contain any human parasites.

FAMILY I. PARAMPHISTOMIDÆ Fischoeder, 1901, restricted.

Definition.—Pyriform paramphistomoidea with ventral pouches absent.

Type Genus.—*Paramphistomum* Fischoeder, 1901.

Classification.—The Paramphistomidæ are classified into the following subfamilies: *Paramphistominæ* Fischoeder, 1910, restricted; *Cladorchiinæ* Fischoeder, 1901; and *Diplodiscinæ* Cohn, 1904; but of these only the second concerns us.

These suborders may be recognized as follows:—

A. Oral sucker without evaginations *Paramphistominæ.*

B. Oral sucker with evaginations *Cladorchiinæ.*

SUBFAMILY CLADORCHIINÆ Fischoeder, 1901.

Definition.—Paramphistomidæ with oral sucker with evagination.

Classification.—The Cladorchiinæ can be subdivided into the *Stephanopharynginæ* Stiles and Goldberger, 1910, with circular evagination, and *Cladorchiinæ sensu stricto* Fischoeder, 1910, with paired evagination. This last subdivision contains the following genera: *Cladorchis* Fischoeder, 1901, which is the type genus; *Pseudodiscus* Sonsino, 1895; *Chiorchis* Fischoeder, 1901; *Tasiorchis* Fischoeder, 1901; *Pseudocladorchis* Daday, 1907; *Microrchis* Daday, 1907; *Pfenderius* Stiles and Goldberger, 1910; and *Watsonius* Stiles and Goldberger, 1910; of which the last is of importance in tropical medicine.

It may be remarked that this subfamily will probably soon be made a family, and its divisions subfamilies.

Watsonius Stiles and Goldberger, 1910.

Definition.—Cladorchiinæ without genital sucker, with lobate or lobulate testes, without cirrus pouch, and with each oral invagination single.

Species.—*Watsonius watsoni* (Conyngham, 1904) Stiles and Goldberger, 1910.

Watsonius watsoni (Conyngham, 1904) Stiles and Goldberger, 1910.

Synonyms.—*Cladorchis watsoni* (Conyngham, 1904), *Amphistomum watsoni* (Conyngham, 1904), *Paramphistomum watsoni* (Conyngham, 1904).

Definition.—Watsonius with the characters of the genus.

History.—*Watsonius watsoni* was first discovered in the duodenum and upper part of the jejunum of a negro who had come from Adamawa, in late German West Africa, to Northern Nigeria. Since its discovery it has been reported near Lake Chad. The type was first described by Conyngham, later by Shipley, and in 1910 by Stiles and Goldberger.

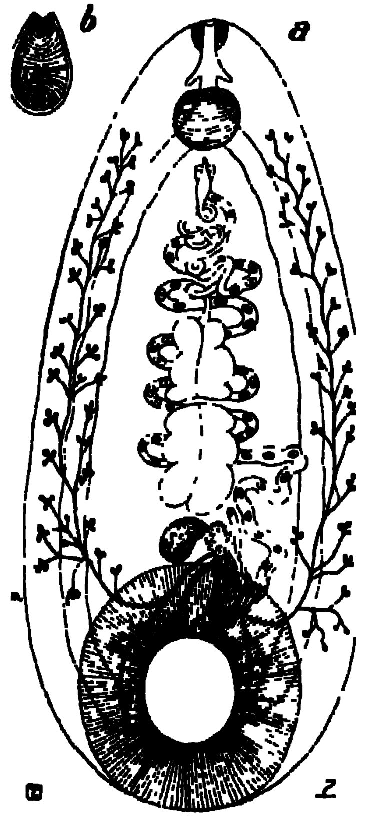

FIG. 212.—*Watsonius watsoni* (After Shipley, emended by Leiper.) *a*, Schematic; *b*, natural size.

Morphology.—The parasite is reddish-yellow when fresh, 8 to 10 millimetres in length by 4 to 5 millimetres in breadth. In shape it is oval or pyriform. The ventral sucker is large and situated posteriorly and subterminally, while the oral sucker is so small as to be hardly worthy of being considered a true sucker. It has a pair of lateral caudal irregularly globular suctional pouches. The pharynx is spherical, with two lateral diverticula, called the 'pharnygeal pouches.' The œsophagus divides into two long intestinal cæca about the level of the junction of the anterior third with the posterior two-thirds of the body, and is here surrounded by a sphincter muscle. The excretory pore opens slightly to the left of the middle line dorsal to the posterior sucker. The excretory vesicle is relatively small, and lies over that sucker. The genital papilla is situated in the mid-ventral line, about the junction of the anterior quarter with the posterior three-quarters of the body, and on it open the canal of the cirrus and the metatrema. The testes, which lie one behind the other, are deeply lobulated. The vas deferens runs into a vesicula seminalis, which opens into the cirrus canal, but has no true cirrus pouch.

The ovary lies close behind the testes, and rather to the right of the body. The ovarian duct curves backwards, and is almost at once surrounded by the shell gland, when it may be called the 'oötype,' which just behind the shell gland receives the vitellarian duct and the inner end of Laurer's canal. The uterus, full of eggs, coils over the testes and runs as far forwards as their anterior border, where it becomes thick and muscular, and is called the 'metatrema.' The eggs are large (122 to 130 μ in length by 75 to 80 μ in breadth).

Life-History.—The life-cycle is not known, but it is believed that the usual host is a herbivorous animal.

Pathogenicity.—It may perhaps cause diarrhœa and anæmia. A post-mortem showed the mucosa slightly congested.

Diagnosis.—By recognition of the eggs or adults in the fæces.

Treatment.—The eucalyptus and chloroform mixture advised for ankylostomiasis (Chapter LXXV.).

FAMILY II. GASTRODISCIDÆ Stiles and Goldberger, 1910.

Definition.—Paramphistomoidea with rather discoidal bodies divided by a transverse constriction into cephalic and caudal portions. Ventral pouch absent. Venter with many large papillæ. Acetabulum ventral at caudal end.

Type Genus.—*Gastrodiscus* Leuckart, 1877; the other genus is *Homalogaster* Poirier, 1883.

Gastrodiscus Leuckart, 1877.

Definition.—Gastrodiscidæ with bodies slender anteriorly and broadened posteriorly. The latter contains the genital glands. The acetabulum is small. The ventral pouch is absent. The oral sucker has paired evaginations, and leads into an œsophagus with muscular thickening. The cæca are long, not wavy, and end post-testicularly. Male organs:—These are two branched testes, and a cirrus pouch which is not completely closed. Female organs:—Ovary and shell gland are post-testicular; vitellaria are extracæcal; and the uterus intercæcal. Laurer's canal is prevesicular.

Type.—*Gastrodiscus ægyptiacus* Cobbold, 1876, in the horse.

Other Species.—*G. hominis* in man; *G. secundus* Looss, 1907, in the horse; *G. minor* Leiper, 1913, in the pig in Uganda and Nigeria.

Gastrodiscus hominis Lewis and McConnell, 1876.

Synonym.—*Amphistomum hominis* Lewis and McConnell.

Definition.—*Gastrodiscus* 5-8 mm. in length and 3-4 mm. broad.

History.—It was first described in 1876 by Lewis and McConnell, who found it in hundreds attached by its posterior sucker to the mucosa of the cæcum, vermiform appendix, and ascending colon of an Assamese. Since then it has been reported in natives of India, and perhaps it may be common. We have not met with it in Ceylon, though there was a small jar in the Medical College Museum labelled *Amphistomum hominis*, but without a history.

Leiper has made *G. hominis* the type of a new genus *Gastrodiscoides*, distinguished from *Gastrodiscus* by the absence of papillæ on the venter and the position of the genital pore on the cone.

Morphology.—The parasite is reddish-coloured, 8 to 10 millimetres in length and 4 to 5 millimetres in greatest breadth, tapering to 2·5 millimetres in front. The thickness is about 4 millimetres. The posterior end of the body presents a larger disc, on the hinder border of which lies the acetabulum. The rest of the body is thin, tapering to the mouth. The genital pore is at a level with the bifurcation of the intestine. The testes are double, with a sinuous vas deferens. The uterus and the yolk glands are situated laterally. The eggs are oval, 0·15 millimetre in length and 0·072 millimetre in breadth.

Pathogenicity.—It is not known whether these parasites cause any disease. It occurs in 5% of the pigs in French Indo-China.

SUPER-FAMILY FASCIOLOIDEA Stiles and Goldberger, 1910.

Synonym.—*Distomata* Retzius, 1782.

Definition.—Prostomata with acetabulum ventral and always separated from the posterior extremity by some part of the genital apparatus. Oral sucker present; cæca two in number. Hermaphrodites or with separate sexes.

Type Family. *Fasciolidæ* Railliet, 1895.

Classification.—The super family may be classified into the following families as follows:

A. *Hermaphrodites*:—
  I. Oral sucker without collar of strong pointed spines:—
    (*a*) Ovary in front of testes:—
      1. Genital pore in front of ventral sucker—*Fasciolidæ*
      2. Genital pore not in front of ventral sucker:—
        (A) Genital pore surrounded by a pseudo-sucker—*Heterophyidæ*.
        (B) Genital pore not so surrounded:—
          (C) Cuticle with pointed spines—*Troglotremidæ*.
          (D) Cuticle without pointed spines—*Opisthorchiidæ*.
    (*b*) Ovary behind testes—*Dicrocœliidæ*.
  II. Oral sucker with a dorsal and lateral, but not ventral, fold or collar bearing pointed spines—*Echinostomidæ*.
B. *Sexes separate*—*Schistosomidæ*.

FAMILY FASCIOLIDÆ RAILLIET, 1895.

Definition.—Fascioloidea, hermaphrodites with oral sucker without spiny collar, with ovary in front of the testes and genital pore behind the ventral sucker. Vitellaria well developed, extending dorsally and ventrally. Cirrus and vagina without spines. Uterus poorly developed. Excretory vesicle much branched. Eggs large.

Classification.—The Fasciolidæ are divided into two subfamilies as follows:—

A. Body with shoulder; receptaculum seminis absent; intestine branched—*Fasciolinæ*.
B. Body without shoulder; receptaculum seminis present; intestine not branched—*Fasciolopsinæ*.

SUBORDER FASCIOLINÆ Odhner, 1910.

Definition.—Fasciolidæ with a shoulder separating the head from the body, with a much branched intestine, without a receptaculum seminis.

Remarks.—This subfamily contains the genus Fasciola, which concerns us.

Fasciola Linnæus, 1758.

Definition.—Large Fascioloidea with leaf-like bodies, with the anterior end shaped into a conical head and with the ventral sucker situated near the mouth. Cuticle covered with spines.

Type Species.—*Fasciola hepatica* Linnæus, 1758.

Fasciola hepatica Linnæus, 1758.

Synonyms.—*Distomum hepaticum* Retz, 1786, *Fasciola humana* Gmel, 1789; *D. caviæ* Sons, 1890; *Cladocœlium hepaticum* Stoss, 1892.

Definition.—*Fasciola* with long cephalic cone, converging sides, small acetabulum situate some distance behind the oral sucker. Eggs 130-145 × 70-90 microns.

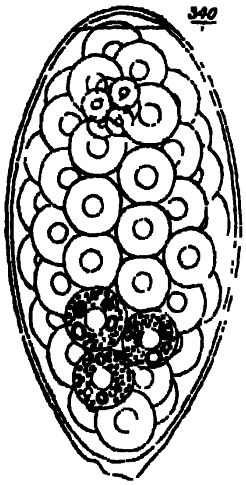

FIG. 213.—EGG OF *Fasciola hepatica*.

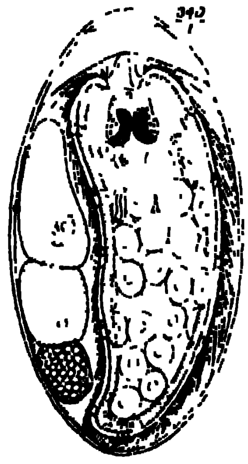

FIG. 214.—THE MIRACIDIUM OF *Fasciola hepatica*.

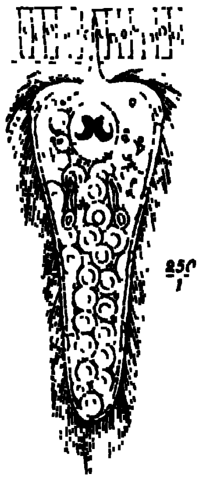

FIG. 215.—THE LARVA OF *Fasciola hepatica*.

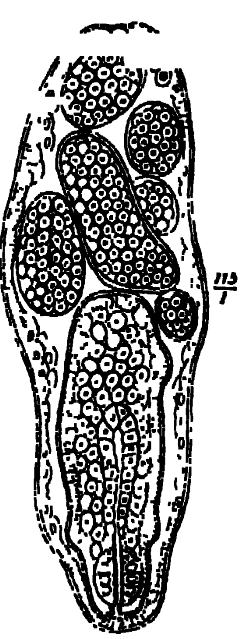

FIG. 216.—THE SPOROCYST OF *Fasciola hepatica*.

(After Thomas, from the *Quarterly Journal of Microscopical Science*.)

History.—*Fasciola hepatica*, the liver-fluke, is a parasite of sheep, oxen, goats, horses, and many other herbivorous animals, in Europe, North Africa, North and South America, Australia, Tasmania, Japan, China, Burma, and India. It is said to be extremely common in Burma and Egypt.

It has been found in man several times, and apparently usually in the liver, but it has been recorded in the bloodvessels, in a swelling on the sole of the foot, in abscesses about the head, and in a swelling in the right hypochondriac region. It is probable that *Distomum oculi humani* Ammon, 1833, and *Monostomum lentis* Von Nordmann, 1832, may have been young liver-flukes.

Morphology.—*Fasciola hepatica* is a flat, oval animal, with an anterior triangular projection. Length, 20 to 30 millimetres; breadth, 8 to 13 millimetres. The cuticle is covered with minute pointed scales directed backwards.

There are two suckers—an oral, which is situated at the anterior end of the animal and surrounds the mouth opening, and a ventral, the acetabulum, which is a muscular cap situated in the median line near the junction of the anterior projection with the rest of the body. The mouth leads into a muscular pharynx, which passes via a short œsophagus into the intestine, which divides just in front of the genital aperture into two tubes running to the posterior end of the body, giving off numerous branched cæca.

The excretory system starts with dilated tubules, into which project the cilia of the so-called flame cells. The ducts, which freely anastomose, open into a main duct, which runs directly backwards to open at a median pore at the posterior end of the body.

The two testes are much-branched tubes, lying in the middle of the body, of equal size, one lying in front of the other; from each a vas deferens runs as far as the ventral sucker, where it opens into an elongated sac, the vesicula seminalis, from which the ductus ejaculatorius runs to the end of a large muscular organ, called the cirrus which lies in a sac situate just in front of the ventral sucker. The genital opening through which the cirrus can be protruded is situated between the two suckers on the ventral surface.

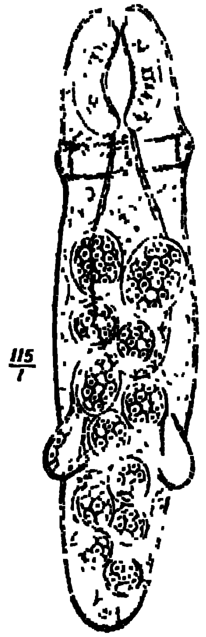

Fig. 217.—The Redia of *Fasciola hepatica*

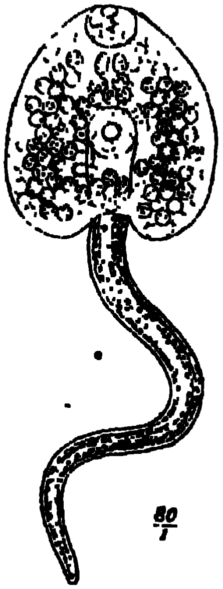

Fig. 218.—The Cercaria of *Fasciola hepatica*.

(After Thomas, from the *Quarterly Journal of Microscopical Science*.)

The branched and tubular ovary lies on the right, in front of the anterior testes. The ovarian ducts run backwards to join the middle line with the median vitellarian duct from the yolk reservoir, into which open the vitellarian ducts from the large branched yolk glands lying on either side of the body, from the level of the ventral sucker to the posterior extremity.

The junction of these two ducts is surrounded by the shell gland, and forms a much-convoluted tube, the uterus, which is joined close to its commencement by a little tube, Laurer's canal, opening on to the dorsal surface. The uterus, which is generally full of eggs, opens on the left side of the base of the cirrus.

The nervous system consists of a nerve collar around the pharynx, from which two nerve cords run backwards along the sides of the body.

Life-History.—The ovum starts from the ovary and travels along the ovarian duct, where it is fertilized, after which it is surrounded by a large number of yolk cells, and then by a shell formed from the secretion of the shell gland. The egg now passes forwards into the uterus, and is evidently deposited in the bile-passages and escapes in the fæces. It is oval, yellowish-brown, with a cap-like lid 0·13 to 0·145 millimetre in length by 0·07 to 0·09 millimetre in breadth, and is seen to enclose a mass of yolk cells with one ovum, which now segments and grows, using up the yolk cells, forming a young form, called a 'miracidium,' 0·13 by 0·027 millimetre, which in a few weeks escapes by the opercular opening if the egg is in water, and, being ciliated, swims about as a conical larva, with a little anterior papilla and two eye-spots. It has a cuticular epithelium, under which are muscular layers, and contains a simple sac, like an alimentary canal, a cerebral ganglion, and an excretory system. There is a segmentation cavity (forming a body cavity) between the alimentary canal and the body-wall.

It now bores its way into the pulmonary cavity of some snail by means of its anterior papilla; otherwise it dies in about eight hours. The varieties of snail hosts are: *Limnæa truncatula* Muller, in Europe, Asia, Africa; *L. oahuensis* in the Sandwich Islands; *L. viator* Orb in South America; *L. humilis* Say in North America, in which it loses all its organs, and increases in size rapidly, while cells grow from the wall into the primary body cavity, so that a cyst is formed, called the 'sporocyst.' This has an external cuticle, a thin muscular layer, and an epithelial lined cavity, containing collections of cells, which develop into cylindrical forms, possessing a simple, short, tube-like alimentary canal, with a pharynx, glands, and intestine, and a genital pore near the anterior end. These forms, which are called *Rediæ*, after the celebrated biologist Redi, force their way out of the sporocyst by making a wound, which heals readily, and then wander about the snail, being especially abundant in the liver. When fully formed they have a ridge running round the anterior end, and a pair of blunt processes for locomotion posteriorly.

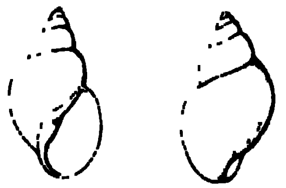

FIG. 219.—*Limnæa truncatula* MÜLLER.

Inside the *Rediæ* cells bud off from the body-wall and form the *Cercariæ* which are not unlike a young *Fasciola* with a tail

The *Cercariæ* possess cutaneous glands for the purpose of secreting the cyst-wall of the next stage. They escape from the *Rediæ* by means of the genital pore, and, leaving the snail, swim about in the water for some time, finally becoming encysted on grass or water-weeds, and are then eaten by sheep, inside which they escape from the cyst, and, working their way along the bile-ducts, develop in six weeks into sexually mature flukes.

Habitat.—The liver-fluke usually lives in the sheep, in which it causes the disease called '**sheep-rot**'; but infection can spread to man.

Pathogenicity.—It causes the disease 'Halzoun' in North Lebanon by entering the pharynx. It is probably *Hexathyridium venarum* Treutler, found in the anterior tibial vein, and the worms found in the portal vein by Duval at Rennes in 1842; by Vital from Constantia in 1874, by Giesler, in 1850, in a foot; by Harris, in Liverpool, in an abscess. It may be *Distomum oculi humani* Ammon, 1833; *Monostomum lentis* Von Nordmann, 1832; and the *Distomum ophthalmicum* Diesing, 1830.

Fasciola gigantica Cobbold, 1856.

Synonyms.—*Fasciola angusta* Railliet, 1895; *F. gigantea* Cobbold, 1858.

Definition.—Fasciola with short cephalic cone, almost parallel sides, large acetabulum situate close behind oral sucker. Eggs 150-190 × 75-90 microns.

Remarks.—*F. gigantica*, which is nearly allied to *F. hepatica*, is found in herbivora in Africa, and is believed to have occurred in a man, for a parasite somewhat resembling it was expelled from the lung during a fit of coughing associated with hæmoptysis, but there is some doubt as to whether it was not different from Cobbold's species. Its length was 26 to 28 millimetres and its breadth 6 to 8 millimetres, but it was contracted. It caused fever, cough, and slight hæmoptysis.

Subfamily Fasciolopsinæ Odhner, 1910.

Definition.—Fasciolidæ without shoulder between head and body, with simple zigzag intestines, and with a receptaculum seminis.

Type Genus.—*Fasciolopsis* Looss, 1896.

Fasciolopsis Looss, 1896.

Definition.—Fasciolinæ with large ventral sucker elongated posteriorly to form a sac. Cirrus pouch, long and cylindrical. Laurer's canal present.

Type Species.—*Fasciolopsis buski* Lankester, 1857.

Classification.—Four species are known to occur in man, and they can be recognized as follows:—

A. *Spines present on cuticle:*
  I. Vitelline acini very large—*Goddardi*.
  II. Vitelline acini not large—*Kwan's fluke* (?).
B. *No spines on cuticle:*—
  I. Cirrus sac conspicuous:—
    (*a*) Cirrus pouch very long, broad, convoluted, powerfully built—*Fülleborni*.
    (*b*) Cirrus pouch not so long, narrow, straight, not powerfully built—*Buski*.
  II. Cirrus sac inconspicuous—*Rathouisi* (?).

Fasciolopsis buski Lankester, 1857.

Synonyms.—*Distomum buski* Lankester, 1857; *D. crassum* Busk, 1859; *nec* v. Siebold, 1836; *Distomum rathouisi* Poirier, 1887.

History.—*Fasciolopsis buski* is a very large trematode, which was first discovered by Busk in the duodenum of a Lascar who died in the Seamen's Hospital in 1843. In 1857 it was named by Lankester, and in 1859 described by Cobbold.

It appears to be by no means uncommon in man and pigs in South China, and is known in Borneo, the Straits Settlements, Assam, and India. In 1910 *F. rathouisi* Poirier, 1887, was regarded as the same as *F. buski* Lankester, 1898, but at the present time some authorities go back to the older view that they are separate species—*e.g.*, Odhner says they are the same, and Ward that they are separate, because the cirrus sac is convoluted and not conspicuous while that of *F. buski* is straight and conspicuous.

Morphology.—It is a large, thick, brown, smooth trematode, 24 to 70 millimetres in length and 5·5 to 14 millimetres in breadth. The oral sucker and acetabulum are in the proportion of 0·5 : 2·0. The pharynx is globular, and there is a prepharynx, with a sphincter. The œsophagus is short, and the intestinal cæca are not branched, and extend to the posterior border. The genital pore is situated anteriorly to the acetabulum, but the most remarkable feature is the very long cirrus, about one-fourth the length of the body. The testes lie posteriorly, with the ovary and the uterus in front. The yolk glands are extensive, like those in *F. hepatica*.

Life-History. The eggs are 0·12 to 0·13 millimetre in length and 0·077 to 0·08 in breadth, and the larval stages are said to occur in shrimps.

Habitat.—The intestine of the pig and man.

Pathogenicity.—It is believed to cause dysenteric diarrhœa, wasting, and jaundice at times.

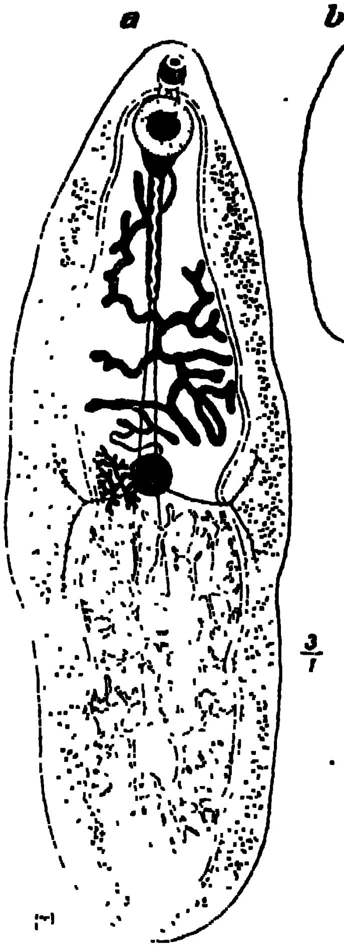

Fig. 220.—*Fasciolopsis buski.*
(After Odhner, from the *Centralblatt für Bakteriologie.*)
a, Schematic ; *b*, natural size.

Fasciolopsis fülleborni Rodenwaldt. 1909.

History.—This worm was discovered and described by Rodenwaldt in 1909, being found in the motions of an Indian in Hamburg.

Morphology.—The parasite is very large, measuring from 30 to 50 millimetres in length and from 14 to 16 millimetres in breadth. The oral sucker and acetabulum are in the proportion of 0·75 to 0·9. There is a prepharynx and pharynx, but no œsophagus.

The intestinal cæca are long and wavy, and extend to the posterior end. The genital apertures lie in front of the acetabulum.

The cirrus sac is very long and well developed, and the testes lie behind the ovary and the oötype. The latter is much larger than in *F. buski*, and is oval instead of being round. The yolk glands extend from the acetabulum to the posterior end of the body, being situated laterally. The excretory vesicle is well developed.

The eggs measure 0·1 millimetre in length by 0·073 millimetre in breadth.

Habitat.—Intestine of man.

Pathogenicity.—The patient harbouring it was suffering from fever, which had been diagnosed as typhoid.

Kwan's Fluke (= F. goddardi ?).

Under this term Heanley has described a trematode found by Dr. Kwan King Hung in a child in the island of Hong Kong.

Morphology.—In length it is 2 inches, in breadth ½ inch. The cuticle possessed spines. The intestine was not clearly seen, but the cæca were unbranched. The testes were large and placed one behind the other. The

ovary was branched, and it—the shell gland and the yolk glands (which met each other posteriorly)—resembled those of *F. buski*.

Pathogenicity.—The patient suffered from vomiting, which resulted in the expulsion of the flat-worms.

Fasciolopsis goddardi Ward, 1910.

Definition.—Fasciolopsis with spines and very large vitellaria.

Remarks.—This fluke, which is imperfectly known, was found in Shanghai, China and measures 22 × 9 mm.

FAMILY HETEROPHYIDÆ ODHNER, 1914.

Definition.—*Fascioloidea*, hermaphroditic, with the ovary in front of the testes, genital pore behind the ventral sucker, and surrounded by a pseudo-sucker, which is behind or on a level with the acetabulum, and has its muscles blended with the body musculature and not sharply differentiated therefrom.

Type Genus. *Heterophyes* Cobbold, 1866.

Classification.—The two genera which concern us can be differentiated as follows:—

A. Acetabulum and genital suckers ventrally situate and separate—*Heterophyes*.

B. Acetabulum and genital suckers dextro-laterally situate and surrounded by a complex musculature—*Metagonimus*.

GENUS: HETEROPHYES Cobbold, 1866.

Synonyms.—*Cotylogonimus* Luhe, 1899; *Cœnogonimus* Looss, 1899.

Definition.—Heterophyiidæ with suckers ventrally situate, with a narrow, movable, anterior portion, and a broader, less movable, posterior portion, which contains the genitalia. Cuticle with scale-like spines; suckers widely separated; œsophagus long. Genital pore placed laterally, behind the ventral sucker, and surrounded by a genital prominence with chitinous rodlets. No cirrus pouch. The testes are at the posterior end, and the ovary in a median position between them. Yolk glands are small, and situated at the sides posteriorly.

Type Species.—*Heterophyes heterophyes* v. Siebold, 1852.

Heterophyes heterophyes v. Siebold, 1852.

Synonyms.—*Distomum heterophyes* v. Siebold, 1852; *Mesogonimus heterophyes* Railliet, 1890; *Cœnogonimus heterophyes* Looss, 1900; *Cotylogonimus heterophyes*, Braun, 1901.

Definition.—Heterophyes with ventrally situate and separate acetabular and genital suckers.

History.—This minute parasite was discovered by Bilharz in the intestine of a boy in Cairo in 1851, and again a little later, but the third observation was not till 1891 by R. Blanchard; since then Looss has found it in Alexandria and Cairo, where he says it is not uncommon. Leiper has recorded several cases in Chinese seamen.

It is also found in dogs and cats in Egypt, Japan, and Formosa; in man in Khartoum (eggs 0·026 × 0·013 mm.), also adults; and in dogs in the same town.

Morphology.—*Heterophyes heterophyes* is pear-shaped, very narrow in front, broad behind; 2 millimetres in length by 1 millimetre in breadth, but can stretch to quite double this length. Cuticle with rectangular scales, and with numerous glands on the anterior ventral surface. Oral sucker 0·1 millimetre and ventral 0·35 millimetre in diameter. Œsophagus relatively long. Intestinal cæca end posteriorly near each other. Testes situated posteriorly, not quite on the same level on each side of the excretory vesicle; ducts join in a large vesicula seminalis, from which a canal unites with the metatrema, and then discharges into the genital cavity, the pore of which is placed laterally, surrounded by an annular muscular elevation, provided with seventy-five to eighty branched chitinous spines, probably intended to help in sexual intercourse.

The ovary lies medianly, and its duct passes backwards to join the receptaculum seminis, which is just in front of the testes.

Here also joins the vitellarian duct of the yolk glands, which also lie laterally in the posterior third of the body. The uterus is coiled throughout the posterior part of the body. The canal of Laurer is present. The eggs have thick shells, and are 0·03 millimetre in length and 0·017 millimetre in breadth, containing a miracidium.

Habitat.—Small intestine.

Life-History.—Unknown.

Pathogenicity.—Perhaps nil, but the parasite is very small, and may therefore be overlooked.

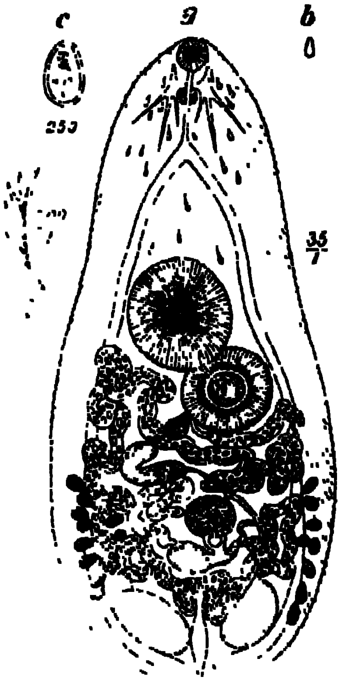

FIG. 221.—*Heterophyes heterophyes.*

(After Looss, from Braun's 'Animal Parasites of Man,' English edition.)

a, Schematic × 35; *b*, natural size; *c*, eggs × 250; *d*, spine × 700.

GENUS METAGONIMUS Katsurada, 1913.

Synonym.—*Yokogawa* Leiper, 1913.

Definition.—Heterophyiidæ with suckers dextro-laterally situate.

Type Species.—*Metagonimus yokogawai* Katsurada, 1913.

Metagonimus yokogawai Katsurada, 1913.

Synonym.—*Yokogawa yokogawai* Leiper, 1913. Leiper now believes that this fluke is the same as one previously described by Kobayashi as *Loxotrema ovatum*, n.g., n.sp.

Definition.—Metagonimus 1·5-2·5 × 0·4-0·7 mm., with body covered with nail-shaped spines about 10 microns in length, with a characteristic sac-like acetabulum placed deeply in the body and not opening on the ventral surface, but dextro laterally.

History.—It was found in Japan in the upper or middle part of the jejunum, rarely the cæcum, of man and mammals. They enter and destroy the solitary glands.

Morphology.—*Metagonimus yokogawai* is a small fluke possessing the characters given above. The oral sucker is 77-85 microns in diameter. The testes are elliptical and situate posteriorly. The ejaculatory ducts open with the uterus into a genital sinus, which opens into a pit at the front of the ventral sucker.

The ovary is spherical, and lies in the middle of the posterior part of the body. A receptaculum seminis and a Laurer's canal are present. The vitellarian acini lie on each side in the posterior part of the body. The uterus forms three to four transverse coils.

Life-History.—The eggs are elliptical, 28 × 16 microns, double contoured and yellowish brown, with an operculum, but no shoulder, and a knob at the narrower end.

Muto found cercaria in the liver of *Melania libertina*, in Kaishu, Korea, where metagonimiasis is common. On breaking up the liver in water, it was found that the cercaria became encysted under the scales of uninfected goldfish kept in the water. Kittens fed with these fish became infected in twelve to fifteen days.

The cercariæ also live in a trout, *Plecoglossus altivelis*, rarely in other fish. Infection takes place by eating raw fish, and the period, judging by dogs, is seven to sixteen days for the eggs to appear in the fæces.

Pathogenicity. It causes chronic diarrhœa in man.

FAMILY TROGLOTREMIDÆ ODHNER, 1914.

Definition. Fascioloidea hermaphroditic, with ovary in front of testes, genital pore just in front or just behind rim of acetabulum, but not surrounded by a pseudo-sucker, and with the cuticle completely covered with pointed spines. Vitellaria well developed and for the most part dorsally situate. More or less flattened worms 2-3 mm in length, with extreme posterior end prolonged into a small appendage, with ventral surface flat or somewhat hollowed, and dorsal surface vaulted. Musculature in forms living in cysts poorly developed. Pharynx present. Gut diverticula terminate a short distance from the posterior end. Genital pore immediately in front or immediately behind the rim of the acetabulum in the middle line or slightly to the left. Cirrus usually absent. Pars prostatica and seminal vesicle present. Testes symmetrical. Ovary in front of the testes. Vitellaria well developed. Uterus long and much coiled, with small eggs, or short and kinked with large eggs

Remarks.—Odhner formulated this family in Zoologiska Bidrag fran Uppsala in 1914 for *Distomum acutum*, in the frontal sinuses of *Mustela putorii*; *D. gastrophilum* from cysts in the pylorus of *Phocæna communis*, for *Collyriclum faba* from *Sylvia hortensis* and for *Paragonimus ringeri*, etc.

Type Species.—*Troglotrema* Odhner, 1914.

GENUS PARAGONIMUS Braun, 1899

Definition.—Troglotremidæ with thick, oval, or broad, fusiform bodies, almost circular on transverse section. Cuticle, with sac-like spines. Suckers separated by half the length of the body

The intestinal cæca are wavy, and run to the posterior end of the body, but are unbranched. The excretory vesicle runs from the pharynx backwards to its aperture on the posterior margin of the body. The genital pore is just behind the ventral sucker. There is no cirrus pouch, and no receptaculum seminis.

Type Species.—*Paragonimus westermanii* Kerbert, 1878.

Classification.—There are five species, but *P. rudis* Diesing, 1850, from a Brazilian otter, and *P. compactus* Cobbold, from an Indian ichneumon, are not well known. According to Ward the other three may be distinguished as follows, but Japanese workers do not accept these characters as of specific value:—

A. Chisel-shaped spines:—
  I. Arranged in circular rows in groups—*Ringeri*.
  II. Arranged in circular rows singly—*Kellicotti*.
B. Lancet-shaped spines:—
  Arranged in circular rows in groups—*Westermani*.

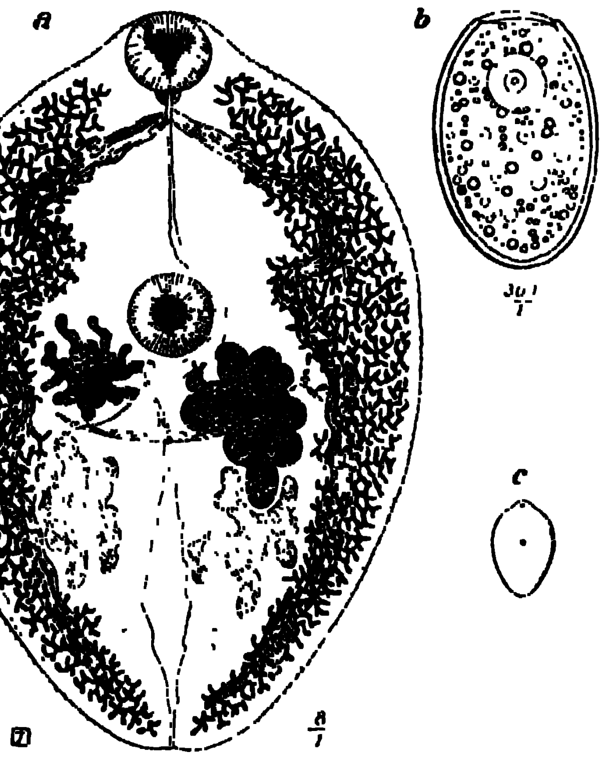

FIG. 222. *Paragonimus ringeri*.
(After Looss, from Mense's 'Tropenkrankheiten.
a, Schematic × 8; *b*, eggs × 300; *c*, natural size.

Paragonimus ringeri Cobbold, 1880.

Synonyms.—*Distoma ringeri* Cobbold, 1880; *D. hepaticum* Miura, *D. pulmonale* Baelz, 1883; *D. pulmonis* Suga, 1883; *D. cerebrale* 1889; Yamagiwa, 1890; *Mesogonimus westermani* Railliet, 1890; *M. pulmonale* Stossich, 1892.

History.—*Paragonimus westermani* was discovered by Kerbert in 1878 in the lungs of two Bengal tigers, which died respectively in the Zoological Gardens of Amsterdam and Hamburg.

In 1880 Baelz found in the sputum of cases of hæmoptysis bodies which he took to be psorosperms, and therefore called the disease gregarinosis pulmonum, but when these were referred to Leuckart he said that they were eggs of a *Distomum*. In the same year Manson found what he took to be eggs of some parasite in a case of hæmoptysis, in a Chinaman from Northern Formosa, and later he saw a Portuguese with hæmoptysis and obscure thoracic symptoms, who lived in Tamsui in North Formosa.

This man died in Formosa, and Dr. Ringer, who performed the post-mortem, discovered in the lungs a minute, fleshy, slightly flattened, oval body, grey in colour, and about a quarter of an inch in length, which expelled some brownish material from a minute orifice near one end.

This specimen was sent to Manson, who noted the same eggs as he had found in the Chinaman already mentioned, and then forwarded the parasite to Cobbold, who, rightly thinking it new to science, named it *Distomum ringeri*, the name now in use. In 1883 Baelz, having found specimens in the lungs, named it *D. pulmonale*. In 1890 Otani and Yamagiwa proved that it could occur in other parts of the body besides the lungs by finding it in the brain, where it produced symptoms of Jacksonian epilepsy. Stiles and Looss defined its zoological position; Ward found it in cats, Railliet in dogs, and Stiles in hogs; while the best description of the lesions caused by it is that by Musgrave in 1907, who found it in the Philippine Islands.

It is very common in Japan, and is found in China, Korea, and North America, a human case being reported from Mexico by Naunyn.

In 1908 Ward found *P. kellicotti* in pigs, dogs, and cats in North America.

Morphology.—The parasite varies from a reddish-brown to a light slate colour when first removed from the body, but soon becomes greyish on exposure to the air. In shape it is oval, with a somewhat flattened ventral surface, and is capable of slight alterations of its appearance by protruding and retracting its head, and by altering its ventral sucker so that it may appear terminal. The cuticle is covered with scale-like spines, which may be capable of being moved. The oral sucker is spherical and terminal, 0·63 to 0·97 millimetre in diameter. The ventral sucker is situated in the anterior half of the body, and is 0·76 to 1·31 millimetres in diameter. The œsophagus is short, and divides into the two wavy cæca. The genital pore may be indistinct, and is always small, lying close to and behind the ventral sucker. The testes lie about, but not quite on, the same level on each side of the median line just behind the uterus. There is neither a cirrus nor a cirrus pouch. The ovary is opposite and slightly posterior to the uterus, which is visible just posterior to the ventral sucker. The yolk glands lie at the sides, and their branches almost meet dorsally, while ventrally they only extend to the intestinal cæca. Laurer's canal is present. The eggs are oval in shape, of a reddish-brown to a light yellow in colour, with a length from 0·08 to 0·1 millimetre, and a breadth from 0·052 to 0·075 millimetre. They possess an operculum, and contain the ovum and yolk cells.

The excretory vesicle is well developed, and extends from the pharynx backwards.

Life-History.—According to Nakagawa, the miracidia infect the snails *Melania libertina* and *Melania obliquegranosa*.

Nagakawa in Formosa found encysted larvæ in fresh-water crabs:—1. *Geothelphusa obtusipes*. **Synonyms.**—*Potamon obtusipes, Thelphusa rubra*. 2. *Geothelphusa dehaanii*. **Synonyms.**—*Potamon dehaanii, Thelphusa berardi*, and perhaps—3. *Eriocheir japonicus*. **Synonym.**—*E. formosa*.

According to Sadao Yoshida, in the first two, the larvæ are found in the liver, rarely in the gills or muscles, and in the last chiefly in the gills, muscles, and hypoderm, and rarely in the liver.

Dogs and cats have been infected by these observers from the crabs, when the larva, escaping from the cyst in the intestine, penetrates the wall near the jejunum and enters the abdominal cavity, perforates the diaphragm, and, entering the subpleural tissue, may pierce its way into the lung and encyst or pass into the neck (and perhaps so to the brain, etc.). The lungs are their favourite seat, and the only one in which they attain maturity.

Kakami, on the other hand, says that cercariæ may be found in *Melania libertina*, and that they get into drinking-water and so infect people directly.

Pathogenicity.—It causes paragonimiasis in man.

FAMILY OPISTHORCHIIDÆ BRAUN, 1901, *emendavit* STEPHENS, 1916.

Definition.—Fascioloidea, hermaphroditic, with oral sucker without collar of spines. Ovary in front of testes. Genital pore behind ventral sucker. Cuticle without pointed spines. Small to medium flukes tapering anteriorly. Cirrus absent, but receptaculum seminis and Laurer's canal present. Eggs small.

Classification.—The family is divided into subfamilies as follows:—

A. Excretory pore terminal; bladder long, dorsal to testes.
   Uterine coils not overlapping intestinal cæca—*Opisthorchiinæ*.

B. Excretory pore ventral; bladder short, ventral to testes.
   Uterine coils overlapping intestinal cæca—*Metorchiinæ*.

SUBFAMILY OPISTHORCHIINÆ LOOSS, 1899, *emendavit* Stephens, 1916.

Definition.—As above.

Classification.—The genera important to us can be distinguished as follows:—

A. Testes lobed:—

I. With long retractile process projecting from ventral surface and carrying out its apex the acetabulum and the genital pore—*Paropisthorchis*.

II. Without such process:—

Vitellaria from acetabulum to ovary in one mass—*Opisthorchis*.

Vitellaria divided into one mass in front of and another behind the ovary—*Amphimerus*.

B. Testes branched:—

Branches cover intestinal cæca ventrally—*Clonorchis*.

Type genus.—*Opisthorchis* R. Blanchard, 184

Opisthorchis R. Blanchard, 1845.

Definition.—Opisthorchiinæ with long flattened body and somewhat pointed anterior extremity, suckers small, intestinal cæca unbranched, yolk glands situate laterally and not extending beyond the ventral sucker in front, testes in the posterior part of the body, one behind the other.

Type Species. *Opisthorchis felineus* Rivolta, 1885.

Classification. The species of this genus are separated from one another with great difficulty.

The following are found in man: *Opisthorchis felineus* Rivolta, 1885; *Opisthorchis viverrini* Poirier, 1866.

These two species are distinguished as follows:—

A. Cuticle without spines—*Felineus*.

B. Cuticle with minute spines—*Viverrini*.

Opisthorchis felineus Rivolta, 1885.

Synonyms.—*Distoma conus* Gurlt, 1831, *nec* Creplin, 1825; *D. lanceolatum* v. Siebold, 1836, *nec* Mehlis, 1825; *D. sibiricum* Winogradoff, 1892; *D. tenuicolle* Mühl, 1896, p.p.

Definition.—Opisthorchis with cuticle without spines.

Remarks.—*Opisthorchis felineus* lives in the gall-bladder and bile-ducts of the domestic cat, and is also found in dogs in Europe. The North American species is different (*O. pseudo-felineus*).

In human beings it is apparently a common parasite in Siberia, where it was first found by Winogradoff in Tomsk.

Morphology.—It is reddish-yellow in colour, with a conical neck at the level of the ventral sucker, marked by a shallow constriction.

The length is from 8 to 11 millimetres and the breadth 1·5 to 2 millimetres. The testes lie in the posterior part of the body, one behind the other. The yolk glands are situate on either side of the middle third of the body, beginning behind the ventral sucker and terminating about the level of the ovary.

The genital pore is close in front of the ventral sucker.

The eggs are oval, with a well-defined operculum (30 μ by 11 μ).

Life-History.—The parasites live in the bile-duct, and the eggs, containing a ciliated miracidium, escape in the fæces. Complete development is not known, but cercaria have been found in fish which infect men and cats.

Pathogenicity.—It causes inflammation, dilatation of the bile-ducts in man, with atrophy of the liver substance, ascites, and icterus.

Opisthorchis viverrini Poirier, 1886.

Definition.—Opisthorchis with cuticle covered with minute acicular spines. Ovary multilocular. Branches of intestine almost reach the hinder end of the body, and the ovary and testes are deeply lobed.

Remarks.—This trematode, which belongs to the Indian civet-cat, was obtained by Kerr from prisoners at Chiengmai, and recognized by Leiper.

Infection.—Infection is probably by eating raw or partially cooked fresh-water fish.

Paropisthorchis Stephens, 1912.

Definition.—Opisthorchiinæ with lobed testes and with ventral process on which are situate the ventral sucker and the genital pore.

Type Species.—*Paropisthorchis caninus* Barker, 1912.

Paropisthorchis caninus Barker, 1912.

Definition.—Paropisthorchis with the generic characters.

Remarks.—Cobbold in 1858 found a little fluke, *Distomum conjunctum*, in the bile-ducts of *Canis fulvus* Lewis, the American fox.

Fourteen years later Lewis and Cunningham found the same fluke in Indian pariah dogs, and in 1874 McConnell found what was thought to be the same fluke in human beings in Calcutta. In 1903 Braun pointed out that the American and Indian flukes were different, and named the latter *Opisthorchis noverca* (*vide infra*, Amphimerus).

In 1912 Barker separated the parasite of the Indian pariah dog from the human, calling the former *O. caninus*; and in the same year Stephens created a separate genus for it. Leiper still maintains, however, that these two forms, in man and dog, are identical.

It is not known to occur in man.

Amphimerus Barker, 1912.

Definition.—Opisthorchiinæ without ventral process, but with lobed testes and vitellaria divided by the position of the ovary into anterior and posterior lobes.

Type Species.—*Amphimerus noverca* Braun, 1903.

Remarks.—This genus was created for Braun's *Opisthorchis noverca*, which, as explained above according to Stephens, only applies to McConnell's flukes, found in two Mohammedans in Calcutta.

Amphimerus noverca (Braun, 1903).

Definition.—Amphimerus with the characters of the genus.

Morphology.—It is lancet-shaped, with anterior and posterior extremities, pointed body, covered with spines; 9·5 to 12·7 millimetres in length and 2·5 millimetres in breadth, with two suckers very close together, the anterior being larger than the posterior. The genital pore opens just in front of the ventral sucker. The pharynx is sphæroidal, and the intestinal cæca extend far back. The two testes are very distinct, the anterior rounded and the posterior lobate. The ovary is slightly lobate, and it and the uterus are situated medianly. The yolk glands lie laterally in the middle third, extending from behind the ventral sucker to the back of the testes. There is no cirrus pouch. The eggs are oval (0·034 by 0·021 millimetre).

Habitat.—The dog and man.

Pathogenicity.—Not known.

Clonorchis Looss, 1907.

Definition.—Opisthorchiinæ characterized by the fact that the testes are not notched or lobate, but distinctly ramified, the branches crossing the intestinal cæca on their ventral side and extending very near the body margin. The excretory vesicle is simply an unpaired tube, which becomes somewhat widened at its anterior end, assuming sometimes the shape of an irregular triangle.

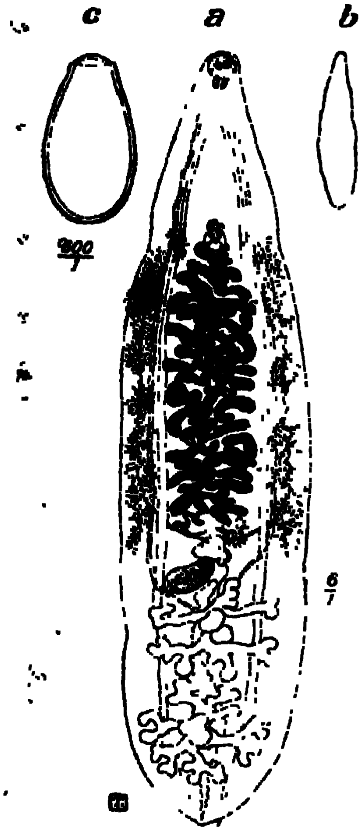

Fig. 223.—*Clonorchis sinensis.*

(After Looss, from the *Annals of Tropical Medicine and Parasitology.*)

a, Schematic; *b*, natural size; *c*, egg × 500.

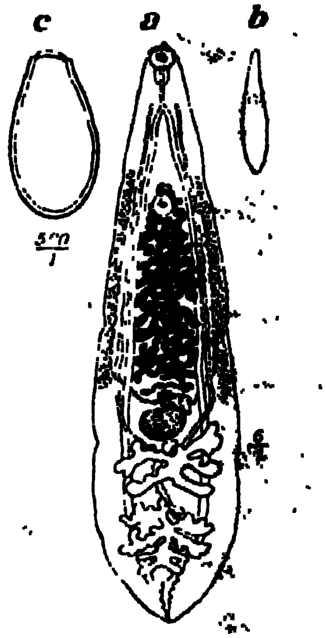

Fig. 224.—*Clonorchis endemicus.*

(After Looss, from the *Annals of Tropical Medicine and Parasitology.*)

a, Schematic; *b*, natural size; *c*, egg × 500.

Species.—*Clonorchis sinensis* Cobbold, 1875; *Clonorchis endemicus* Baelz, 1883; but the work of Kobayashi in 1917 tends to show that they are one and the same species.

Clonorchis sinensis Cobbold, 1875.

Synonyms.—*Distoma sinense* Cobbold, 1875; *D. spathulatum* Leuckart, 1876; *Distomum hepatis innocuum* Baelz, 1883.

Definition.—Clonorchis with the generic characters.

History.—*Clonorchis sinensis* was first discovered by McConnell in 1874 in the liver of a Chinaman. It was believed to be an *Opisthorchis*, but in 1907 Looss gave reasons why it should be placed in the new genus *Clonorchis*. As far as is known it occurs principally in China and Japan, and has not yet been found in animals.

Remarks.—It may be the same as *Clonorchis endemicus* Baelz, 1883; *Distoma hepatis endemicum sive perniciosum* Baelz, 1883; *Distoma japonicum* R. Blanchard, 1886. In 1883 flukes were first described in the liver of human beings in Japan by Kiyono, Nakahama, Suga, and Yamagata, and a little later in the same year Baelz reported the occurrence of two hepatic distoma in Japan.

1. *Distoma hepatis innocuum*, up to 20 millimetres in length, with a lighter-coloured uterus of larger volume, with slightly larger ova, 21 to 36 μ in length by 18 to 20 μ in breadth, and with a black granular pigment in its excretory apparatus and body parenchyma. It caused little or no symptoms in human beings, and was found accidentally in post-mortems.

2. *Distoma hepatis endemicum sive perniciosum*, which was smaller, 8 to 11 millimetres in length, and did not possess the above characters, while its eggs were only 20 to 30 μ in length by 15 to 17 μ in breadth.

Kobayashi finds that Looss's differences between *C. sinensis* and *C. endemicus* do not hold good. They were (1) size; (2) discontinuity of the vitellaria; (3) pigmentation; (4) size and shape of the egg. In the experimentally reared forms there are no such constant differences.

It is found in Japan, where it is common, and in Annam and Tonkin, in man, cats, dogs, and pigs.

Morphology.—*Clonorchis sinensis* is a white, or yellowish-red, or brownish, narrow trematode, 13 to 19 millimetres in length and 3 to 4 millimetres in breadth. The pigmentation is due to the deposit of fine yellowish or brown granules in the body parenchyma. The ramifications of the testes are long, the anterior arising from four and the posterior from five main stems, with sometimes ventral bulgings. The ovary is trilobate, but may show three to six smaller lobules. The yolk glands reach from the ventral sucker to the level of the ovary, and are peculiar in that certain groups of follicles remain undeveloped. In perfectly mature specimens the seminal vesicle extends back as far as the middle of the uterus. The eggs are generally narrowed towards the anterior end, and have a rather high lid, with a sharply projecting brim (these peculiarities may be absent.) The egg is 29 μ in length and 16 μ in breadth.

Life-History.—Kobayashi has found the cysts in the muscles of fish—*Pseudorasbora parva*, *Leucogobio güntheri*, *Leucogobio mayedæ*, and *Carassius auratus*—and was able to infect cats by feeding with the infected flesh. He also found cysts in other fish—*Acheilognathus lanceolatus*, *A. limbatus*, *A. cyanostigmus*, *Paracheilognathus rhombeus*, *Pseudoperclampus typus*, *Abbottina psegma*, *Biwia zezera*, and *Sarcocherlichthys variegatus*. These fish are the second intermediate host. The first intermediate host and the method of infection of the fish are unknown, but *Melania libertina* is suspected.

Habitat.—It is found in cats, dogs, hogs, and men.

Pathogenicity.—Enlargement of the liver, and diarrhœa.

A Possible Feline Clonorchis (or Opisthorchis).

Looss draws attention to the fact that Ijima, in 1886, describes a *Distomum* from the liver of a cat in Japan, with fine spines, and smaller than *C. endemicus*, which is to be looked upon as a normal parasite of the cat. It is only 1·5 millimetres in length by 0·9 millimetre in breadth. It may be a *Clonorchis* or an *Opisthorchis*.

Katsurada, in 1900, published a paper based upon seventy-six post mortems with an enormous number of parasites, among which he mentioned three found in a man from the province of Saga, with an average length of 5·10 millimetres and breadth of 0·96 millimetre, which Looss considers can only be explained as an infection with a feline species.

Habitat. Cats and man (?).

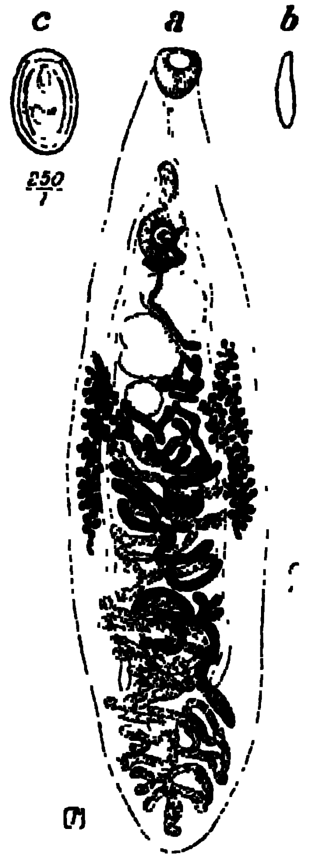

FIG. 225.—*Dicrocœlium dendriticum* Rudolphi.

(After Looss, from Mense's 'Tropenkrankheiten.')

a, Schematic × 6; *b*, natural size; *c*, eggs × 250.

FAMILY DICROCŒLIIDÆ

ODHNER, 1910.

Definition.—Fascioloidea, hermaphroditic, without spiny collar around the oral sucker, and with the ovary behind the testes.

Type Genus.—*Dicrocœlium* Dujardin, 1845.

Dicrocœlium Dujardin, 1845.

Definition. Dicrocœliidæ with lancet-shaped bodies, without spines, and with suckers placed close together. Intestine does not reach the posterior end. Genital pore close behind the pharynx, with a cirrus pouch in front of the ventral sucker, just behind which the testes lie with the ovary in the median line behind them. The uterus lies behind the ovary and testes, extending as far back as the posterior border. The yolk glands are small, and situated in the middle quarter of the lateral areas of the body. The excretory vesicle is tubular. Ova dark brown. Worms live in the liver and gall-bladder, rarely in the intestine.

Type Species. *Dicrocœlium dendriticum* Rudolphi, 1819.

Dicrocœlium dendriticum Rudolphi, 1819.

Synonyms.—*Fasciola lanceolata* Rudolphi, 1803, *nec* Schrank, 1790; *Distomum lanceolatum* Mehlis, 1825; *Dicrocœlium lanceolatum* Dujardin, 1845; *Dicrocœlium lanceatum* Stiles and Hassall, 1896.

History.—Bucholz appears to have been the first to discover these worms in the gall-bladder in Weimar, and, later, Chabert in the intestines of a girl in France, and Kirchner in Weimar. Since then they have been noted in Italy and Egypt. They are found in the bile-ducts of herbivorous and omnivorous animals in Europe, North Africa, Asia, and North and South America.

Morphology.—*Dicrocœlium dendriticum* is a small trematode, measuring 8 to 10 millimetres in length by 1·5 to 2·5 millimetres in breadth. It is pointed in front and narrow behind, so that the widest point is just behind the yolk glands. Cuticle is smooth; the oral sucker is terminal, and about the same size as the ventral (0·5 to 0·6 millimetre). The intestine bifurcates just in front of the genital pore, which is situate in the median line in front of the ventral sucker, behind which the two testes lie, from which the vasa deferentia run forwards to form a cirrus lying in a cirrus sac

The ovary lies behind the posterior testis; there is a receptaculum seminis and a Laurer's canal. The yolk glands lie in the lateral portion of the middle fifth of the body, the posterior portion of which is filled up by the large coiled uterus. The eggs are thick-shelled, and yellowish to brown in colour, with a length of 38 to 45 μ and a breadth of 22 to 30 μ

Life-History.—Not known, but suspicion rests on *Planorbis marginatus* and land-snails.

Pathogenicity.—No special symptoms.

FAMILY ECHINOSTOMIDÆ Looss, 1902.

Definition.—Fascioloidea, hermaphroditic, with a fold or collar bearing a row or rows of pointed spines on the dorsal and lateral aspects of the oral sucker. The rows of spines are continued laterally on to the ventral corners, and the number of spines is constant for each species. The corner spines are large or specialized.

Classification.—The family is divided into two subfamilies as follows:—

A. Cirrus sac does not reach beyond acetabulum. Without strong rosethorn hooks—*Echinostominæ*.

B. Cirrus sac reaches beyond acetabulum. With strong rosethorn hooks *Himasthlinæ*

SUBFAMILY ECHINOSTOMINÆ Looss, 1899.

Definition.—As above.

Type Genus.—*Echinostoma* Rudolphi, 1809.

Classification.—*E. malayanum* Leiper, 1911, has been placed by Odhner in the genus *Euparyphium* Odhner, so that it now becomes *Euparyphium malayanum*, as, according to Leiper, it is probably the same as *Artyfechinostomum sufrartyfex* Lane, 1915, which Lane found in a girl of eight years of age on the Ragnik Tea Estate in Assam. In 1916 Stephens pointed out that Lane's genus did not possess the strong rosethorn hooks of the Himasthlinæ. In 1917 Lane pointed out that as Odhner's principal character of the Echinostominæ was that the cirrus sac usually reaches to the centre of the acetabulum, but not beyond it, while that of *A. sufrartyfex* reaches 0·75 mm., therefore it is not a member of the Echinostominæ.

GENUS ECHINOSTOMA Rudolphi 1809.

Synonym.—*Fascioletta* Garrison, 1908.

Definition.—Echinostominæ, with small elongated bodies, broader anteriorly than posteriorly, with characteristic circumoral ring of spines and with other spines on the body, and with large prominent acetabulum. Œsophagus short, intestinal cæca unbranched. Excretory vesicle tubular. Genital pores anterior to the acetabulum. Testes compact, situate in the median line one behind the other. Cirrus and pouch well developed. Ovary compact; no receptaculum seminis; Laurer's canal present. Yolk glands well developed in the posterior fifth of the body; well developed shell gland and uterus, which lies between the ovary behind and the acetabulum in front. Ova large and operculated.

Remarks.—With regard to the position of *Echinostoma*, it should be observed that some authorities do not classify it under the Fasciolidæ, but in a special family Echinostomidæ which we adopt.

Type Species. The type species is *Echinostoma revolutum* (Froelich, 1802), of which the synonym is *Distoma echinatum* Zeder, 1803. Another species of importance in tropical medicine is *E. ilocanum* (Garrison, 1908).

Echinostoma ilocanum Garrison, 1908.

Synonym.—*Fascioletta ilocana* Garrison, 1908.

History.—*Echinostoma ilocana* was discovered and described by Garrison, who in 1907 noticed peculiar eggs in the fæces of Philippino prisoners in Bilibid Prison in Manila and subsequently, after treatment with male-fern, obtained a small number of trematodes. Quite recently Odhner has shown that it belongs to the genus *Echinostoma*, family Echinostomidæ.

Morphology. *Echinostoma ilocana* is a very small trematode, measuring 4 to 6 millimetres in length by 0·75 to 1·35 millimetres in breadth and 0·5 to 1 millimetre in thickness. Posteriorly it is attenuated. The acetabulum is about three times the size of the oral sucker, which is either terminal or slightly ventro-subterminal. The prepharynx is long, the pharynx globular; the œsophagus short, bifurcating just anterior to the genital pore into the intestinal cæca. The genital pores open separately a little behind the halfway point between the pharynx and the acetabulum.

The cirrus pouch is well developed, and contains posteriorly the vesicula seminalis, into which open the vasa deferentia, and which gives rise to the long coiled cirrus. Each testis shows an anterior and a posterior lobe. The ovary is globular, the yolk glands well developed, and the uterus fairly developed. Ova 88·8 to 114·7 μ long by 53·5 to 81·0 μ broad.

Life-History.—Nothing is known of the life-history beyond the fact that a miracidium hatches in about ten days after the eggs have left the host.

Habitat.—The intestine of man in Luzon, in the Philippine Islands.

Pathogenicity.—It is probable that the worm is non-pathogenic.

GENUS EUPARYPHIUM Odhner.

Euparyphium malayanum Leiper, 1911.

Synonym.—*Echinostoma malayanum* Leiper, 1911.

History.—In 1911 Leiper received two consignments of flukes from Dr. Macaulay of Singapore and from Dr. Stanton of Kuala Lumpur which had been collected from the intestine of a Tamil in the Malay States.

Morphology.—It is a thick, fleshy trematode, light brown in colour, 12 millimetres in length, 3 millimetres in breadth, and 1·3 millimetres in thickness. The oral sucker is situated on a kidney-shaped anterior portion, which is somewhat detached from the rest of the parasite by a furrow on either side. This circumoral disc is surrounded by a row of forty-two stout spines. The cuticle of the body is unevenly furnished with spines. The acetabulum is several times larger than the oral sucker. The oral sucker lies in the middle third of the circumoral disc, and leads into a spheroid muscular pharynx, and so into the œsophagus, which bifurcates immediately behind the pharynx into two branches, which are simple and end blindly at the posterior end of the body.

The deeply lobed testes lie one behind the other behind the acetabulum; there is a well-developed cirrus pouch and a long, thick cirrus The ovary is smooth, and lies immediately in front of the anterior testis and just behind the acetabulum. The yolk glands are numerous, extending from the acetabulum to the posterior end of the body. The brown eggs are few in number and large in size.

Habitat.—Leiper does not think that this worm is a normal parasite of man, and considers that domesticated animals, especially cats and dogs, should be investigated for it.

Pathogenicity.—Not stated.

SUBFAMILY HIMASTHLINÆ Odhner, 1910.

Definition.—Echinostomidæ in which the cirrus sac extends caudad to the acetabulum.

Remarks.—The only genus with which we are concerned is:—

GENUS ARTYFECHINOSTOMUM Clayton-Lane, 1915.

Definition.—Himasthlinæ without strong rosethorn hooks.

Remarks.—There has been much disput [illegible] to whether this is a good genus or not.

Type Species.—*Artyfechinostomum sufrartyfex* Clayton-Lane, 1915.

Artyfechinostomum sufrartyfex Clayton-Lane, 1915.

Nomenclature.—Leiper has pointed out that this name clashes with the recommendations of the International Rules: 'The use of proper names in the formation of compound generic names is objectionable.' However, the name cannot now be changed.

History.—The worm was found in a girl, aged eight years, on the Ragnik Tea Estate in Assam, and was thought by Leiper to be probably the same as *Euparyphium malayanum*; but in 1917 Clayton-Lane showed that the cirrus sac extended 0·75 mm. caudad to the acetabulum, a fact agreeing with the definition of the subfamily.

FAMILY SCHISTOSOMIDÆ Looss, 1899.

Definition.—Fascioloidea with separate sexes, and with genital pore posterior to the elevated acetabulum. No pharynx. Intestinal caecare unite to form a single intestine.

Type Genus.—*Schistosoma* Weinland, 1858.

Schistosoma Weinland, 1858.

Synonyms.—*Gynæcophorus* Diesing, 1858; *Bilharzia* Cobbold, 1859; *Thecosoma* Moquin-Tandon, 1860

Definition.—Schistosomidæ with long filiform *females* and shorter *males*, with body considerably widened behind the acetabulum. In this part the lateral walls can curve ventrally to form an almost closed *canalis gynæcophorus*, within which the female is enclosed. No cirrus pouch. No pharynx No Laurer's canal. Eggs with spines and no lids. Miracidia ciliated with large glandular cells discharging anteriorly beside gastric sac. Development in various snails. Cercariæ with forked tails and no eye spots. Enter vertebrate hosts through skin or mucosa, and pass into blood-vessels.

Classification.—The species known to occur in man may be recognized as follows (*S. magna* Cobbold, 1852, found in a monkey *Cercocebus fuliginosus* is represented to-day by only a piece of a male, which Leiper says cannot be recognized as belonging to a human species):—

A. Cutiele with spines:
  I. *Male*, four to five large testes; *femdle*, ovary posteriorly situate. *Eggs*, terminal spined. *Development* in subgenera and species of *Bullinus*—*Hæmatobium*.
  II. *Male*, eight small testes; *female*, ovary anteriorly situate. *Eggs*, lateral spined. *Development* in species of *Planorbis*—*Mansoni*.

B. Cuticle nearly smooth, only a few spines seen in fresh condition along margin of canal
  Male, six to eight testes, *female*, ovary almost in middle of body. *Eggs* with small lateral spines or thickenings. *Development* in species of *Blanfordia*—*Japonicum*.

Schistosoma hæmatobium Bilharz, 1852.

Synonyms.—*Distomum hæmatobium* Bilharz, 1852; *D. capense* Harley, 1864; *Bilharzia hæmatobia* Cobbold, 1859

Definition.—Schistosoma with spiny cuticle. *Males* with four to five large testes and with intestinal caeca uniting late to form a short single intestine. *Females* with ovary in the posterior half of the body. Uterus very long, with many terminal spined eggs. Vitellaria in posterior fourth of the body. Development of cercariæ in subgenera and species of *Bullinus*.

History.—*Schistosoma hæmatobium* was discovered in the portal vein of a man in 1851 by Bilharz in Cairo, and later by Harley in

1864 in a patient from the Cape of Good Hope. Since then it has been found widely distributed through Africa (Egypt, Sudan, Tunis, Algiers, West Coast, including the Gold Coast, East Coast, and South and Central Africa), which is its endemic centre, and in Asia, in Syria, Arabia, Mauritius, Persia, India. Only imported cases occur in Ceylon.

Other species are known in sheep, horses, oxen, etc.

In 1915 Leiper discovered its complete life-history in the snail and its method of entry into the vertebrate.

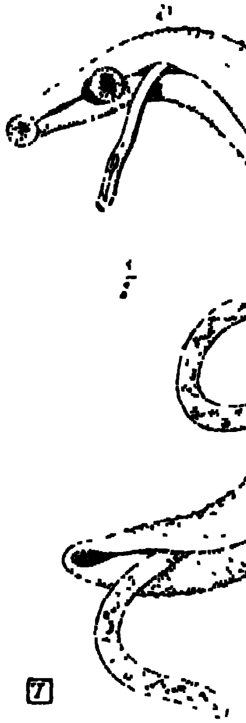

Fig. 226. *Schistosoma hæmatobium.* (After Looss, from Mense's 'Tropen krankheiten').

This drawing shows the female worm enclosed in the gynæcophoric canal of the male.

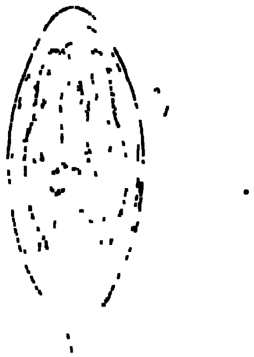

Fig. 227. Egg of *Schistosoma hæmatobium* (× 250). (After Looss, from Mense's 'Tropenkrankheiten.')

Morphology.—**Male.**—The male is whitish in colour, and from 12 to 14 millimetres in length, with a greatest width behind the ventral sucker of 1 millimetre. It is really thin and flat though it may look cylindrical, because the lateral margins are turned ventrally inwards, enclosing a canal called the 'gynæcophoric canal,' in which the female lies. The whole body is covered with projections tipped with short spines, which enable it to cling to the wall of the bloodvessel. The oral sucker looks ventrally. The ventral sucker is situate near to it. There is no pharynx, but the œsophagus is long and covered with numerous glands, and bifurcates just in front of the ventral sucker into the intestinal cæca, which unite behind the testes into a median trunk. The excretory pore is at the posterior end, situated a little dorsally. There are four to five testes, from which the vas deferens runs to a vesicula seminalis, from which an ejaculatory duct proceeds to the genital pore situated behind the ventral sucker at the beginning of the gynæcophoric canal.

Female.—The female worm is long, thin, being 20 millimetres in length (*i.e.*, longer than the male) and 0·25 millimetre in breadth (much thinner than the male). Posteriorly it is coloured dark brown, because of the colour of the contents of the intestine. The cuticle is smooth, except in the sucker and at the tail end, where there are large spines. The alimentary canal is much the same as in the male. The ovary is median, and the ovarian duct,

taking origin at the posterior end, runs forward to join with the vitellarian duct from the single yolk gland, which lies about the middle of the body. The junction of the two ducts is at first narrow and surrounded by the shell gland, but it soon dilates into the uterus, which runs forwards to end in the genital pore, just behind the ventral sucker. The eggs are bluntly spindle-shaped, yellowish in colour, slightly transparent, and provided with a thin shell, without a lid, but possessing a terminal spine, which may be absent at the posterior end. They measure from 0·12 to 0·19 millimetre in length [illegible] millimetre in breadth, but vary considerably.

Life-History.—The young immature and mature males and females are found in the portal system.

Looss notes that it is not uncommon to find males alone in the portal vein, and, further that they are all of the same age. Eventually they pair, and now the male carries the female along that vein down the inferior mesenteric vein to the bladder, which is a fairly direct route, but Looss considers that they may be chemically attracted to the bladder, for their journey is against the blood stream, and they are enabled to perform it by means of the bristles on the male cuticle.

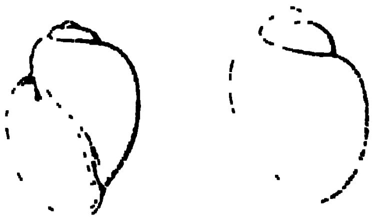

FIG. 228.—*Bullinus contortus* MICHAUD, 1829.

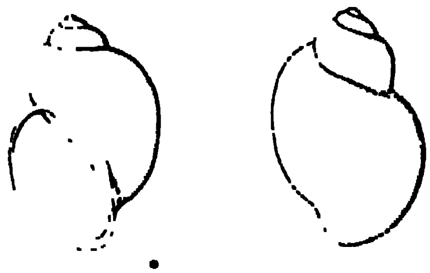

FIG. 229. *Bullinus dybowskii* FISCHER, 1891.

The length of time occupied by the journey is not known, and probably varies considerably. Arrived in the veins of the bladder, the real oviposition begins, and Looss is inclined to think that the female can push the head (close to which is the genital opening) into the capillaries, and thus lay the eggs directly into these channels, where they are held in position by contraction of the capillary upon them. Looss thinks that it is probable that the worms may live three years in these vessels, producing during that period large numbers of eggs, which work their way like any other foreign body into the lumen of the bladder, probably by means of the contractions of that organ.

Leiper finds that in experimentally infected monkeys eggs begin to appear about ten weeks after infection.

Egg.—During their journey through the tissues the eggs increase in size from 0·08 to 0·09 μ in length and 0·03 to 0·04 μ in breadth in the oötype to 0·13 to 0·15 μ in length and 0·04 to 0·06 μ in breadth in the urine, while the embryo develops, so that when they are voided in the urine they contain a well-developed miracidium; but during this journey many die and become calcified. It is not known how long an egg must take before it escapes in the urine, but Looss points out that even the presence of an egg with a true miracidium is no evidence that the parent worms are alive.

Miracidium.—These eggs will simply die, unless they gain access to water, in which they hatch, and the ciliated miracidium escapes and swims about. In the so-called body cavity of this miracidium there are germinal cells.

Intermediate Hosts.—When miracidia are allowed to hatch out in water containing suitable and unsuitable snails, they crowd round and enter the former, while they neglect the others. In a short time all the miracidia have disappeared from the water containing suitable snails.

The snails which are suitable are those in which Leiper found the development to proceed viz., *Bullinus contortus* Michaud, 1829; *B. dybowskii* Fischer, 1891, and *B. innesi* Bourguignat. In South Africa Becker has experimentally implicated *Bullinus* (*Physopsis*) *africanus* as an intermediary.

Within these molluscs the miracidium makes its way into the liver and becomes changed into a smooth-walled sac the sporocyst —from which are formed daughter sporocysts, and from these cercariæ. In any case the cercaria is the end of this stage, and is alone the infective organism.

In some of our experiments we so heavily infected our snails that they died, but in nature this does not take place.

Cercariæ.—If an infected snail is allowed to remain in clear water it is amazing the quantities of cercariæ which may escape therefrom into the water and swim about.

Infection.—Leiper has shown that these cercariæ may penetrate the skin and infect animals. They may also penetrate the mucosa of the mouth and throat, and then by gradual growth and differentiation of the organs become male or female adult worms.

Pathogenicity.—It is usually the cause of urinary schistosomiasis, or, as it is better known, vesical Bilharziosis, but occasionally it may give rise to Bilharzial Dysentery.

Schistosoma mansoni Sambon, 1907.

Definition.—Schistosomum with spiny cuticle. *Male* with eight small testes. The gut forks unite early, and hence the straight intestine is long. *Female* with ovary in the anterior half of the body. Uterus very short, with only one lateral spined egg present at a time. Vitellaria in posterior two-thirds of body. *Development of cercaria* in *Planorbis boissyi* in Egypt and the Sudan, and *P olivaceus* Spix in Brazil, and *P. guadelupensis* in Venezuela.

Historical.—In 1851 Bilharz in Egypt noted that certain female worms possessed uteri containing lateral-spined eggs, and later Sonsino considered that these worms should be made into a species separate from those with terminal-spined eggs, but nothing came of it. In 1902 Castellani in Uganda noted that some patients had only lateral-spined eggs in the fæces and no ova in the urine. In

1903 Manson observed the same fact in a patient from the West Indies. In 1907 Sambon created a new species, *Schistosoma mansoni*, for the following reasons:—

1. Lateral-spined eggs are never found in the urine, but only in the fæces, and never occur in the bladder, only in the rectum and liver.
2. The egg is oval in shape, with a lateral spine, while that of *S. hæmatobium* is oblong and lanceolar in shape, with a terminal spine, and that of *S. japonicum* oval or roundish, with a lateral very small spine in about 75 per cent. of those examined by Looss.

The lengths and breadths are different. *S. mansoni*, 112 to 162 μ by 60 to 70 μ, *S. hæmatobium*, 110 to 120 μ by 46 to 50 μ; *S. japonicum*, 75 to 90 μ by 53 to 75 μ.

3. The males are apparently similar, but the females have a difference in the genital tract, which has been described by Fritsch and when mature contain lateral-spined ova in the uterus.
4. The geographical distribution of *S. mansoni* and *S hæmatobium* is different. *S. hæmatobium* is alone found in the Cape; *S. mansoni* is the only species in the West Indies and in South America.

Looss in Egypt immediately challenged Sambon's statements, but the history of this polemic will be found in the earlier editions of this book. We have all through felt that Bilharz, Sonsino, Manson, and Sambon, were right, and Ward always supported Sambon, and now this has been proved experimentally by Leiper to be correct.

In 1909 Da Silva described the adult worms as follows:—

Males The male measures 12 millimetres in length by 0·448 millimetre in breadth in the middle The ventral sucker is 0·540 millimetre behind he oral sucker.

The anterior end shows six sexual masses composed of testes and seminal vesicles The posterior end is tapering The spinous papillæ are not so marked as in *S hæmatobium*

Females The female worms measure 11·5 to 15 millimetres in length by 0·168 millimetre in breadth in the middle The distance between the two suckers is 0·224 to 0·252 millimetre. It is thickest in the middle, and tapers to each extremity. The anus opens 0·336 millimetre in front of the tip of the tail The oviduct is much shorter than in *S hæmatobium*, and enters the vitelline ducts after only a short turn. The uterus contains laterally spined eggs The eggs measure 140 μ by 62 μ, with 18 μ as the length of the spiculum The miracidium escapes by a transverse rupture of the shell, and measures 153 μ by 72 μ.

In 1911 Flu, in studying the Bilharziosis in Surinam, concluded that *S. mansoni* is distinct from *S. hæmatobium* because (1) *S hæmatobium* has eggs differently shaped from those of *S mansoni* ; (2) the anterior border of the lateral folds in the male *S hæmatobium* forms almost a right angle with the anterior portion of the body, while in *S mansoni* the transition is more gradual; (3) the ovaries of *S mansoni* have always a more or less winding course, a character not described for any other species of *Schistosoma* ; (4) the oötype is asymmetrical in relation to the long axis of the worm; the oviduct opens laterally on the ventral side where the shell gland is situate; (5) *S. mansoni* lives in the region of the mesenteric veins, and *S. hæmatobium* predominates in the pelvic veins; (6) *S. mansoni* gives rise to an illness like katayama disease, and never to the bladder symptoms produced by *S. hæmatobium*: (7) the morbid anatomy of cases invaded by *S. mansoni* agrees with those invaded by *S. japonicum*, and differs considerably from those caused by *S. hæmatobium*; (8) the geographical distribution is in opposition to Looss's view that the lateral-spined eggs are unfertilized because they are the only eggs found in Brazil, the Antilles, and Surinam.

He also found a single type of egg with lateral spine in the uterus and oötype of sixty females.

In 1915 Leiper's work in Egypt proved that the miracidium developed in a special snail, *Planorbis boissyi*, and that the vertebrate could be infected by the skin or oral mucosa.

In 1917 Chalmers and Pekkola in the Anglo-Egyptian Sudan have experimentally infected the same snail with the miracidia, and obtained cercariæ, and in the same year Lutz carried out similar experiments in Brazil with *P. olivaceus*.

In 1917 Iturbe, working in Caracas, Venezuela, found that the miracidia could infect *Planorbis cultratus* and *P. guadelupensis*, but the latter was more easily infected, and showed typical cercariæ by the end of the sixth week. He considers it to be the true carrier of the infection there. He noted that it was easier to infect animals *per os* than by the skin. He found no less than 120 out of 400 specimens of *P. guadelupensis* to be naturally infected around Caracas. The 'rediae' described by him have since been recognized as immature stages of a new species of Tetracotyle.

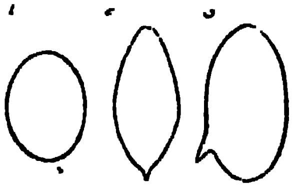

FIG. 230.—OUTLINES OF TH OF (1) *S. japonicum* (WITHOUT SPINE); (2) *S. hæmatobium*, (3) *S. mansoni*. (After Sambon)

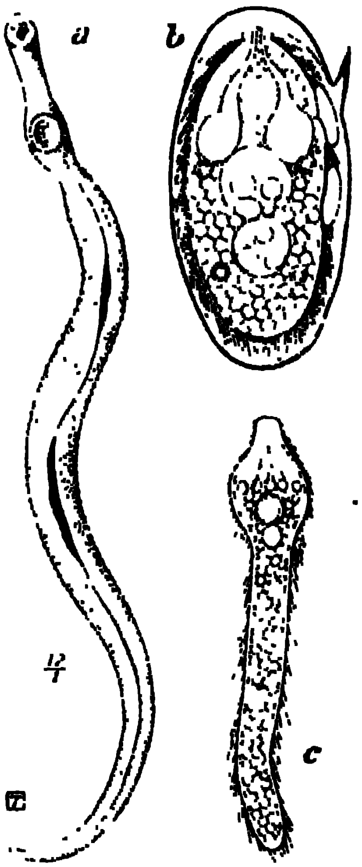

FIG. 231.—*Schistosoma mansoni* (After Holcomb) *a*, Male; *b*, egg; *c*, larva.

Morphology.—Sufficiently described above.

Life-History.—The adults live chiefly in the mesenteric veins, and the ova pass into the submucosa of the large bowel and through this into the fæces, and so escape from the body. The egg is oval, 112-162 × 60-70 microns, and possesses a well defined lateral spine.

The miracidia quickly hatch when placed in water in the tropics, and swarm around *Planorbis boissyi*, into which they disappear so rapidly that in twenty minutes none will be visible in the water.

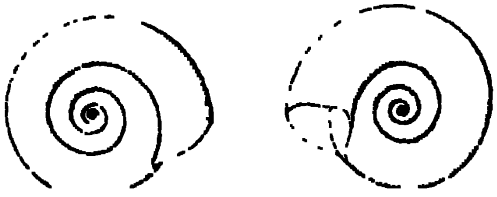

FIG. 232. *Planorbis boissyi* POTIEZ AND MICHAUD, 1838.

They pass to the liver of the mollusc and form sporocysts, rediæ, and cercariæ and finally end in cercariæ, which, leaving the snail and swimming about the water, enter the skin or mucosa of the mouth or throat and so infect man.

Pathogenicity. -*S. mansoni* is the cause of intestinal schistosomiasis (Chapter LXXIX.)

FIG. 233. SPOROCYSTS OF *Schistosoma mansoni* SAMBON, 1907, STILL PARTIALLY EMBEDDED IN TISSUE FROM THE LIVER OF THE PLANORBIS.

(After Leiper, from 'Researches on Egyptian Bilharziosis.')

FIG. 234. CERCARIA OF *Schistosoma mansoni* SAMBON, 1907.

(After Leiper.)

Schistosoma japonicum Katsurada, 1904.

Synonym. *Schistosomum cattoi* Blanchard, 1905.

Definition. -Schistosoma with a nearly smooth cuticle. *Male* with a few spines or protuberances along the margins of the gynæcophoric canal in the fresh condition. Testes six to eight, irregularly elliptical. Intestinal cæca unite very late and form a very short intestine. *Female* with ovary almost in the middle of the body. Vitellaria do not reach the posterior extremity. Uterus long, with many eggs, showing small lateral spines or thickenings. *Development of cercariæ* in species of *Blanfordia*.

History.- -For several years an endemic disease, characterized by enlargement of the liver and spleen, fever, diarrhœa with mucus and blood in the motions, associated with ascites and cachexia and extreme weakness, had been observed in the provinces of Yamanashi and Hiroshima of Central Japan and Saga of Kiushu. Eggs containing a miracidium were to be found in the liver and other organs.

Katsurada then examined cats in the neighbourhood, and found numerous *Schistosoma* in the portal veins of two cats in the province of Yamanashi, in which there were eggs exactly similar to those found in the above-mentioned disease. Catto a little later found the same parasite in a Chinaman from the province of Fukien. Logan and others have found it in Chinamen in the province of Hunan, Nicols in a case from the Philippines, and Manson and Sambon in cases from China.

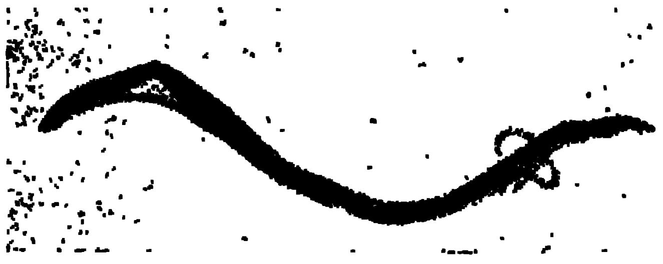

FIG. 235.—*Schistosoma japonicum* KATSURADA, 1904. MALE AND FEMALE. (From a photograph by J. J. Bell.)

With regard to the life-history, in 1908 Fujinami and Nakamura immersed cattle, cats, and dogs in water containing many miracidia from *S. japonicum*, but no infections followed. They then immersed a second series in rice-fields, ditches, and streams, reputed to be sources of infection, and heavy infections with *S. japonicum* resulted, the young parasites, 0·15 mm. in length, being found in the portal system on the third day after immersion.

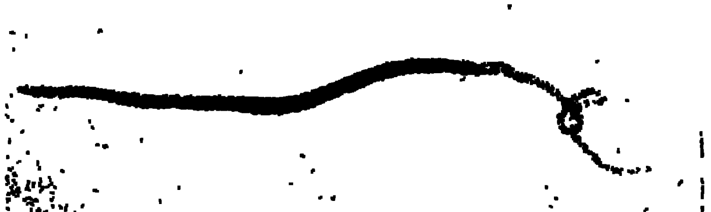

FIG. 236.—*Schistosoma japonicum* KATSURADA, 1904. FEMALE. (From a photograph by J. J. Bell.)

In 1911 Miyagawa described smaller forms as seen in the cutaneous tissues and peripheral vessels in two to twenty-four hours after immersion.

In 1913 Miyairi, experimenting with local snails, found a sporocyst in an unidentified snail.

In 1914 Miyairi and Sudzuki found a snail with a dark shell with seven spirals to be heavily and naturally infected with cercariæ, and, taking non-infected young samples, were able to find that the miracidia penetrated the cuticle of the snail, and found their way to the gills and the wall of the alimentary canal, where in twelve days the first rediæ appeared and gradually concentrated in the bile-ducts, where they grew and formed second rediæ. Mice were immersed in the water in which the full-grown snails were kept, and after three weeks many *S. japonicum* specimens were found in their livers.

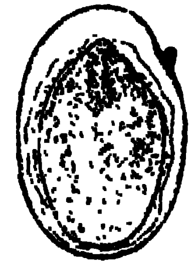

FIG. 237.—Egg of *Schistosoma japonicum*. (After Leiper.)

In 1914 Leiper confirmed this work in Japan, having recognized morphologically the cercariæ originating in sporocysts, mistermed rediæ by the Japanese authorities. The mollusc in question was named *Katayama nosophora*. *Katayama* is a synonym of *Blanfordia*.

In 1916 Narabayashi showed that man, cattle, horses, goats, pigs, cats, and dogs, are naturally infected by *S. japonicum*, which contains ferments which can digest albumen in an alkaline medium. He also found that in dogs and guinea pigs, after penetrating the skin, most of the parasites enter the venous blood stream, though some few enter arteries or lymphatics. Eventually they all enter the right side of the heart and are scattered all over the lungs, at the bases of which they collect and then migrate through the mediastinum, diaphragm, and liver into the portal system, while a few re-enter the circulation and reach the rectum.

Morphology. In general it resembles *S. hæmatobium*, but the cuticle of the female is smooth and that of the male has only the few spines mentioned above. There are no 'bosses.'

Male.—8-10 millimetres in length, 0·53 millimetre in breadth, with acetabulum larger than oral sucker. Œsophagus with two bulbs. Junction of intestinal cæca far back, and united intestine only one-fifth to one sixth of body length. The lateral excretory canals open into a dorsal pore. Testes six to eight in anterior part of hind body, from which the vasa efferentia unite into a common vas deferens, which opens just behind the acetabulum. Seminal vessels present.

Female.—8-26 millimetres in length and about 0·4 millimetre in breadth. Suckers armed with fine spines. Body thicker behind ovary, behind which gut forks unite. Ovary elliptical, dilated behind where the oviduct arises, and running forwards joins the vitellarian duct. Vitellaria well developed, lying behind the ovary, but not quite reaching the posterior end of the body. Shell gland at the junction of the oviduct with the vitellarian duct. Canal forms an oötype, and then becomes the uterus, which opens just behind the acetabulum.

Life-History.—The eggs vary from 50 to 300, and *in utero* are soft, and so can form various shapes. *Ex utero* they are oval, faintly yellow, and double contoured, 83·5 × 62·5 microns, and have small lateral spines or thickenings, and at the opposite side cap-like thickenings.

The miracidia hatch out quickly and develop into cercariæ in

Blanfordia nosophora. The cercaria is barrel-shaped, tapering towards the anterior end, mouth with two short lancet-shaped bristles. Small ventral sucker at posterior one-sixth of body. Hinder end with three pairs of poison glands, from each of which a duct runs forwards to open into the mouth. Two pairs of laterally placed flame cells with vessels. In the middle of this body there is an oval light brown body with a small anterior canal. The cercariæ penetrate the skin, pass via the veins to the heart, and so to the lungs, from the bases of which they penetrate the mediastinum, diaphragm, liver, and so enter the portal vein, from which the eggs pass to the submucosa and mucosa of the colon and cause growths. The adult worms can live at least two years in the vertebrate.

Pathogenicity.—The cercariæ, while entering the skin, cause the disease *kabure*, and in the body *katayama disease*.

Christophers and Stephens' Schistosoma.

Christophers and Stephens in 1903 described a *Schistosoma* egg which differs from the usual descriptions, and may belong to a new and as yet unknown species or genus, but it was found with ordinary *S. hæmatobium* eggs, and may therefore be an abnormality. The egg was found in Madras; it was of an elongated, spindle shape, with a long snout-like process extending from the broader end (205·2 μ by 53·2 μ).

New Schistosoma.

In 1904 Salomone and Bello found portions of a worm which they think may be a new *Schistosoma* in a patient suffering from hæmaturia contracted in Brazil. It may, however, have been a *S. mansoni* which very occasionally occurs in the bladder wall and is a common infection in Brazil.

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CHAPTER XXV

CESTOIDEA

Cestoidea—History—Morphology—Life History—Habitat—Classification—Cestodes in man—References.

CESTOIDEA Rudolphi, 1808

Definition. Platyhelmia without alimentary canal in any stage of the life cycle, with segmented body, in which the epidermis, which has sunk into the parenchyma, secretes a thick cuticle. Lime-secreting cells are developed in greater or less number, and form calcareous concretions. Organs of fixation of a variable character are developed. The habitat of the adult worm is typically the intestine, and that of the larval form some other part of the body, normally that of another host.

History. It is believed that cestodes were known to the ancients, and that the reason why Moses, who figures largely in the history of Tropical Medicine, forbade the Israelites to eat pigs and such animals, was because of the parasites known to exist in their flesh.

Aristotle knew the proglottides of tapeworms, and as early as 1502 *Taenia* was distinguished from *Bothriocephalus*. Tyson (1683) discovered the head of the tapeworm of a dog. Redi (1687-1705) came to the conclusion that *Cysticerci* were animals, and Zeder (1800) formed them into a separate group, *Cystici*; but Kuchenmeister in 1851 proved by feeding experiments that these were only the larvæ of tapeworms, and that, as a rule, two different kinds of animals were required as hosts in order that the life-cycle might take place.

Leuckart, Braun, Fuhrmann, Looss, Sonsino, Grassi, Blanchard, von Linstow, Luhe, Stiles, Leiper, and Sambon may be mentioned as investigators who have greatly improved our knowledge of these parasites.

Morphology. There are two groups of cestodes, one called the Cestodaria containing genera with only a single segment, and another Cestoda, in the restricted sense of the word, which includes all forms possessing a scolex and segments. It is with this latter group that we are now concerned.

The true cestodes are easily recognized by their band-like segmented body, which is usually of a white colour. They are broad and large posteriorly, becoming narrower and narrower till the place is reached where they are attached to the intestinal wall. This anterior end is called the 'scolex,' while the segments are called 'proglottides.' The scolex is divisible into a broader anterior portion called the head, and a narrower posterior portion, the neck.

The head is provided with muscular suckers, which keep it attached to the mucous membrane of the bowel. Often there are also hooks present on some part of the head, not infrequently on an anterior projection called the rostrum. The neck is constricted, and shows posteriorly faint rings indicating the commencement of new segments, which are always formed from the neck.

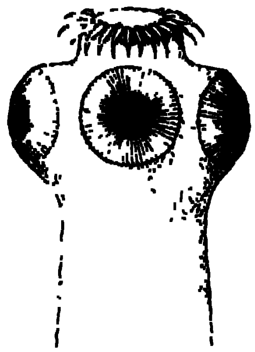

FIG. 238.—HEAD OF *Taenia solium*. (After Leuckart.)

Behind the head come the proglottides, the youngest being those situated anteriorly, and the most fully developed posteriorly. Their number is very variable, and their size increases from before backwards. They contain the male and female sexual organs.

The whole surface of the worm is covered by a thick, non-chitinous cuticle, said to contain a quantity of lime salts, under which lies a basal membrane; beneath this come the cuticular muscles, and then the cortical parenchyma, in which lie the sunken epithelial cells, nerve cells, sense organs, excretory cells, etc. Among these cells are peculiar calcareous corpuscles, varying from 3 to 30 μ in diameter, and having essentially the structure of a fat cell, that is to say they are composed of concentrically deposited calcareous material enclosed in a cell with a nucleus at one side. These corpuscles are highly characteristic of a Cestode. The calcareous matter is composed of 79 per cent. organic matter and 21 per cent. of lime salts in the form principally of the carbonate, but also of an albuminate and a urate. Their function is not understood; perhaps it is skeletal, perhaps protective.

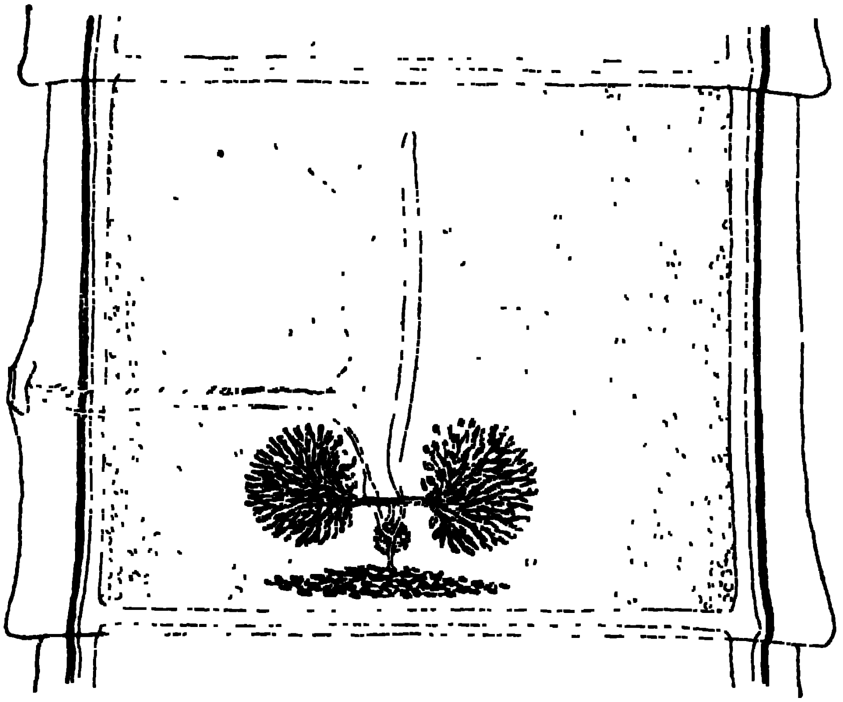

FIG. 239.—MATURE SEGMENT OF *Taenia saginata* GOEZE, 1782. (After Leuckart.)

In the cortex come the longitudinal muscles, beneath which are the transverse muscles, which enclose a central area of the parenchyma called the medullary layer, and therefore separate cortical from medullary layers.

There is no alimentary canal, and the excretory system with its flame cell terminations consists of anastomosing capillaries emptying into a dorsal and ventral collecting tube on each side of the body, which run from the scolex to the last proglottis, where they open to the exterior. In the originally posterior proglottis there is a pear-shaped excretory vesicle in the middle of the posterior edge, but this arrangement is lost when this proglottis drops off, and then the tubes open as a rule separately on the last proglottis. The nervous system consists of one ganglion in the scolex and two nerve cords. The generative organs gradually develop in the proglottides as they grow older, the youngest having no trace of them. With the exception of the end portions, these organs lie in the medullary layer of the body.

The male organs, which are the first to reach maturity, usually consist of numerous follicular testes scattered over the dorsal portion of the medullary layer, but may be consolidated into one to three glands. The efferent ducts from these unite about the middle of the proglottis into a vas deferens, which, after a wavy convoluted course, enters a cirrus pouch and terminates in the genital atrium near the vaginal orifice.

The female reproductive organs consist usually of two ovaries, which lie near the ventral surface of the medullary layer, from which a common oviduct runs to join with the spermatic duct, which, after travelling a certain distance, is dilated to form a receptaculum seminis, and continued as the vagina to the female opening in the genital atrium. After the junction with the spermatic duct, the oviduct is joined by the common duct of the yolk or vitellogene gland or glands, and then, forming the ootype, receives the ducts of the shell gland, and passes on to enter the uterus. This is usually a blind tube, but may open by a special aperture on the same or the opposite surface to that on which the genital atrium is found.

When the uterus becomes laden with eggs, it is apt to alter its appearance and become branched, and grows, filling up the proglottis, while the male generative organs atrophy and disappear (*vide* Fig. 253, p. 614).

Life-History.—The proglottis can fertilize itself with or without the use of the cirrus, or different proglottides may fertilize one another. In any case, the receptaculum seminis receives the spermatozoa, which travel down the spermatic duct, and, meeting the ovum, fertilize it. The fertilized ovum now obtains its yolk (vitellus) and its shell, and then passes into the uterus, from which it may escape by the uterine orifice when there is one, or not until the proglottis is destroyed.

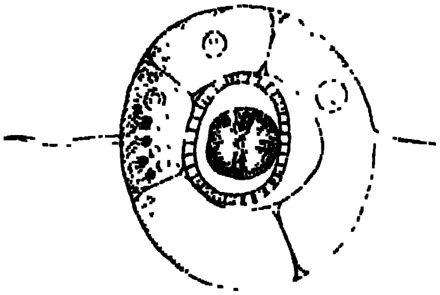

FIG. 240.—UTERINE EGG OF *Tænia saginata*. (× 375.) (After Leuckart.)

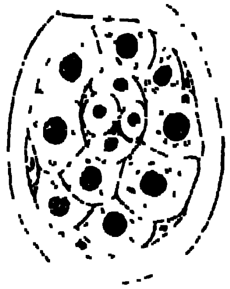

FIG. 241.—OVUM OF *Dibothriocephalus latus*. (After Leuckart.)

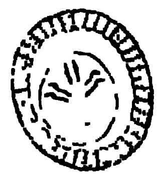

FIG. 242.—FÆCAL EGG OF *Tænia solium*. (× 300). (After Leuckart.)

Development usually begins in the uterus. An egg is as a rule oval in form, enclosed in a brown or yellow shell with or without an operculum. This shell contains food yolk and the developing embryo, whose cells form two membranes—an outer in contact with the shell, and an inner in contact with the embryo.

The outer envelope and the shell are soon lost, and when the embryo appears in the fæces it is surrounded by its inner envelope, the embryophore, and has developed six hooks. In this stage of development it is called an onchosphere.

It will therefore be evident that the so-called egg as seen in the fæces is not an egg at all, but the onchosphere with its embryonic envelope, which in certain species may be ciliated.

When the onchosphere enters the alimentary canal of a new host, generally of a different class from the original host it throws off its envelope, and works its way into the tissues by its hooks until it arrives in some suitable organ, when it throws off its hooks, encysts, and forms either a little bladder-like cyst, from the wall of which the scolex develops (the whole being called a '*Cysticercus*'; if the cyst is small, it is called a 'cysticercoid'; and if in addition it has a caudal appendix, a 'cercocystis'), or it develops directly into the scolex without the intervention of a cyst, forming a plerocercoid (πλήρης, full; κέρκος, a tail). These wanderings of the onchosphere in search of a suitable resting-place may produce unpleasant symptoms if there are a number of parasites. The time occupied in the transformation of an onchosphere into a *Cysticercus* varies, being from two to six months, or longer.

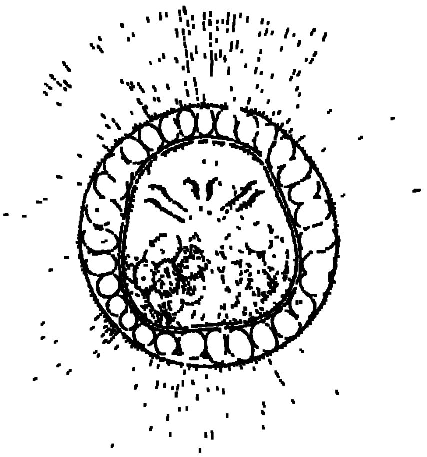

FIG. 243.—FREE CILIATED EMBRYO OF *Dibothriocephalus latus*.
(After Leuckart.)

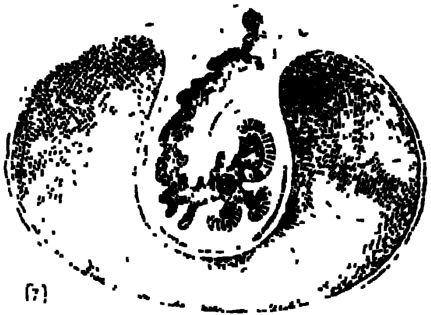

FIG. 244. CYSTICERCUS OF *Tænia saginata* GOEZE, 1782.
(After Leuckart.)

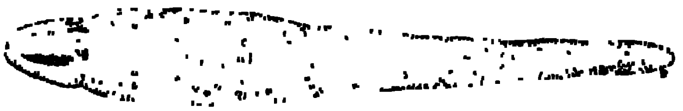

FIG. 245. PLEROCERCOID OF *Dibothriocephalus latus*.
(After Leuckart.)

With but rare exceptions the *Cysticercus* does not develop further until it enters another and different host, though some, like *Hymenolepis murina*, which is said to have its larvæ in the villi and its adults in the intestine of the rat, infest only one host.

Often the *Cysticercus* is found in a herbivorous animal, while the tapeworm occurs in a carnivorous or omnivorous animal. Infection is direct by feeding, for in the alimentary canal the cyst dies off, and leaves the scolex, which develops in the course of a few weeks into an adult tapeworm, whose span of life appears to be about a year, but may be much more or much less. An example is *Cysticercus fasciolaris* of the mouse, which becomes *Tænia crassicollis* in the cat. Abnormalities are often met with in the segments.

Habitat. As a rule the adult lives in the alimentary canal usually of a vertebrate, but they may be found in the liver and pancreas. They are capable of active movements during life. Food is obtained by osmosis from the contents of the alimentary canal.

Classification.—The classification followed is that of Monticelli, given by Braun in Bronn's 'Klassen und Ordnung des Thierreichs.'

The *Cestoidea* Rudolphi, 1808, are divided into *Cestoidaria* Monticelli, 1892, which are Cestodes consisting of a single segment containing a single set of reproductive organs, and *Cestoda sensu stricto* Monticelli, 1892, which are the typical cestodes with a scolex and segments. The subclass Cestoda are divided into orders as follows:—

Cestoda Sensû Stricto Monticelli, 1892.

Synonyms.—*Pollaplasiogonei* E. Blanchard, *Cestodes digeneses* van Beneden, *C. polyzoa* Lang.

Definition.—Cestodes in which the adult worm consists of a scolex and proglottides.

ORDER I. PSEUDOPHYLLIDEA *Carus*, 1863.—**Synonyms.**—*Bothriocephaloidea*. Scolex armed or unarmed, with two usually slightly developed, groove-like suckers, with three genital orifices. Vitellaria situated laterally. Eggs with or without a lid.

ORDER II. TETRAPHYLLIDEA *Carus*.—Scolex armed or unarmed, with four very motile pedunculated or sessile bothridia, or with four round suckers, no uterine orifice; cirrus and vagina open at the sides. Vitellaria situated laterally.

ORDER III. CYCLOPHYLLIDEA *van Beneden*.—Scolex with four suckers, between which there is an apical rostellum with or without hooks; segmentation distinct; no uterine orifice; vitellogene gland single, placed behind the ovary. Eggs without lids.

ORDER IV. DIPHYLLIDEA *Carus*.—Head stalk armed with hooklets, with solex, rostellum, and two bothridia.

ORDER V. TRYPANORHYNCHA *Diesing*.—Scolex with two or four bothridia, and four retractile armed rostella.

The only orders which contain parasites found in man are I. and III.

CESTODES IN MAN.

The cestodes which are found in man may be classified as follows:—

Order	Family	Subfamily.	Genus	Subgenus.	Species.
Pseudophyllidea	Dibothriocephalidæ	Dibothriocephalinæ	Dibothriocephalus		1. D. latus.
					2. D. cordatus.
					3. D. parvus.
					4. D. grandis.
					5. D. braunii.
			Diplogonoporus		
			Sparganum		6. S. mansoni.
					7. S. prolifer.
					8. S. baxteri.
		Ligulinæ	Braunia		9. B. jassyensis.
Cyclophyllidea	Tæniidæ	Dipylidiinæ	Dipylidium		10. D. caninum.
			Hymenolepis	Hymenolepis	11. H. nana.
					12. H. diminuta.
				Drepanidotænia (?)	13. H. lanceolata (?).
		Davaineinæ	Davainea		14. D. madagascariensis.
					15. D. asiatica.
		Tæniinæ	Tænia	Tænia	16. T. solium.
				Tæniarhynchus	17. T. saginata.
					18. T. africana.
					19. T. hominis.
					20. T. philippina.
					21. T. confusa.
					22. T. bremneri.
			Echinococcus		23. E. granulosus.
					24. E. multilocularis.

Two tapeworms are not included in this list: *Tænia (Tænia) tæniæformis* Bloch, 1750, a tapeworm found in cats, and *T. (Tænia) pisiformis* Bloch, 1780, a tapeworm found in rabbits, because no definite evidence exists that man has ever been infected by them.

At the time of writing, man alone is known to be the host of the adults of the following worms: *Tænia solium*, *T. saginata* (there is probably no doubt about this), *T. africana*, *T. hominis*, *T. philippina*, *T. confusa*, *T. bremneri*, *Dibothriocephalus parvus*, *Hymenolepis nana* (?), *Davainea madagascariensis*, *D. asiatica*. Other hosts may yet be found.

The following are only occasional parasites in man: *Dibothriocephalus latus* (true host may perhaps be the dog?), *D. cordatus* (true host, the seal and walrus), *Hymenolepis diminuta* (true host, the rat and mouse), *Drepanidotænia lanceolata* (true host, ducks and geese).

Therefore in man there is the question of intestinal tæniases to be considered. But cysts may also develop in man from *T. solium* and *Echinococcus granulosus* and *multilocularis*. From the species of *Sparganum* larval forms give rise to somatic tæniiases. These affections, with their treatment, will be considered later, as will the treatment.

It must be noted that the cysticercus of *T. saginata* is not included, as it is very doubtful whether it has ever been found in man.

Cysticercus acanthotrias Weinland, 1858, is the same as *C. cellulosæ* —*i.e.*, the larva of *T. solium*.

The following tables, modified from Stiles, may be of help, as they give the names of recognition of the genera, and the species of *Tænia*, as determined by the head or the segment, and also a scheme for recognizing the eggs.

Table of Genera.

A. Head with two elongated or slit-like suckers; uterus forms a rosette; genital pores ventral—*Dibothriocephalidæ*.

I. *Tapeworms*.—Single set of genital and uterine pores present in medium ventral line—*Dibothriocephalus*.

Double set of uterine and genital pores present in ventro submedium line—*Diplogonoporus*.

II. *Plerocercoids* (*Sparganum*). Probably larval forms of this group.

B. Head with four cup-shaped suckers, uterus does not form a rosette, genital pores lateral—*Tæniidæ*.

I. Large forms, ripe segments 9 to 35 millimetres long. Uterus median, with lateral branches—*Tænia*.

II. Smaller forms, ripe segments up to 7 millimetres long.
 (a) Genital pores single, rostellum with no more than two hooks.
  (1) Suckers not armed. Three testes in each segment—*Hymenolepis*.
  (2) Suckers armed with hooks. 15 to 50 testes in each segment—*Davainea*.
 (b) Genital pores double, rostellum with several rows of hooks—*Dipylidium*.

Table of the Species of Tænia found in Man.

A. SPECIMEN IS A TAPEWORM.

Head Characters.

I. Head armed with hooks. Subgenus: *Tænia*. Species: *T. solium*.

II. Head unarmed. Subgenus: *Tæniarhynchus*.
 (1) Circular ring around head behind the suckers, which are directed postero-anteriorly—*T. hominis*.
 (2) Without circular ring.
  (a) Head cuboid, 1·5 to 2 millimetres in diameter; suckers 0·7 to 0·8 millimetre in transverse diameter—*T. saginata*.
  (b) Head small, 1·38 millimetres broad, 1·03 millimetres thick, 0·17 millimetre long; suckers 0·63 millimetre in transverse diameter—*T. africana*.
  (c) Head small cuboid, 1 to 1·5 millimetres in diameter, 0·75 millimetre thick, and 1 millimetre long; suckers 0·34 to 0·37 millimetre in transverse diameter—*T. philippina*.

III. Head not known—*T. confusa*, *T. bremneri*.

Segment Characters.

I. *Segment Longer than Broad.*

(a) Only in the last 100 segments—*T. saginata*.
(b) In the last half of the worm—*T. solium*.
(c) In nearly the entire worm—*T. confusa*.
(d) In the entire worm—*T. africana*.
(e) Known segments very large, 28·6 by 8·5 millimetres on an average—*T. bremneri*.
(f) Unknown.—*T. hominis*.

II. *Segment Broader than Long.*

Except in the terminal segments, which are equilateral or slightly longer than broad --*T. philippina.*

B. Specimen is a Cysticercus.

I Small bladder-worm with one scolex - *Tænia.*
  (*a*) Head armed—*T. solium*
  (*b*) Head unarmed (very rare, if ever present)- -*T. saginata.*
II. Large bladder-worm with brood capsules, inside which are the scolices - *Echinococcus.*

C. Specimen is an Egg

I With an operculum - -*Dibothriocephalidæ.*
68 to 71 μ × 45 to 50 μ *D. latus.*
75 to 80 μ × 50 μ *D. cordatus*
63 48 μ to 50 μ brownish *D. grandis.*

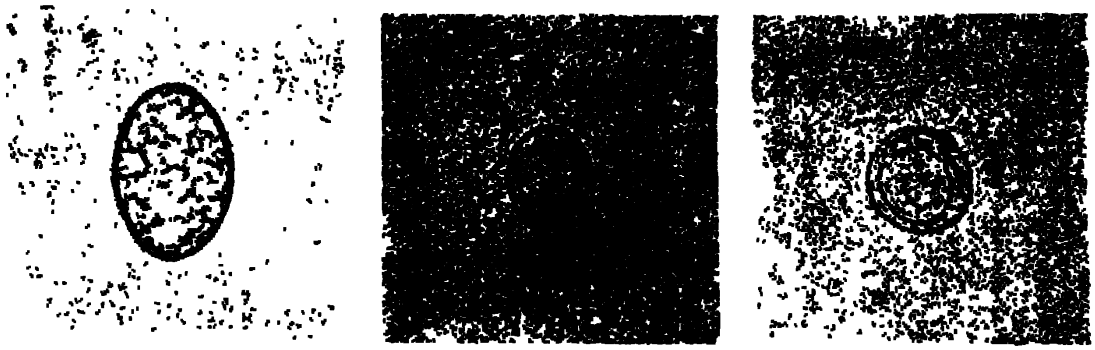

Fig. 246. *Dibothrio-cephalus latus*
Fig. 247. *Tænia solium*
Fig. 248.- -*Dipylidium caninum.*

Figs. 246-248. Eggs of Cestode Worms from Human Fæces.
(From photographs by J. J. Bell.)

II Without an operculum and with a six hooked embryo -*Tæniidæ.*
  (*a*) Egg with a thick, radially-striated, inner shell or embryophore *Tæniinæ.*
    (A) Embryophore round or oval, 39×33 μ. Africa—*T. africana*
    (B) Embryophore oval, whitish to yellow, 39 × 30 μ. America *T. confusa.*
    (C) Embryophore, 38 × 30·4 μ. Africa- -*T. bremneri.*
    (D) Embryophore oval, 35 to 41, μ × 26 to 35 μ. Philippines *T. philippina.*
    (E) Embryophore, ovoid, rusty brown, 35 to 40 μ × 20 to 30 μ Cosmopolitan and common -*T. saginata*
    (F) Embryophore almost round; brown, 31 to 30 μ. Not uncommon in the tropics---*T. solium.*
    (G) Egg and embryophore unknown. Asiatic Russia- - *T. hominis.*
  (*b*) Egg with a thin, membranous inner shell.
    (1) *Not in Capsules- -Hymenolepis.*
      (*a*) Egg oval or globular, with two distinct membranes—outer 30 to 60 μ, inner 16 to 34 μ- -mammillate projection at each pole- *H. nana.*

(b) Egg round or oval; outer membrane, 54 to 86 μ; yellowish, may be radially striated; inner membrane, 24 to 40 μ × 20 to 35 μ, with not very evident mammillate projection at each pole. *H. diminuta.*

(c) Egg oval or spherical, outer membrane, 50 to 100 μ × 35 to 100 μ, inner membrane 30 to 40 μ × 25 μ, occasionally polar papillae, very rare in man. *H. lanceolata.*

In Capsules.

Eight to twenty [illegible] in a capsule, egg spherical, 43 to 50 μ. *D. caninum.*

One to three eggs in a capsule, with calcareous corpuscles. Eggs with two shells and two mammillate projections, onchosphere, 8 μ. *D. madagascariensis.*

Egg capsules without calcareous corpuscles, mature eggs not observed. *D. asiatica.*

ORDER I. PSEUDOPHYLLIDEA Carus

This order has three families [illegible] P[illegible] Amphitretidae. The first [illegible] contains human parasites.

Family Dibothriocephalidae [illegible] Pseudophyllidea with variously developed suckers, and a uterus which forms a rosette. Eggs with opercula. There are two subfamilies with species found in man: (1) Dibothriocephalinae, (2) Ligulinae.

Subfamily 1. Dibothriocephalinae. The suckers or bothria are more or less definite slit-like furrows. Proglottides distinct, and drop off in groups. Genus 1. *Dibothriocephalus*, Genus 2. *Diplogonoporus*, Genus 3. *Sparganum.*

Dibothriocephalus Lühe, 18[illegible]

Synonyms. *Diphyllobothrium* Cobbold, 1858 (con[illegible] o be correct name by some authors); *Bothriocephalus pro parte* Rud[illegible] o, *Dibothrius pro parte* Rudolphi, 1819, *Dibothrium pro parte* Diesing.

Dibothriocephalinae with a more or [illegible] longated, unarmed scolex with flat suckers cutting deeply into the head [illegible] ngle genitalia in each proglottis. [illegible] (3) *D. cristatus*, (4) *D. parvus.*

Dibothriocephalus latus Linnaeus, 1758.

Synonyms. *Taenia lata* L., 1748, *T. vulgaris* L., 1758, *T. membranacea* Pallas, 1781, *T. tenella* Pallas, 1781, *T. dentata* Batsch, 1786, *T. grisea* Pallas, 1796, *Bothriocephalus latus* Bremser, 1819, *Dibothrium latus* Diesing, 1850, *B. balticus* Küchenmeister, 1855, *B. cristatus* Davaine, 1874, *B. latissimus* Bugn., 1886.

History. This tapeworm has long been known in Europe, especially in French Switzerland and the Baltic provinces, Germany, and in many other parts. It is however well known in Asia, Turkestan, and Japan; in Africa about the Lake Ngami, in Madagascar, and in North America.

It occurs in man, and dogs, and cats.

Morphology. It is about 9 metres in length, with some 3,000 to 4,200 segments; colour yellowish grey. Scolex elongated, almond-shaped, 2·5 millimetres in length, with two deep laterally placed suckers. Neck very narrow, and of variable length.

Proglottides very broad (10 to 20 millimetres), breadth being greater than the length; postero-lateral angles project. Testes situated dorsally; vas deferens has a vesicula seminalis and a cirrus sac which opens dorsally. Vaginal opening directly behind this, leading into a receptaculum seminis. Yolk glands in pairs, shell gland behind, ovaries on each side of the median line behind. Uterus is arranged in a rosette, with four to six convolutions.

and possesses its own separate opening. The genital orifices are two in number: a transverse slit for the cirrus pouch and the vagina, and a posterior roundish opening for the uterus. Calcareous bodies present. The brown eggs are oval, 68 to 71 μ in length, and 45 μ in breadth, with an operculum.

Life-History.—The egg remains undeveloped for a longer or shorter time, and eventually a six-hooked onchosphere enclosed in a ciliated embryophore, escapes through the lid opening, after undergoing a preliminary development in a species of *Cyclops*, then gets into certain fish, particularly *Esox lucius* (pike), *Lota vulgaris* (Miller's thumb), *Perca fluviatilis*, *Salmo umbla*, *Trutta vulgaris*, *T. lacustris*, *Thymallus vulgaris*, *Coregonus lavaretus*, *C. albula*, and *Onchorhynchus perryi* in the muscles of which it becomes a plerocercoid.

When these fish are eaten, the plerocercoids quickly develop into the tapeworm, eggs appearing in the fæces in some twenty-one to twenty-four days.

Habitat.—Man, dog, cat and fox.

Pathogenicity.—It produces a severe form of anæmia, together with fever (99° to 104° F.) in some cases, and a quick pulse, which is supposed to be due to the action of a toxin.

Dibothriocephalus cordatus R. Leuckart, 1863.

Synonym.—*Bothriocephalus cordatus* R. Leuckart, 1863.

This parasite is commonly found in the seal, the walrus, and the dog in Greenland and Iceland. It may infest man.

Morphology.—The principal features are the short, broad, heart-shaped head with the grooves on the flat surface, the absence of the neck, and the length only 1 to 1¼ metres. Uterine rosette with six to eight loops. Eggs with lids 75 μ in length by 50 μ in breadth.

Dibothriocephalus parvus Stephens, 1908.

This parasite was found by Elkington in Tasmania in 1906 in a Syrian aged thirty-seven, who had not long arrived from his native country.

Morphology.—Scolex not known. Proglottides with darkly coloured central, uterine rosette with four to five loops on each side of the median line; largest segment, 5 by 2 millimetres. Genital atrium 0·4 to 0·5 millimetre behind the anterior margin, uterine opening some distance behind the genital atrium. Calcareous bodies were not seen. Eggs 59 by 40 μ.

Diplogonoporus Lönnberg, 1892.

Synonym.—*Krabbea* R. Blanchard, 1894.

Bothriocephalinæ with short scolex, powerful suckers, no neck, and two sets of genitalia side by side in each proglottis.

Type Species.—*Diplogonoporus balænopteræ* Lönnberg, 1892.

Diplogonoporus grandis R. Blanchard, 1894.

Synonym.—*Krabbea grandis* R. Blanchard.

So far this parasite has only been observed twice in Japanese in Hiogo, Japan.

Morphology.—Scolex unknown. Proglottides 1·5 millimetres broad in front and 2·5 millimetres broad behind, very short, only 0·45 millimetre. Two ventral grooves on either side of the median line with the genital pores. Uterus with few loops. Eggs brown; thick shell, 63 to 68 μ in length and 50 μ in breadth, with opercula.

Diplogonoporus brauni Léon, 1907.

Two specimens of this worm have been found in Roumania.

Morphology.—The worm presents the appearance of a thick, opaque, greyish ribbon 12 centimetres in length, marked by slight transverse rings and with a dorsal and ventral sucker which mark a division of the head into two unequal parts. There is no neck. The genital orifices are double, with a double genital apparatus in each ring. The vitellogene glands are situate peripherally. No genital sinus, no calcareous corpuscles.

Sparganum Diesing, 1850.

A collective group of larval stages of Dibothriocephalidæ which have not reached a stage in their development at which they can be determined generically: *Sparganum mansoni*, *S. prolifer*, *S. baxteri*.

Sparganum mansoni Cobbold, 1883.

Synonyms.—*Ligula mansoni* Cobbold, 1883; *Bothriocephalus liguloides* R. Leuckart, 1886; *Dibothrium mansoni* Ariola, 1900.

This larva was found by Manson while making a post-mortem on a Chinaman in Amoy, lying under the peritoneum near the kidneys and over the iliac fossæ; he also found one free in the pleural cavity. Scheube discovered another specimen in the urethra of a Japanese, and Sonsino a third in an Egyptian jackal.

Morphology.—Long, white ribbon-shaped parasites, with feeble movements. No head or definite structure visible. Length, 30 to 35 centimetres; breadth, 3 to 12 millimetres. At the broader end there is a sort of papilla. There is no reproduction by fission.

Sparganum prolifer Ijima, 1905.

Synonym.—*Plerocercus prolifer* Ijima, 1905.

In 1905 Ijima found this worm in a woman living near Tokio, and in 1907 Gates found the same or a similar worm in a man in Manatee, U.S.A.

Morphology.—The larva which lies enclosed in a cyst, may attain 1 to 12 millimetres in length by 2·5 millimetres in breadth. The head at the narrow end is motile, and capable of evagination and invagination. It shows an apical depression, which perhaps serves as a sucker, but there are no true suckers or other organs of attachment.

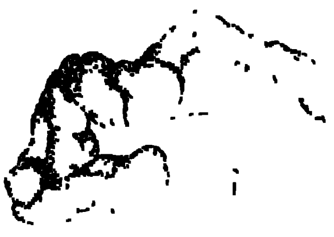

FIG. 249.—*Sparganum prolifer* IJIMA. (After Stiles.)

Calcareous spherical corpuscles can be found anywhere, except in the head. No genitalia are to be seen, but there is a good muscular and excretory system and food-reserve bodies. It can multiply by transverse division, and supernumerary heads may become independent, and may assume bizarre and irregular shapes. The adult is unknown.

Habitat.—It lives in the subcutaneous tissue and elsewhere in man.

Pathogenicity.—It produces nodules in the skin and fascia between the muscles and in the abdominal cavity. Associated with these nodules there may be considerable swelling of the integument, and, in fact, a condition not unlike elephantiasis may arise. Also there may be acne-like spots all over the body causing itching, which may lead to the escape of a worm from the spot. When a nodule is cut open, a cyst is found containing one or two worms, either filled with a watery fluid, or with a jelly or slime-like substance. Apparently after weeks or months the cyst-wall may become firm and thick, and encapsulate the worms. This condition may last for years, and apparently can kill the victim, who may be literally ' eaten up of worms.'

Sparganum baxteri Sambon, 1907.

This Dibothriocephalid larva was found by Baxter in an abscess in the thigh of a Masai in late German East Africa.

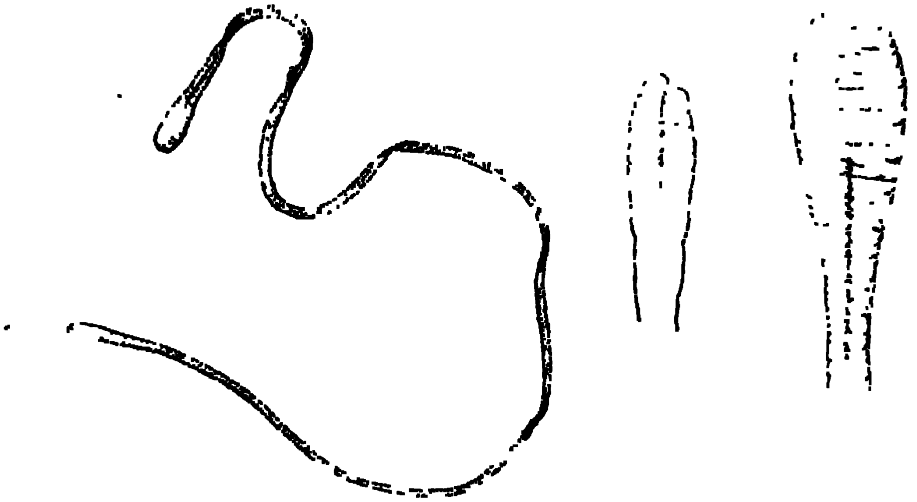

FIG. 250. *Sparganum baxteri* SAMBON.
(After Sambon.)

Morphology.—It has a long unsegmented body, 15 centimetres in length and 1 millimetre in breadth, with numerous irregular transverse folds, and a distinct longitudinal groove on the ventral surface. Anterior extremity is 2 millimetres broad, with a completely invaginated head; posterior extremity, 1·2 millimetres broad, with a shallow medium slit.

Leon has described a new tapeworm in man which he has referred to the Ligulinæ, in which it requires a new genus called *Braunia jassyensis* Leon 1908.

ORDER III. CYCLOPHYLLIDEA van Beneden.

There is only one family with human parasites.

FAMILY TÆNIIDÆ Ludwig, 1886.

Scolex globular or pyriform, with unarmed suckers, and an armed or unarmed rostellum. Vagina posterior to the cirrus. Mostly parasitic in mammals. Larval stage a cysticercus or cysticercoid. Subfamily 1. Dipylidiinæ; Subfamily 2. Davaineiinæ; Subfamily 3. Tæniinæ.

SUBFAMILY 1. DIPYLIDIINÆ Stiles, 1896.

Definition.—Tæniidæ, with armed rostellum and unarmed suckers. Genital pores marginal. Genitalia simple or double.

Uterus becomes divided into ovarium follicles, or entirely atrophied, and the eggs are set free into the parenchyma. Eggs with thin transparent shells, with or without appendages.

Genera.- (1) *Dipylidium*; (2) *Hymenolepis*.

Dipylidium R. Leuckart, 1863.

Definition. Dipylidiinæ of medium or small size, with retractile rostellum armed with several rings of alternating hooks, which have a broad basis. Genitalia duplicated, with pores on each side of a proglottis. Eggs with a double shell.

Dipylidium caninum Linnaeus, 1758.

Synonyms. *Tænia canina* Leuckart 1758, *Moniliformis* Pallas, 1781; *T. cucumerina* Blochmann, 1782; *T. elliptica* Batsch, 1786; *Dipylidium cucumerinum* Leuckart, 1863.

Dipylidium is frequently found in the dog and the cat, which are its proper hosts; in man it is only an accidental and rare parasite, having been first found by Dubois, a pupil of Linnaeus, in 1751. Melnikow showed that the scolex was to be found in the dog-louse (*Trichodectes canis*) and in that of the cat (*T. subrostratus*), as well as in the dog flea (*Ctenocephalus canis* Curtis), the cat flea (*C. felinis* Bouché), and in that of man (*P. irritans*), but how the infection reaches man is not definitely proved. Recently Blanchard has summarized sixty cases in man up to the year 1907, most of which occur among young children.

FIG. 251.—*Dipylidium caninum*. Nest of Eggs × 25. (After a photograph by J. J. [illegible])

Morphology.—It measures 15 to 35 and even to 40 centimetres in length, and the segments are from 1·5 to 3 millimetres in breadth.

The scolex has the typical rostellum, with three to four rings of hooks, diminishing in size from the first circle, where they are 12 to 15 μ, to the last, where they are only 5 to 6 μ in length, and four suckers, which are unarmed.

The genitalia are double, with pores on each side. The eggs are round, from 43 to 50 μ in diameter, with a thin shell.

Life-History.- The ripe proglottides by their own movement pass through the host's anus, and get into the fur, where the eggs infect the dog and cat louse, or flea, in which they develop into cysticercoids (*Cryptocystis trichodectis* Villot, 1882).

The dog bites the louse or flea and infects itself, and may pass on the cysticercoids to man by licking. The cat licks its fur, and gets infected in that manner.

Blanchard thinks that the cat spreads the parasite by infecting milk with the cysticercoids when it steals a drink from a bowl, the contents of which are afterwards given to children.

Hymenolepis Weinland, 1858.

Synonym.—*Diplacanthus* Weinland, 1858, *nec* L. Agassiz, 1842.

Definition.—*Dipylidiinæ* with small head, with armed, well-developed, or unarmed, rudimentary rostellum. Neck long. Proglottides serrated, longer than broad. Genital pores always on the left. Three testes. Eggs with three shells.

Type.—*H. diminuta.* The genus possesses two subgenera, *Hymenolepis* and *Drepanidotænia.*

Subgenus 1. Hymenolepis Sensu Stricto.

With the characters of the genus, but the hooks have the dorsal root much longer than the ventral, and number twenty-four to thirty.

Proglottis narrow, female genitalia ventral to or between testes.

Hymenolepis (Hymenolepis) diminuta Rudolphi, 1819.

Synonyms.—*Tænia diminuta* Rudolphi, 1819; *T. leptocephala* Creptlin, 1825; *T. flavopunctata* Weinland, 1858; *T. varesina* Parona, 1884; *T. minima* Grassi, 1886.

It is a parasite of *Epimys norvegicus*, *E. musculus*, and *E. rattus alexandrinus*, being not uncommon in rats in Ceylon.

The first human specimen was discharged by a child aged nineteen months, and was presented to the Boston Medical Improvement Society by Dr. Ezra Palmer in 1842. Since then a number of cases have been recorded in Philadelphia, Sicily, Italy, France, South America, and the West Indies.

Morphology.—The worm measures 20 to 60 centimetres in length, and up to 3·5 millimetres in breadth. The head is very small, only 0·2 to 0·5 millimetre in diameter, club shaped, and has a rudimentary, unarmed rostellum and four elliptical suckers. The segments measure 0·66 millimetre in length by 3·5 millimetres in breadth. The anterior proglottides show a yellow spot (hence the name *T. flavopunctata*), caused by the distended receptaculum seminis. The posterior proglottides show a brownish-grey colour, due to the mature uterus. The genital pore is situated laterally. The eggs are oval, with a diameter of about 60 μ.

Life-History.—It is a common parasite in rats and mice, while the cysticercus is said to live in the larva and imago of the meal-moth (*Asopia farinalis*), in an earwig (*Anisolabis annulipes*), and in the beetles *Acis spinosa* and *Scaurus striatus*, it is not likely that rat fleas are important, as the cysticercus has been found in *Ceratophyllus fasciatus* by Nicoll and Minchin, and Johnston in Australia has found it in *Xenopsylla cheopis*.

The infection in man is mostly among infants and children.

Hymenolepis (Hymenolepis) nana von Siebold, 1852.

Synonyms.—*Tænia murina* Dujardin, 1845, *nec* Gmelin, 1790; *T. nana* von Siebold, 1852, *nec* van Beneden, 1867; *T. ægyptiaca* Bilharz, 1852; *Diplacanthus nanus* Weinland, 1858.

This is the dwarf tapeworm of man, and was discovered by Bilharz in the ileum of a boy who died of meningitis in Cairo. It is found in Egypt, Europe, North and South America, Siam, and Japan, and is by no means a rare parasite in man. Calandruccio estimates that 10 per cent of the children in Sicily are affected. Stiles reports 4·8 per cent. for 125 children in Washington. The number found varies from one or two to several thousands in one individual.

There is doubt as to whether this worm is or is not identical with *Hymenolepis nana var. fraterna* Stiles, 1906, which is common in rats and mice. Probably it is distinct from this parasite, because Grassi and Looss were unable to transmit it to mice.

Morphology.—It is the smallest tapeworm in man, measuring only 10 to 15 millimetres in length, and from 0·5 to 0·7 millimetre in breadth.

The head is globular, and provided with a rostellum with one ring of twenty-four to thirty hooks, which are very small, 14 to 18 μ in length. The neck is relatively long.

There are about 150 proglottides 0·4 to 0·9 millimetre in breadth and 0·014 to 0·030 millimetre in length. The genital pore is marginal. The mature uterus contains about thirty or more eggs, which are oval and measure 30 to 48 μ, and contain onchospheres measuring 16 to 19 μ in diameter.

Life-History.—It is believed that the cysticercus will be found in some insect.

The nearly related *T. nana var. fraterna* completes its development entirely in the rat, for the cysticercus develops in the villus, while the adult lies in the lumen of the intestine.

Pathogenicity.—Owing to its small size it is apt to be overlooked, but there is no doubt that it spreads in crowded institutions and poorer families. Apparently, when the parasite occurs in small numbers no symptoms result but in considerable numbers disturbance may occur, which has been assigned by Mingazzini to the effects of toxins.

Treatment.—Male-fern is the best treatment (*vide* Chapter LXXV.).

Prophylaxis. While it is doubtful whether *T. nana* and *T. nana var. fraterna* are the same or different species, it will be necessary to guard against the contamination of food by rats and mice. Moreover, it must be remembered that the infection spreads in crowded dwellings, and therefore isolation of the infected child should be insisted upon.

Subgenus 2. Drepanidotænia Railliet, 1892.

With the characters of the genus but the hooks have a dorsal root much larger than the ventral, and are only eight to twenty in number. Proglottis broad, testes three, alongside which lies female genitalia.

Hymenolepis (Drepanidotænia) lanceolata Blochmann, 1782.

Synonyms.—*Tænia lanceolata* Blochmann, 1782; *T. anserum* Frisch, 1727; *T. acutissima* Pallas, 1781; *T. anseris* Blochmann, 1779; *T. lanceola* Batsch, 1786; *Halysis lanceolata* Blochmann, 1803.

It is common in ducks, geese, and other birds, including the flamingo, and has been found in man in Europe, but the record is considered to be very doubtful; probably the worm should not be included among human parasites.

Morphology.—It is about 30 to 130 millimetres in length and 5 to 18 millimetres in breadth, with a very small globular head. Eggs, with three envelopes, oval (50 by 35 μ).

Life-History.—The cysticercoid lives in a cyclops, which is eaten by ducks and geese.

SUBFAMILY 2. DAVAINEINÆ Braun, 1900.

Definition.—*Tæniidæ.* Rostellum and suckers armed. Eggs mostly encapsuled.

Genus.—*Davainea* R. Blanchard.

Davainea R. Blanchard, 1891.

Definition.—Davaineinæ, with a globular head, armed with two rings of hammer-like hooks and four suckers, surrounded by several rings of hooks.

Species.—*D. madagascariensis*; *D. asiatica*.

Davainea madagascariensis Davaine, 1869

Synonyms.—*Tænia madagascariensis* Davaine, 1869; *T. demarariensis* Daniels, 1895.

This worm was first discovered by Grenet in children at Mayotte (Comores). Over ten infections have been recorded: by Davaine from the Comoro Islands, Leuckart from Siam, Daniels from British Guiana, Blanchard from Nossi-Bé, four by Cherreau from Mauritius, and two by Garrison from the Philippines.

Morphology.—The worm is 25 to 30 centimetres in length, with a maximum breadth of 1·4 millimetres. The scolex has four large suckers and a rostellum, with ninety hooks (18 μ long). The proglottides number from 500 to 700, being 2 millimetres long by 1·4 millimetres broad. Genital pores are unilateral, and near the proximal corner. Testes number about fifty, with a long vas deferens and a fusiform cirrus pouch. The receptaculum seminis is long and broad. The uterus is composed of a number of tubes, rolled up on each side into an almost spherical coil. When mature, these windings uncoil and fill the proglottides; then they lose their walls, and the eggs, lying free in the parenchyma, become surrounded by proliferating cells, which form capsules for them.

As many as 300 to 400 of these capsules may exist in one proglottis, arranged in transverse rows.

The egg consists of the usual two membranes and an onchosphere, which is 8 by 15 μ.

Life-History.—The life-history is unknown, but it is suggested that the cysticercus may be found in the cockroach (*Periplaneta orientalis* or *P. americana*).

Allied genera are common in rats, hares, fowls, pigeons, turkeys, pheasants, partridges, grouse, and other birds.

Davainea asiatica von Linstow, 1901.

Synonym.- *Tænia asiatica* von Linstow, 1901.

This worm was found in a person in Aschabad, near the northern frontier of Persia, and consists of 750 proglottides without a head. The genital pores all lie on the same lateral border. The testes are globular, the cirrus pouch pyriform. The female organs lie anteriorly, with a large ovary and a small vitellogene gland. There is a large receptaculum seminis The uterus breaks into sixty to seventy large egg follicles. Nothing is known about the appearance of the mature egg, or about the life-history

SUBFAMILY 3. TÆNIINÆ Stiles, 1896.

Definition. - *Tæniidæ*, usually of considerable length, with segments longer than they are broad. Scolex with either a rostellum armed or unarmed, or an apical sucker. Genital pores irregularly arranged on the lateral borders. Genitalia single. Testes numerous, placed laterally. Ovary shell and vitellogene gland situated posteriorly. Uterus, a single median trunk, from which lateral branches develop later. Eggshell thin; embryonic envelope (embryophore) thick, with radial stripes. Cysticercus generally in herbivora, adults in carnivora.

Tænia Linnæus, 1758.

Definition.– Tæniina with the characters of the subfamily. The genus *Tænia* is subdivided into three subgenera:

Subgenus 1. *Tænia* Linnæus, 1758. Type: *T.* (*Tænia*) *solium.*

Subgenus 2. *Tæniarhynchus* Weinland, 1858. Type: *T.* (*Tæniarhynchus*) *saginata*

Subgenus 3. *Multiceps* Goeze, 1782. Type: *T.* (*Multiceps*) *cœnurus*. This, however, is not a human parasite.

Tænia (Tænia) solium Linnæus, 1758.

Synonyms. *T. cucurbitina* Pallas, 1766; *T. pellucida* Goeze, 1782; *T. vulgaris* Werner, 1782, *T. dentata* Batsch, 1786; *Halysis solium* Zeder, 1803; *T. armata humana* Brera, 1808

The name ' solium ' is derived from a Syrian term *schuschl*, meaning a chain, which has arrived at its present form by being first turned into Arabic and finally into Latin. It is often called the armed tapeworm.

This worm is cosmopolitan in its distribution, for it can be found wherever a pig and a man can live, for the cysticercus lives in the pig, man, and rarely in sheep and dogs, while the tapeworm only lives in man. Even monkeys appear not to be capable of infection.

It seems to be more widespread in the tropics than in the Temperate Zone. It is not uncommon in Ceylon, and it is apparently common in Panama.

Morphology.—Length usually 2 to 3 metres, but may reach 8 metres. Mature segments measure 5 to 6 millimetres in breadth. Scolex provided with a rostellum, which may be pigmented and is armed with a double row of alternately large and small hooks, which number from twenty-two to thirty-two, and with four hemispherical suckers. The neck is long. Proglottides number from 800 to 900, with a length of 10 to 12 millimetres in mature segments. Genital pore lateral and irregularly alternate. The mature uterus has seven to ten ramified lateral branches, and contains three ovaries, the third being formed by subdivision of the one on the side of the genital pore. Eggs globular, pale yellow in colour, from 31 to 38 µ in diameter.

Life-History. — The adult worms live solely in the human intestines, from which the onchospheres with their envelopes escape in the fæces, and are apt to be eaten by pigs, or these may be infected by contaminated food or water. The cysticercus, often called *Cysticercus cellulosæ* (synonym, *C. acanthotrias*), develop in the flesh of the pig. If this flesh is eaten in an undercooked condition, the cysticercus infects the human being and forms the tapeworm. Occasionally man becomes infected with *Cysticercus cellulosæ*, most commonly in the brain, then the eye, the muscles, liver, lungs, etc., where they are sometimes few, sometimes numerous. This infection must be due to contaminated food or water.

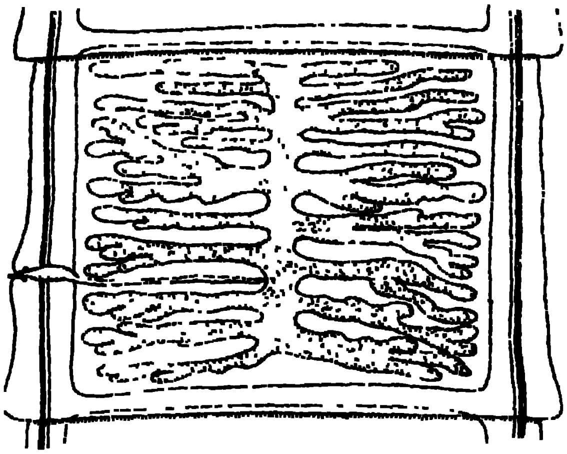

FIG. 252.—PROGLOTTIS OF *Tænia solium* LINNÆUS. (After Stiles.)

The tapeworm can live for years in the intestine of man. A variety called *T. solium, var. abietina* Weinland, originally found in a Chippewa Indian belongs probably to this species.

Pathogenicity.—The intestinal symptoms are not severe, but colicky pains and diarrhœa alternate with constipation. The patient may slowly emaciate. The danger of this infection is the entry of eggs into the human being and the formation of cysticerci in the organs.

Treatment.—Warn the person affected to be very careful to keep his hands clean, and to avoid infecting himself and other people with the eggs. Kill the tapeworm with extract of male-fern given in capsules (four to eight of 10 minims each), or in emulsion on an empty stomach, and followed after four to six hours by a saline purgative.

Prophylaxis.—Fæces should be so treated as not to infect pigs, and the flesh of these animals should be carefully cooked.

Tænia (Tæniarhynchus) saginata Goeze, 1782.

Synonyms.—*T. solium* Linnæus, 1707, *pro parte*; *T. cucurbitina* Pallas, 1781, *pro parte*; *T. inermis* Brera, 1802, *T. dentata* Nicolai, 1830; *T. lata* Pruner, 1847, *Bothriocephalus tropicus* Schmidtmuller, 1847, *T. mediocanellata* Kuchenmeister, 1855; *T. zittavensis* Küchenmeister, 1855; *T. tropica* Moquin-Tandon, 1860.

This is the unarmed beef-worm or the fat tapeworm, which has a cosmopolitan distribution, the adult being known only in man and the cysticercus in cattle, though it can be produced experimentally in a number of animals. It is very common in the tropics, especially in Africa, and particularly Abyssinia, the Sudan, and Asia.

Morphology.—It measures 4 to 8 to 10 metres in length, and has been said to attain much greater length. A mature segment is 4·7 millimetres in breadth. The head possesses four hemispherical, often pigmented, suckers, and a sucker in place of a rostellum. The neck is long. The proglottides number about 1,000 segments, with a length of about 16 to 20 millimetres when mature, The genital spores are arranged irregularly at the sides, and the median uterus produces twenty to thirty-five ramified lateral branches. Malformations of the segments are not uncommon. Eggs globular, often with the original shell, to which may be attached one to two filaments and the two embryonic envelopes, as well as the onchosphere. The inner embryonic envelope is oval, striated, measures 30 to 40 μ in length by 20 to 30 μ in breadth. Segments can escape *per anum* by their own action.

Life-History.—The adult worm lives in man, the cysticercus requiring some fifty-four days (Perroncito quoted Leuckart) to develop, so that proglottides are seen, and the embryophore, escaping in the faeces, enters cattle by means of contaminated food or water, and develops in their muscles into the *Cysticercus*

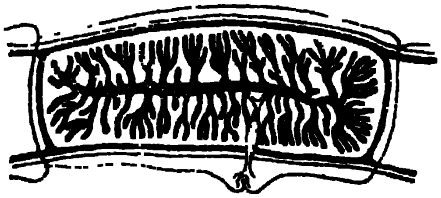

FIG. 253.—PROGLOTTIS OF *Tænia saginata* GOEZE.
(After Stiles.)

bovis, which is rather small—only 7·5 to 9 millimetres in length and 5·5 millimetres in breadth. The tongue and the muscles of mastication, especialy the pterygoids, are chiefly affected.

Man becomes infected by eating under-cooked meat. It can live in him for a number of years. The cysticercus very rarely occurs in man.

Pathogenicity.—It is believed to be more difficult to kill medicinally than *T. solium*, and to produce more severe anaemia.

Treatment.—As for *T. solium*.

Prophylaxis.—Prevent human faeces contaminating the food of cattle, and have the meat, especially the tongue and the pterygoid muscles, inspected in the slaughter-house. In African beef animals also common in the muscles of the shoulder, foreleg, back, rump, and hindquarters. Only in extensive infections and exceptionally in slight invasions, it is found in the lymph glands, lungs, liver, brain and œsophagus which, therefore, ought also to be inspected.

Tænia (Tæniarhynchus) africana von Linstow, 1900.

Two specimens of this worm were found in a negro in late German East Africa, at Langenburg, near Lake Nyassa.

Morphology.—It is about 1·4 metres in length. The scolex is provided with an apical sucker in place of a rostellum, and also with four ordinary suckers. The neck is very short. The proglottides vary in length and breadth, according to position, but always broader than long, in the portion discovered. This species is as yet not clearly defined from *T. saginata*.

The ripe segments are 9 millimetres broad by 1·20 millimetres thick. Their number is about 600. The genital pore is irregularly alternate on the lateral border. The testes are very numerous, and the vas deferens much convoluted, with a thick, pear-shaped cirrus pouch. The cirrus is beset with bristles, as is the vagina. The receptaculum seminis is large. The ovary is large and double, and the vitellogene gland is situated at the posterior border. The mature uterus consists of a median portion with fifteen to twenty-four non-ramified lateral branches.

The embryophore is thick, with radial markings, round or oval (39 by 33 μ).

Life-History.—The life-history is not known, but it is suggested that the cysticercus may live in *Bos indicus*, the hump-backed cow, the flesh of which the natives of East Africa eat raw.

Tænia (Tæniarhynchus) hominis von Linstow, 1902.

This worm was found by Anger in a man in Aschabad in Siberia.

The length was 70 millimetres. The scolex had a rudimentary rostellum without hooks. There were four unpigmented suckers, behind which there was a ring-shaped swelling. Nothing further is known about this parasite.

Tænia (Tæniarhynchus) philippina Garrison, 1907.

This specimen was found by Hare in a prisoner in Bilibid Prison, in the Philippine Islands, in 1905.

Morphology.—The length is 80 to 100 centimetres; maximum breadth 1 centimetre. Head cuboid, with an unarmed retractile rostellum and four suckers. Neck segmental. Proglottides number about 800, being sexually mature about the 470th. Mature proglottides 4 to 5 millimetres in width and 0·8 to 1 millimetre in length. Surfaces and margins extend posteriorly in an elongated cuff-like projection over the succeeding segment. Testes 130 to 160 μ in length, and from 60 to 80 μ in breadth. Vas deferens without vesicula seminalis; cirrus and pouch present. Genital pore situated irregularly on the lateral borders. Ovaries, with two unequal transversely elongated lobes, close against the vitellogene gland. Vagina without setæ and with two coils. Uterus stem with a V-shaped course posteriorly, and with four to six distinct coils anteriorly. Mature uterus very compact, with a median stem and numerous long, slender dichotomous branches.

Embryophore oval, 35 to 41 μ long, and 26 to 35 μ broad.

Life-Cycle.—Life-history not known.

Tænia (?) **confusa** Ward, 1896.

This worm has so far only been found in Lincoln, Nebraska, U.S.A.

Morphology.—Length about 8½ metres, breadth 5 millimetres, scolex unknown. Segments much longer than they are broad, 27 to 35 millimetres long by 3·5 to 5 millimetres broad. Genital pore irregularly placed behind the middle of the lateral border. Testes numerous, vas deferens not much coiled, cirrus pouch thick-walled. Cirrus beset with little hairs. Receptaculum seminis globular; ovary small and double, bean-shaped. Vitellogene gland narrow and triangular; shell gland globular. Uterus, when mature, consists of a median trunk, and fourteen to eighteen short dichotomous branches on each side. Embryophores are oval, thick, and striated (39 by 30 μ).

Life-Cycle.—Nothing is known.

Tænia (?) **bremneri** Stephens, 1907.

This worm was found by Dr. Bremner in a Fullani woman in Northern Nigeria.

Morphology.—The head is not known. The segments examined measured, on an average, 28·6 by 8·5 millimetres, but ranged from 21 by 6 millimetres to 32 by 29 millimetres in size. The central uterine axis has twenty-two to twenty-four ramified lateral branches, and one terminal branch with four to five ramifications. The genital pore is prominent, and lies behind the middle of the segment. Eggs measure on an average 38 by 30·4 μ.

Leiper considers that these large segments are relaxed *Tænia saginata*.

Life-Cycle.—Nothing is known at present about the life-history.

Echinococcus Rudolphi, 1801.

Synonym. *Acephalocystis* Laennec, 1804.

Species. *Echinococcus granulosus* Batsch, 1786; *E. multilocularis* Huber 1896.

Echinococcus granulosus Batsch, 1786.

Synonyms.—*Tænia echinococcus* Zeder, 1803, Siebold, 1853; *T. nana* van Beneden 1861, *nec* Siebold 1853, *Echinococcifer echinococcus* Weinland, 1861.

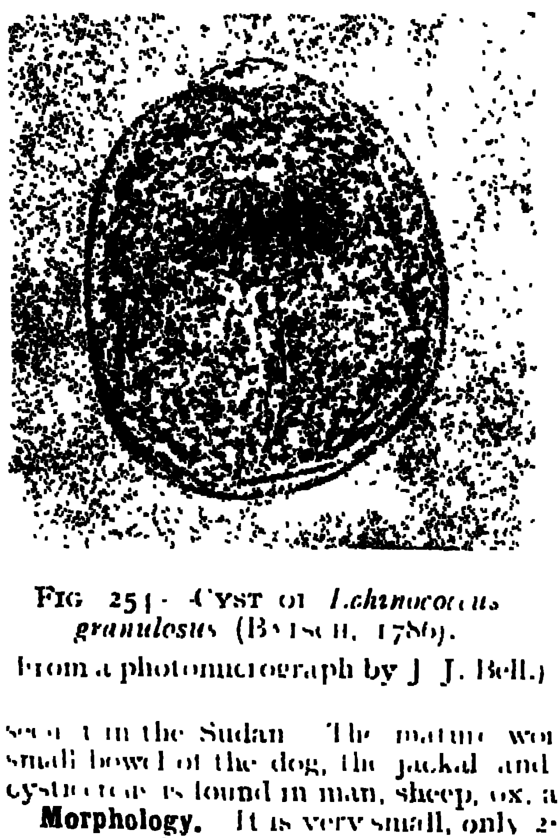

FIG. 254.—Cyst of *Echinococcus granulosus* (Batsch, 1786).
(From a photomicrograph by J. J. Bell.)

Hydatid disease appears to have been known since the days of Hippocrates. In 1684 Redi suggested that the cysts were animal in origin, and in 1766-67 Pallas clearly showed their relationship to tapeworms (*Tænia hydatigena*).

It appears doubtful whether there are two species of worms associated with hydatid disease, but the appearance of the larvæ and the geographical distribution tend to separate the genus into two species. *Echinococcus granulosus* causes the cystic form of hydatid disease. It is found most markedly in Iceland and Australia, but also exists all over Europe, and is known in New Zealand. It is rare in India, and the only case we have seen in Ceylon came from South Africa, where it occurs, but Begbie has recently described another case in Ceylon. It is known in the Philippine Islands, and is not uncommon in Egypt and Algeria, and we have seen it in the Sudan. The mature worm, which is very small, lives in the small bowel of the dog, the jackal and the wolf in large numbers, while the cysticercus is found in man, sheep, ox, and pig.

Morphology. It is very small, only 2·5 to 5 to 6 millimetres in length, and is composed only of a scolex and three to four segments. The scolex has four suckers and a rostellum armed with a double row of twenty-eight to fifty hooks, which vary in size, the larger being 40 to 45 μ in length, and the smaller 30 to 38 μ in length. The genital pores alternate.

The testes are numerous, the vas deferens spirally coiled, the vitellogene gland double, the shell round. The mature uterus has only lateral protuberances, no true branches, and the eggs may form heaps.

The egg is globular, 30 to 36 μ in diameter.

Life-Cycle.—The dog infects man with the onchospheres, usually directly when being petted. Infection may, however, be brought about by contaminated food.

On arrival in the stomach, the onchosphere escapes from its embryophore and bores its way into the liver or some other organ. Here it grows, and forms a cyst with a thick outer cuticle, inside which is fluid enclosed by a layer of parenchyma, the endocyst, composed of two layers of cells. The irritation caused by the growth of this cyst produces a connective-tissue coat, formed by the organ in which the cyst is growing. The cyst in this condition is called an acephalocyst (*Echinococcus cysticus sterilis*), and is often found in cattle.

The next stage is the formation of the brood capsule. The inner layer of the endocyst grows inwards, forming large numbers of small hollow capsules (brood capsules), which have the endocyst externally and the cuticle internally. On these capsules heads develop. The cyst now forms the *Echinococcus cysticus fertilis*, found in domestic animals.

In man, however, daughter-cysts appear between the strata of the cuticle, into which cells belonging to the endocyst have found their way and formed cysts, with an external cuticular and an internal parenchymal layer. These cysts may, of course, bulge, and escape externally or internally. If externally, they then lie between the capsule and the mother-cyst and form *Echinococcus hydatidosus var. exogenus*, or if internally, they fall into the interior of the mother-cyst and form *Echinococcus hydatidosus var. endogenus* These daughter-cysts may remain sterile or produce brood capsules and heads. Granddaughter-cysts may be formed in the same way. The wall of the mother-cyst may disappear, leaving the daughter-cysts free.

Of all these varieties, the endogenous cyst is the most common. It may reach several pounds in weight, with hundreds of daughter-cysts.

In Khartoum cysts fed into dog developed in fourteen days into worms, but not quite sexually mature

It is believed that the usual cycle of life-history takes place in the dog and the sheep. Manson suspects the jackal in India as a spreader of the disease to man. Stirling and Verco lay down the following factors as necessary for the spread of the disease:

1. Sufficiency of infected dogs
2. Domestic herbivora, especially sheep as intermediary hosts.
3. Conditions favourable for the transmission of the parasite from the dog to man.
4. Facility of access to dogs of infected carcasses

Perhaps, however, the egg gains access to the human body through contaminated food and dust

Pathogenicity. -The cysts grow but slowly, consequently organs adapt themselves to the pressure, so that the symptoms may be wanting and depend entirely upon whether the organ can or cannot expand

If, however, fluid escapes from a cyst urticarial eruptions, or even rigors, with local pain and tenderness, may result

Prophylaxis. --Prophylaxis must be on the lines indicated by the factors above mentioned -viz., registration of dogs, destruction of pariah dogs, non-feeding of dogs with raw meat, clean kennels, non-handling of dogs.

Echinococcus multilocularis Leuckart, 1863.

Synonym.—*Echinococcus osteokluster* Huber, 1896.

This is the parasite which causes the alveolar or multilocular form of hydatid disease, which is very different from the ordinary form The disease was first observed by Ruysch in 1721, and was generally looked upon as a colloid cancer, until Virchow in 1856 showed that it had its origin in a worm Mangold and Muller consider that by feeding experiments they obtained from it a *Tænia* different from *E. granulosus* in the hooks and the distribution of the ova.

Melnikow-Raswedenkow gives quite a different life-history for this parasite, which, if correct, will make it a new species. Further, there is the support of Stiles, Stirling, Verco, and others for the differentiation of the parasites from one another.

This form of hydatids occurs in man, sheep, and pigs, but principally in large cattle.

The geographical distribution is interesting, it being mostly found in South Germany, Switzerland, the Austrian Alpine region, Russia, and East Siberia, in which districts it occurs in large cattle and man, whereas it is absent from Iceland and Australia and European districts where sheep are common and where the other form is frequently met with

Morphology.– Melnikow-Raswedenkow says that the cysts are composed of parenchyma internally and externally, the latter being in direct contact with the tissue of the host, and producing, it is said, not merely scolices, but immature amœboid embryos, which spread the cyst by continuity, or may enter the blood-stream and form metastases

An amœboid embryo develops into a much-folded chitinous vesicle, having parenchyma both internally and externally This parenchyma produces poisons which act upon the host The cyst is looked upon as the homologue of a ripe proglottis because it can produce living embryos, for the parenchyma can form scolices, immature embryos without a capsule, and mature ovoid embryos enclosed in a chitinous capsule.

The scolices, however, are frequently destroyed by phagocytosis, because they are situated in direct contact with the host's tissue Hence the failure of feeding experiments, as the scolices arrive in the intestine damaged.

The result of this development is to produce a collection of cysts, measuring from 0·1 to 5 millimetres in diameter, embedded in connective tissue. Disintegration may begin in the centre of the masses of the cysts. Whether the *Tænia* obtained by feeding experiments are the same as *T. echinococcus* or not is uncertain.

Pathogenicity. - It produces a primary tumour in the liver, brain, spleen, kidney, or adrenals, with metastases in different parts of the body The symptoms produced vary with the region affected, but eventually, perhaps after years, lead to anæmia, emaciation, and weakness, which cause death.

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CHAPTER XXVI

NEMATHELMINTHES

Nemathelminthes — Nematoda — Anguillulidæ — Angiostomidæ — Gnathostomidæ — Physalopteridæ — Filariidæ — Dracunculidæ — Mermithidæ — Ascaridæ — Oxyuridæ — Strongylidæ — Metastrongylidæ — Trichostrongylidæ — Ankylostomidæ — Eustrongylidæ — Trichinellidæ — Trichurineæ — Gordiacea — Acanthocephala — References

PHYLUM II. NEMATHELMINTHES.

METAZOA, worm-like in form, tubular, or filiform unsegmented, but covered with a cuticle which may be ringed. Without appendages or limbs, but usually with bristles, hooks, papillæ, or, rarely, suckers. Usually with an alimentary canal, but without any closed vascular system, and without respiratory organs. With a complete absence of cilia. Sexes are separate. Usually parasitic through some part of the life-cycle, in which the larvæ develop in a different host or organ from that occupied by the adult. The larvæ may be free and the adult parasitic, or *vice versa*

Remarks.—The Nemathelminthes are extremely important to the student of tropical medicine, for they include some of the most potent agents of disease—*e.g.*, *Ankylostoma duodenale* and the *Filariidæ*. Recent researches have shown that, no matter how common the worm may appear to be, it is advisable to carefully study it, as it has been found that several species and genera have been included in an old species which was thought to be so well known, that nothing new could be discovered concerning it—*e.g.*, *Ascaris*, in examining specimens of which Leiper has separated two new genera.

Classification.—The Nemathelminthes can be divided into two classes:—

CLASS I.—Anterior end not provided with an armed proboscis; intestine present either complete or in part rudimentary.

This class includes two orders:—

Order I. Nematoda.
Order II. Gordiacea.

CLASS II.—Anterior end provided with an armed proboscis; intestine absent.

Order III. Acanthocephala.

CLASS I.

ORDER I. NEMATODA.

Definition.—Nemathelminthes with white filiform bodies, with usually a complete alimentary canal in the adults, but sometimes this may be represented by only an œsophagus and a rudimentary intestine; with papillæ on the head. The male with one testis, a strongly recurved posterior extremity, and usually spicules. The female with a vulvar opening always distinct from the anus. Egg contains ovum only.

Morphology.—The Nematoda are parasitic, as a rule, but minute sexually mature forms can be met with in moist soil all over the world. The body is enclosed in a thick, transparent, smooth, or ringed cuticle, which may form hooks, spines, or lateral fins.

Under the cuticle comes a syncytium called the epidermis, under which is the peculiar muscular layer cut into four quadrants by thickenings of the epidermis, which project inwards, surrounding dorsally and ventrally a nerve cord, and laterally excretory canals. Under the skin comes the large undivided body cavity, which is not of the nature of a true cœlom, as it is not between the two layers of the mesoblast, but between mesoblast externally and hypoblast internally, and contains a fluid which may represent the hæmolymph fluids of higher animals.

The digestive system consists of a mouth situated at the anterior end, and surrounded by two to six lips, which opens into a thick suctorial œsophagus lined with chitin.

The œsophagus opens into the intestine, which is a thin-walled tube lined by a simple layer of endothelial cells, and leads to the short chitinous rectum, which ends in the anus.

The excretory system consists of two longitudinal tubes lying in the lateral line, and uniting anteriorly by a transverse 'bridge' to open in a pore situated in the mid-ventral line just behind the mouth in the region of the nerve ring.

The nervous system consists of a circumœsophageal ring, with six anterior and six posterior nerve trunks.

The sexes are separate. The male reproductive organs consist of one tube divisible into testis, vas deferens, vesicula seminalis, and ductus ejaculatorius, which opens on the ventral surface of the rectum close to the anus, while the posterior end of the body is modified for sexual purpose with alæ and papillæ. The female reproductive organs consist of two much-coiled tubes divisible into ovary, oviduct, and uterus, which join together to form the simple vagina, which opens about the middle of the body in the mid-ventral line; in some instances just in front of the anus, in others, as in the filaria worms, quite near the head

Biology.—They appear to live upon the juices of the part of the body in which they are found. Generally this is the intestine, the contents of which supply them with ample food. But some of them are capable of entering the villi of the intestine.

Life-History.—Sometimes the life-history is fairly simple, or is supposed to be so, for it is possible that we are not well acquainted with details.

Other life-histories are most complicated, and must be dealt with in detail.

Pathogenicity.—Some of the worms are markedly pathogenic, while others usually produce but slight effects.

Classification.—The Nematoda are classified into—The Non-Bursata, comprising the families: (1) Enoplidæ, (2) Anguillulidæ, (3) Angiostomidæ, (4) Gnathostomidæ, (5) Physalopteridæ, (6) Filariidæ, (7) Dracunculidæ, (8) Mermithidæ, (9) Ascaridæ, and (10) Oxyuridæ; and the Bursata, which are subdivided into the Strongyles, comprising the families (11) Strongylidæ, (12) Metastrongylidæ, (13) Trichostrongylidæ, (14) Ancylostomidæ, and the Pseudostrongyles, comprising the families (15) Eustrongylidæ (16) Trichinellidæ, and (17) Trichosomidæ

The Enoplidæ are free-living, and do not concern us.

The following table gives the parasites known in man, excluding a number of doubtful Filariidæ

Division.	Family.	Genus.	Species.
Non-Bursata.	Anguillulidæ .	Anguillula .	1. A. aceti.
		Anguillulina ..	2. A. putrefaciens
		Rhabditis .	3. R. niellyi.
		Leptodera ..	4. L. pellio.
	Angiostomidæ ..	Strongyloides ..	5. S. intestinalis.
	Gnathostomidæ	Gnathostoma ..	6. G. spinigerum.
	Physalopteridæ	Physaloptera	7. P. caucasica. 8. P. mordens.
	Filariidæ . .	Filaria .. .	9. F. bancrofti. 10. F. ozzardi. 11. (F. inermis ?)
		(Microfilaria) .	12. (M.) powelli 13. (M.) philippinensis.
		(Agamofilaria) .	14. (Agm.) conjunctiva 15. (Agm.) labialis. 16. (Agm.) oculi. 17. (Agm.) georgiana.
		Acanthocheilonema	18. A. perstans.
		Dirofilaria .	19. D. magalhaesi.
		Loa	20. L. loa
		Hamularia	21. H. equi.
		Onchocerca .	22. O. volvulus.
	Dracunculidæ ..	Dracunculus	23. D. medinensis.
	Ascaridæ ..	Ascaris .. .	24. A. lumbricoides. 25. A. maritima. 26. (A. texana.)
		Toxascaris .	27. T. canis.
		Belascaris .	28. B. mystax.
		Lagocheilascaris	29. L. minor.
	Oxyuridæ ..	Oxyuris	30. O. vermicularis.
	Eustrongylididæ	Dioctophyme .	31. D. renale.
	Trichosomidæ ..	Trichinella .	32. T. spiralis.
		Trichuris ..	33. T. trichiura.

Division.	Family.	Genus.	Species.
Bursata.	Strongylidæ	Triodontophorus	34. T. deminutus.
		Œsophagostomum	35. Œ. brumpti.
			36. Œ. stephanostomum var. thomasi.
	Metastrongylidæ	Metastrongylus	37. M. apri.
	Trichostrongylidæ	Nematodirus	38 N. gibsoni.
		Hæmonchus	39. H. contortus.
		Trichostrongylus	40. T. colubriformis.
			41. T. probolurus.
			42. T. vitrinus.
			43. T. orientalis.
	Ancylostomidæ	Ancylostoma	44 A. duodenale.
			45. A. ceylanicum.
		Necator	46. N. americanus.

It is not possible at the present moment to give a scientific and easily workable classification of the Nematoda, because the type genera require revision. We group the various families under the following divisions :--

A. *Nematoda* in which the bursa copulatrix is merely a cuticular expansion not supported by true fleshy rays in the males—*Non-Bursata*.

B *Nematoda* with true bursa copulatrix--*i.e*, supported by fleshy rays in the male-*Bursata*

DIVISION NON-BURSATA.

Leiper gives the following table for differentiation of the non-bursate families which are represented in the parasitic nematodes of man:-

A. Œsophagus a simple cellular tube- *Trichosomidæ*

B. Œsophagus a simple muscular bulb:-

(*a*). Mouth surrounded by several protuberances. Male with one spicule; female with one uterus--*Eustrongylidinæ*.

(*b*) Mouth guarded by large fleshy jaws. Male with two spicules: female with two uteri:-

(1) Jaws two in number: skin smooth--*Physalopteridæ*

Jaws two in number; skin spinous--*Gnathostomidæ*.

(2) Jaws three in number. skin striated- *Ascaridæ*.

(*c*) Mouth a simple pore without buccal capsule:--

(1) Female without vagina: embryos striated. Male with two equal spicules- *Dracunculidæ*.

NEMATODE EGGS.

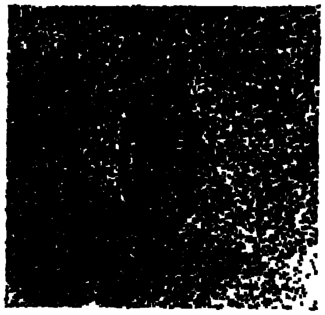


Fig. 255. — *Oxyuris vermicularis* Egg. (× 250.)

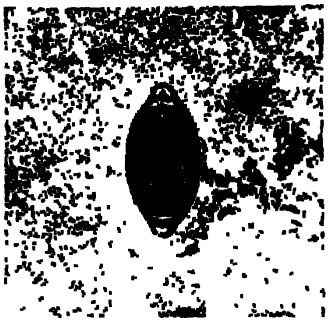


Fig. 256. — *Trichuris trichiura* Egg. (× 250.)

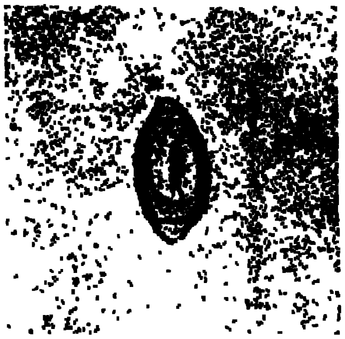


Fig. 257. — *T. trichiura* Egg with Larva. (× 250.)

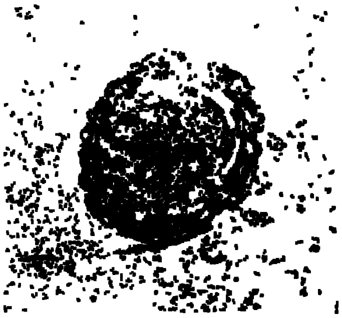


Fig. 258. — *Ascaris lumbricoides* Egg. (× 250.)

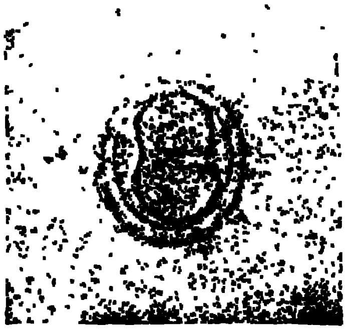


Fig. 259. — *A. lumbricoides* Egg segmenting. (× 250.)

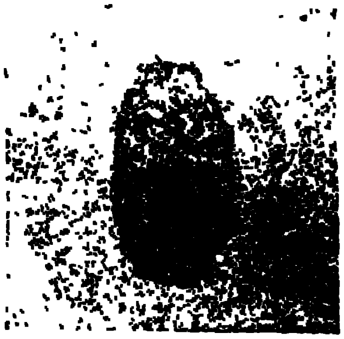


Fig. 260. — *A. lumbricoides* Egg unfertilized.

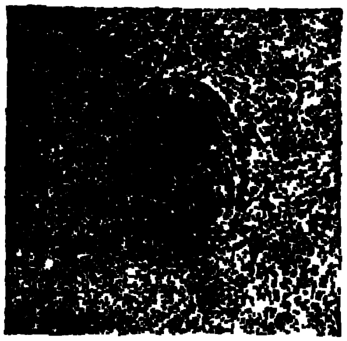


Fig. 261. — *Ancylostoma duodenale* Egg. (× 250.)

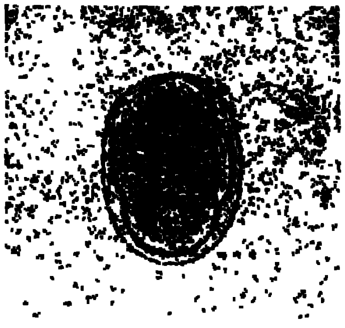


Fig. 262. — *Ancylostoma duodenale* Egg segmenting. (× 250.)

Figs. 255-262.—Nematode Eggs from Human Fæces.

(From photographs by J. J. Bell.)

(2) Female with vagina opening near mouth: uteri convergent: embryos not striated. Male with spicules dissimilar—*Filariidæ*.

(3) Female with vagina in posterior third of body: uteri divergent. Parasitic parthenogenetic adult of *Strongyloides*. [For free-living adults see C (1).]

C. Œsophagus with a double muscular bulb:—

(1) Skin smooth, male with two spicules and accessory piece; female viviparous—Free-living adults of *Angiostomidæ*.

(2) Skin deeply striated, male with one spicule; female oviparous—*Oxyuridæ*.

EGGS OF DOUBTFUL IDENTIFICATION.

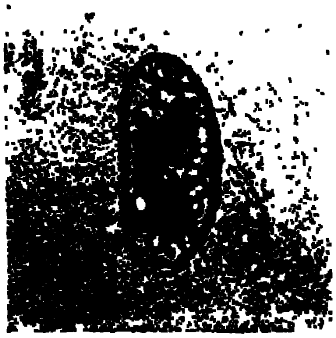


FIG. 263.

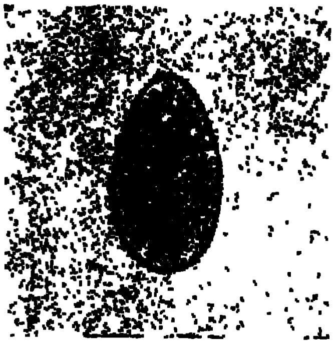


FIG. 264.

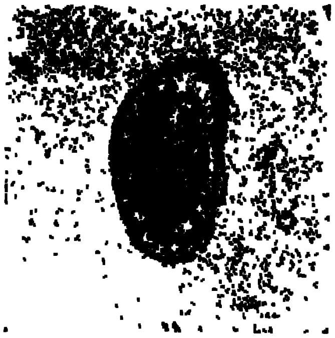


FIG. 265.

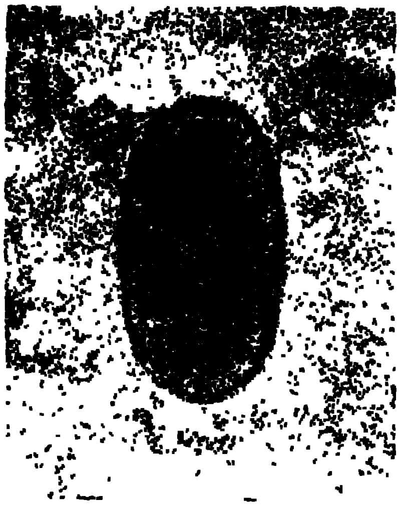


FIG. 266.

FIGS. 263-266.—EGGS OF DOUBTFUL IDENTIFICATION FROM HUMAN FÆCES.

(From preparations and photographs by J. J. Bell.)

FIGS. 263 AND 265.—ABNORMAL EGGS PROBABLY OF *Ascaris lumbricoides*.

NON-BURSATA.

FAMILY 2. ANGUILLULIDÆ.

Very small Nematoda, mostly free-living, rarely parasitic, with an oral cavity armed with a tooth or spine, and an œsophagus with a double dilatation. Male with two spicules, and sometimes a bursa copulatrix. Female with a pointed tail, and a vulva situated in the middle of the body.

Genera.—(1) *Anguillula*, (2) *Anguillulina*, (3) *Rhabditis*, (4) *Leptodera*.

Anguillula Ehrenberg, 1820.

Anguillulidæ with small mouth, œsophagus with two dilatations of which the posterior has valves. Male without bursa, spicules with accessory pieces feather-shaped. Female with the vulva in the hinder portion of the body; uterus asymmetrical.

Anguillula aceti Muller, 1783.

Anguillula aceti is the common vinegar eel, which has several times been reported as occurring in the human bladder, but the method of infection is unknown.

Morphology.—Cuticle not striated, body cylindrical, tapering a little to the anterior, but considerably to the posterior end. Male 1 to 2 millimetres long and 24 to 40 μ broad, with two pre-anal and one post-anal papillæ. Two equal spicules 38 μ long. Female, 2·4 millimetres long and 50 to 72 μ broad. Vulva near the equator. Embryos 222 by 12 μ.

Pathogenicity. Nil.

Anguillulina Gervais and van Beneden, 1859.

Synonym. *Tylenchus* Bastian, 1864.

Anguillulidæ possessing a spine on the oral cavity. Male bursa without papillæ; uterus asymmetrical.

Species.—*Anguillulina putrefaciens* Kuhn, 1879.

Anguillulina putrefaciens Kuhn, 1879.

Synonyms.—*Tylenchus putrefaciens* Kuhn, 1879; *Trichina contorta* Botkin, 1883.

This small nematode lives in onions and it or other varieties may at times find access to the stomach with the food, and be rejected by vomiting as reported by Botkin in 1883.

Rhabditis Dujardin, 1845.

Small Anguillulidæ with no teeth in the oral cavity, with accessory pieces to the two male spicules, and without lateral ridges.

Rhabditis niellyi Blanchard, 1885.

Synonym.—*Leptodera niellyi* Blanchard, 1885.

This parasite was described by Nielly in 1882 in a boy who suffered from an itching papular eruption in Brest, which he had never left.

Morphology.—The parasites measured 0·33 by 0·013 millimetre in width, and possessed a cuticle with delicate transverse striation, a double-bulbed œsophagus, and an intestine, but no genital organs.

Pathogenicity.—The specimens were found in the papules, and also in the blood at the beginning of the illness, but not in the fæces, urine, or sputum.

Life-History. Unknown.

Leptodera Dujardin, 1845.

Anguillulidæ with mouth guarded by two, three, or six lips. Male with or without bursa, which when present, never surrounds the point of the tail. Two equal spicules, and three pre-anal papillæ. Female with the tail prolonged into a long unsymmetrical point.

Leptodera pellio Schneider, 1866.

Synonyms.—*Pelodera pellio* Schneider, 1866; *Rhabditis genitalis* Scheiber, 1880.

Leptodera pellio is merely an occasional parasite in man. Infection arises in rather a peculiar manner. The larva lives in the earthworm (*Lumbricus terrestris*) while the adults exist in decomposing matter in the soil.

The Hungarian peasants use soil for making poultices, from which the little worms apparently make their way into the vaginæ of women and live there. Oerley has shown experimentally that they will live in the vagina of a mouse.

Morphology.—Male, 0·8 to 1·05 millimetres in length, with a bursa supported by seven to ten ribs on each side. Spicules, which are not quite alike measuring 27 to 33 μ in length. Female, 0·9 to 1·3 millimetres in length, with a vulva slightly posterior to the middle of the body.

Pathogenicity. Nil.

FAMILY ANGIOSTOMIDÆ.

Nematoda characterized by heterogony, each species having a free living bisexual rhabdite form and a parasitic hermaphrodite filarial form.

Strongyloides Grassi, 1879.

Synonyms.—*Pseudorhabditis* Perroncito, 1881; *Rhabdonema* Leuckart, 1882.

The parasitic form has an unarmed mouth, long cylindrical œsophagus, which reaches nearly to the middle of the body. The free-living stage has a small mouth, short œsophagus with a double dilatation, in the hinder part of which are small teeth. The male spicules are of equal size.

Strongyloides stercoralis Bavay, 1877.

Synonyms.—*Anguillula intestinalis et stercoralis* Bavay, 1877; *Leptodera intestinalis et stercoralis* Cobbold; *Pseudorhabditis stercoralis* Perroncito, 1881; *Rhabdonema strongyloides* Leuckart, 1883; *R. intestinale* Blanchard, 1886.

History.—This little worm, which is not uncommonly met with in fæces, was first described in 1876 by Normand in the fæces and the intestine of French soldiers just returned to Toulon from Cochin China.

At first it was thought that there were two species—one in the fæces (*Anguillula stercoralis*) and the other in the bowel (*A. intes-*

tinalis)—but Leuckart showed that they were but succeeding stages of one life-cycle. It is found in Europe, Africa, India, Ceylon, Indo-China, China, the Philippines, Oceania, the United States, the West Indies, and Brazil.

The fully-developed worm is found in the duodenum and jejunum, into the mucosa of which it has bored its way deeply.

Morphology.—The parasitic adult worm is very small—2·2 millimetres long and 34 μ broad – with a finely striated cuticle, and a mouth surrounded by four lips, leading into a cylindrical œsophagus, equal in length to one-quarter of the whole body. The anus is just in front of the tip of the tail. Inside this parasite can be seen ellipsoidal eggs. The sex of this parasite is doubtful. Is it a hermaphrodite, in which the male organs, after serving their purpose, have degenerated, or is it a parthenogenetic female? At present these questions cannot be answered definitely. Most probably it is a hermaphrodite. The eggs measure 50 to 58 μ in length by 30 to 34 μ in breadth, and are arranged in strings surrounded by a delicate tubular structure. They occur in the fæces only during attacks of diarrhœa.

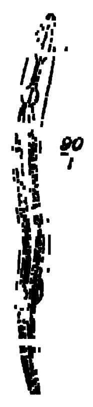


FIG. 267.—RHABDITIFORM EMBRYO OF *Strongyloides intestinalis* BAVAY AS FOUND IN HUMAN FÆCES. (After Looss.)

Life-History.—The eggs are oviposited into the mucosa of the host's intestine, and the embryos hatch and find their way into the lumen, and are evacuated with the fæces. On reaching water or moist earth these embryos grow into adult male and female forms, which conjugate, and then the female lays eggs. The eggs produce free-living rhabditiform embryos, which moult and turn into filariform embryos, which have been shown by Mozocchi and van Durne to penetrate the skin, not through the hair-follicles, but through the horny layer into the rete Malpighii, and so into the corium. The experiments of Fülleborn and V. Schilling-Torgau in infecting tracheotomized dogs or dogs with the œsophagus cut and fixed to the skin with larvæ of *Strongyloides stercoralis* Bavay, 1877, have shown that the more important route is from the skin to the lungs and so via the trachea and œsophagus to the bowels, while a less important route from the skin via the blood-stream directly to the bowel can also take place (*vide* the life-history of *Ancylostoma duodenale*, p. 663). On arrival in the intestine they burrow into Lieberkühn's follicles, and begin to lay their eggs.

Pathogenicity.—The parasite is generally believed to cause a catarrh of the small intestine, though many believe it to be non-pathogenic.

FAMILY 4. GNATHOSTOMIDÆ.

Nematoda, with two large lips and the whole or only the anterior part of the body covered with minute ramified spines. They live often in the tumours in the gut wall of vertebrates, especially mammals.

Two genera: *Gnathostoma* Owen, 1836, and *Tanqua*.

Gnathostoma Owen, 1837.

Synonyms.—*Cheiracanthus* Diesing, 1839; *Liorhynchus* Rudolphi.

Definition.—With the characters of the family.

Remarks.—The genus comprises only intestinal parasites, of which nine species are known in man, alligators, cats, tigers, pigs, etc.

Gnathostoma spinigerum Owen, 1837.

Synonyms.—*Cheiracanthus siamensis* Levinsen, 1889; *Gnathostoma siamense* Levinsen, 1889; *Cheiracanthus robustum* Diesing, 1839.

Remarks.—Only two specimens are known, one a female, which was obtained by Deuntzer from a young Siamese woman in whose breast a hard painful swelling had formed, accompanied with slight fever, and another a male described by Leiper. Nodules the size of beans appeared in the skin, from one of which the worms were extracted. Two other similar cases have recently been reported. Leiper has recently compared a male specimen from man with typical specimens of *G. spinigerum* of the tiger, and declares them to be identical.

Morphology.—*Male.*—10·55 millimetres long by 0·6 millimetre broad, with the anterior half of the body quite straight and terminating in a globular swelling, which carries two large fleshy lips which guard the mouth. Neck only 0·3 millimetre in diameter. In front of the neck the cuticle is provided with eight transversed rows of chitinous hooks, with their points directed backwards. Behind the neck the cuticle has many cuticular laminæ, but the posterior half of the body is without armature.

The mouth is simple, without a vestibule. The paired labial glands open on the lips already mentioned. The œsophagus is 2·4 millimetres long and very muscular, and opens into the chyle intestine, which, being uniformly 0·25 millimetre broad, is with difficulty separated from the rectum, which leads to the cloaca.

There are two pre-anal and two post-anal large nipple-like genital papillæ around the cloaca, and though the cuticle is folded there is no bursal formation; but there are two unequal spicules, 1·1 millimetres and 0·4 millimetre long. There is a distinct muscular ejaculatory duct, 1·5 millimetres long.

Female.—Nine millimetres long by 1 millimetre broad, with eight rows of bristles around the head and spines covering the anterior third of the body. Each spine ramifies into three points, of which the middle is the longest. The anterior end was narrow and the mouth appeared to be bordered by two lips. The posterior end had a three-lobed prominence, at the base of which the anus opened.

Habitat.—Subcutaneous tumours in man in Siam. Allied species live in the stomach of pigs and oxen. The species is said to occur in the pariah dogs of Calcutta.

Pathogenicity.—Man is apparently an aberrant host, for in man only do the worms wander into the connective tissue and form subcutaneous tumours. The species normally lives in the stomach of animals, causing fibrous thickenings.

FAMILY 5. PHYSALOPTERIDÆ.

Physaloptera Rudolphi, 1819.

Physalopteridæ possessing mouth with usually two lips, each with papillæ and teeth. Posterior end of the male lancet-shaped, owing to a widening of the cuticle. The ventral aspect is here covered with cuticular plates, and there are four pairs of pedunculated external papillæ and a number of sessile internal papillæ and unequal spicules. Female; vulva situated anteriorly. Eggs thick-shelled and smooth.

Physaloptera caucasica von Linstow, 1902.

This has only been found once by Ménétries in the alimentary canal of man in the Caucasus.

Male 1·42 millimetres long by 0·71 millimetre broad. Female 27 millimetres long by 1·14 millimetres broad. Eggs 57 by 30 μ.

Physaloptera mordens Leiper, 1907.

Leiper has recently described a large number of cases of infection with *Physaloptera* in natives of tropical Africa, which differed from *P. caucasica* not only in size, but in the length of the spicules in the male.

FAMILY 6. FILARIIDÆ Claus, 1885.

Synonyms.—*Filaridea* Carus, 1863; *Filariadea* Leuckart, 1876; *Filaridæ* Cobbold; *Filarides* Assenova, 1896.

Definition.—Long filiform nematodes with uniform diameter, and a straight head provided with two latero median and four submedian papillæ. Mouth terminal, with two lips, and occasionally a more or less distinct buccal capsule. Œsophagus slender, elongated, and may be divided into two portions, but has no posterior bulb. Mid-gut present, rectum present, anus subterminal.

Males with one or two unequal spicules and a spirally recurved tail, provided with papillæ, and in some cases with lateral alæ. Females larger than the males, with or without a vulva in the gravid worms, which, when present, is situate anteriorly. Uterus usually double. All species parasitic and ovoviviparous, with a change of host in at least certain species.

Type Genus.—*Filaria* Muller, 1787.

The genus *Filaria* was created by Muller in 1787, unfortunately without naming a particular type, which Stiles suggests should be *Filaria martis* Gmelin, 1790 (*F. perforans*). This is found in *Mustela martes* L., the pine marten of Europe, and was one of the parasites originally described by Müller. This parasite requires to be restudied before definite characters can be given for the genus.

Classification.—The subfamilies are *Filariinæ* and *Onchocercinæ*.

SUBFAMILY FILARIINÆ Stiles, 1907.

Filaria Müller, 1787.

Definition.—This is doubtful. Filariidæ with long slender filiform bodies; anterior extremity attenuated, obtuse; posterior very attenuated, more so than the head. Cuticle without transverse striation, and without bosses. Male shorter than the female, with spirally bent tail provided with lateral cuticular alæ, pre- and post-anal papillæ, and unequal spicules. Females longer than males, with vulva situate anteriorly near the mouth.

Synonyms.—*Fileraria* Rudolphi, 1809; *Filaire* Lee, 1840; and some misprints.

Type.—*F. martis* Gmelin, 1790.

Species.—*F. bancrofti* Cobbold, 1877; (?) *F. demarquayi* Manson, 1895.

Some years ago the genus *Filaria* contained a large number of species parasitic in man, but the following genera have definitely been separated from *Filaria*: *Acanthocheilonema*, *Dirofilaria*, *Dracunculus*, *Onchocerca*, and *Hamularia*. At the present time there are only three species known to be human parasites, which are referred to the genus *Filaria*—viz., *F. bancrofti* Cobbold, 1877; *F. ozzardi* Manson, 1897; and *F. inermis* Grassi, 1888; in addition to the embryonic forms included in the collective group (*Microfilaria*) and the immature forms in the collective group (*Agamofilaria*). There are, however, a number of spurious or doubtful forms scattered throughout medical literature and described as human parasites which must be eliminated from the genus, and these are:—

1. *Filaria* (?) *hominis oris* Leidy, 1850.—This probably belongs to the Mermithidæ and may have been a mermis accidentally taken into the child's mouth while eating, say, an apple, because it had an obtuse posterior extremity with a recurved hook.

2. *Filaria* (?) *gigas* Prout, 1902.—Two embryonic *filarial* structures 220 to 340 μ by 8 to 12 μ, found with rounded head and tapering tail ending bluntly, no sheath; stained readily with fuchsin. Low thinks that these might be contaminations—*i.e.*, insect hairs; Looss thinks that they may be cast skins, and as Stiles has also adopted this view the parasite may perhaps be eliminated. Recently Leiper has considered it to be a stained fungoid growth.

3. *Nematoideum tracheale* Cobbold, 1864.

The following can certainly be eliminated:

4. *Filaria* (?) *restiformis* Leidy, 1880, as this is *Agamomeris restiformis*, and belongs to the Mermithidæ.

5. *Filaria* (?) [illegible]. Stiles believes this to be merely *Oxyuris vermicularis*, it may be the embryo of a *Filaria*.

6. *Filaria* (?) *niellyi* is *Rhabditis niellyi*.

7. *Filaria* (?) *zebra* Mon Grand, 1852, is said to be a fibrinous clot, and therefore a species *fictitia*.

The following may have to be eliminated:—

8. *Filaria* (?) *kilimaræ* Kolb, 1898.—These consist of several female specimens once found free in the abdominal cavity of a fallen Kitu warrior. Oral papillæ are said to have been like *Dracunculus medinensis*.

They were 10 to 20 centimetres in length, and 0·5 to 1 millimetre in diameter, white, and resembled *Gordius aquaticus* in general appearance.

With these Kolb classified free-living worms, and therefore doubts are held as to the exact zoological determinations of the species recorded.

9. *Filaria* (?) *romanorum orientalis* Sarcani, 1888.—Observed in the blood of a Roumanian woman; 1 millimetre long by 0·3 millimetre broad, with intestine and generative apparatus developed; believed by some to be an adult threadworm.

The uncertain species are:—

1. *Filaria Species* (?) Cholodkowsky, 1896.—Found in whitlow-like tumours on the fingers of peasants in the Twer Government.

2. *Filaria Species* (?) Prout, 1902.

3. There was a parasite called *Spiroptera hominis* Rudolphi, 1819, which appears to have been spurious, being really *Filaria communis*, of which *Filaria piscium* is a synonym.

Filaria bancrofti Cobbold, 1877.

Synonyms.—*Trichina cystica* Salisbury, 1868, *nec* Rudolphi, 1819; *F. sanguinis hominis* Lewis, 1872; *F sanguinis hominis ægyptiaca* Sonsino, 1874; *F. dermatemica* da Silva Araiyo, 1875; *F. wuchereri da* Silva Lima, 1877; *F. sanguinis hominum* Hall, 1885; *F. sanguinis hominum nocturna* Manson, 1891; *F. nocturna* Manson, 1891.

History.—The *Microfilaria* was discovered in Paris by Demarquay in August, 1863, in the chylocele fluid of a patient from Havana. In 1866 Wucherer found it in Brazil in the urine of patients suffering from chyluria. In 1872 Lewis made the important observation that its true anatomical habitat is the blood. Bancroft, in 1876, discovered the adult female form; Bome, in 1888, discovered the adult male. In 1899 Manson discovered that the *Microfilaria*, on disappearing from the peripheral circulation, resorted to the lungs during the day-time. The parasite is spread by mosquitoes, as discovered by Manson in 1878, who thought that the *Filariæ* escaped from their insect hosts into water, and reached man by this means. Later Bancroft conjectured that *Filariæ* might be inoculated directly into man, and about this time sent infected mosquitoes to Manson in London. Bancroft's material was investigated, at Manson's request, by Low, who discovered that the *Filariæ* migrate to the mouth-parts of their insect hosts after a period of growth within the musculature. A little later, independently, James made the same discovery in India. In the meantime Grassi and Noè investigated the life-history of a corresponding *Filaria* of the dog (*D. immitis*), and demonstrated that it undergoes a similar development also in mosquitoes, choosing, however, the Malpighian tubes instead of the thoracic muscles as the seat of their development. Moreover, Grassi and Noè were successful in inoculating normal dogs by means of mosquitoes fed on infected dogs. Fülleborn and Bahr have most carefully re-studied the subject.

Morphology- *General Characters* The worms are whitish in colour, long, and filiform, with a smooth cuticle, and a globular head terminating in a simple, circular, unarmed, lipless mouth. The tail is rounded.

Sexual Characters.- The male is smaller than the female, and a complete specimen measures on the average 38 millimetres in length and 0·12 millimetre in thickness. In the dead worm the tail is spiral or much incurved, but may be straight during life, according to Maitland. The anus, which is 0·13 millimetre from the posterior extremity, is guarded by two projecting lips. The anal papillæ are not easily defined, but are said to consist of three pairs of pre-anal and three of post-anal papillæ. Leiper has recently figured fourteen pairs.

There are two unequal curved retractile spicules. The larger measures 0·6 millimetre and the smaller 0·2 millimetre in length. They consist of a basal portion, which is broad, rigid, and chitinous, measuring 0·17 millimetre in the larger and 0·12 millimetre in the smaller spicule, and a long, thin, colourless, cylindrical, slightly undulating terminal portion.

The female, while more or less transparent, is longer and thicker than the male, and measuring 76 to 100 millimetres in length, with a thickness of 0·185 millimetre.

The mouth is situated at the anterior extremity, being 8 μ in diameter, and leading into an œsophagus which passes insensibly into the intestine. This terminates in the anus, situated 0·28 millimetre from the incurved posterior end.

The vulva, situate 1·2 millimetres from the anterior extremity, opens into a single vagina, from which two uterine tubules run along most of the length of the body. These tubules contain the eggs and embryos in various stages of development.

Cobb's formula is:-

$$\frac{0\cdot36,\ 3\cdot04\ (?),\ 1\cdot22,\ 99\cdot5}{0\cdot145,\ 0\cdot377\ (?),\ 0\cdot254,\ 0\cdot147}.$$

The numerator indicates lengths from the anterior extremity to (1) base of œsophagus; (2) nerve ring, (3) posterior pharyngeal construction; (4) vulva in females or middle in males, (5) anus. The denominator represents transverse measurements at the same levels. All measurements are expressed as percentages of the total length. At the present time Cobb's formula is not accepted as a reliable guide to the parasitic species.

Life-History.- The males and females may be found coiled together in the lymphatics of the scrotum, the arm, the leg, hydroceles of the cord, epididymis, or testicle, and more rarely in those of the pelvis and abdomen. The males are less numerous than the females.

When placed in saline solutions, they show active movements, coiling and uncoiling themselves for several hours.

In the uterus of the female, as has already been stated, eggs may be noted in all stages of development.

At first nearly round, measuring 50 by 34 μ, and containing a coiled up embryo, the eggs become more and more elongated by the movements of the embryo, until in the anterior part of the uterus they are much longer than broad. Finally, they escape through the genital pore, and enter the lymph-stream, along which they travel through lymphatic vessels and glands, the thoracic duct, the right side of the heart, and the lungs, to reach the peripheral circulation, where they are best seen at night; hence the name *Microfilaria nocturna*. In the blood they appear as little wriggling filiform bodies, knocking the corpuscles about, but not moving from the position in which they are lying. The *Microfilaria* in the blood are said to be a little larger than those in the uterus, which is thought by Penel to be due, not to growth, but to inhibition of fluid by osmosis.

They measure from 290 to 320 μ in length and from 7·5 to 8·4 μ in breadth (Low), and are seen to be long, slender, cylindrical organisms with a rounded anterior and a tapering posterior end, enclosed in a sheath—the vitelline or egg membrane—inside which they are capable of darting backwards and forwards, because it is longer than they are, the empty portion being noted either in front of the anterior or behind the posterior end of the *Microfilaria*. Manson considers that this sheath is of vital importance to the little parasite, as it prevents its using its anterior spine to escape out of the blood-vessel, and so losing the chance of its invading a mosquito.

The anterior rounded extremity is said to possess a thick hemispherical proboscis, carrying a minute apical spine, which is capable of being covered by a retractile and protractile six-lipped prepuce, but this observation requires confirmation.

Behind the anterior end, the body can be seen to be composed of a transversely striated dermo-muscular layer, inside which are a number of closely packed cells whose nuclei show up clearly on staining. Unstained, the central mass appears granular, but the granules are, however, wanting at certain spots, which, following Annett, Dutton, and Elliot may be defined as: (1) A clear anterior area from the front to the first nuclei, (2) an irregular transverse spot situated 21·5 per cent. of the length of the body from the anterior end; (3) a V-shaped or transverse irregular spot at 30 per cent. of the length, called V-spot by Manson; (4) a median line, the central viscus of Manson, whose centre is at 63 per cent. of the length; (5) an irregular oval spot often present at 85 per cent., called the tail-spot by Manson; (6) a small central spot only occasionally present at 91·7 per cent.; (7) the clear posterior area behind the last nucleus.

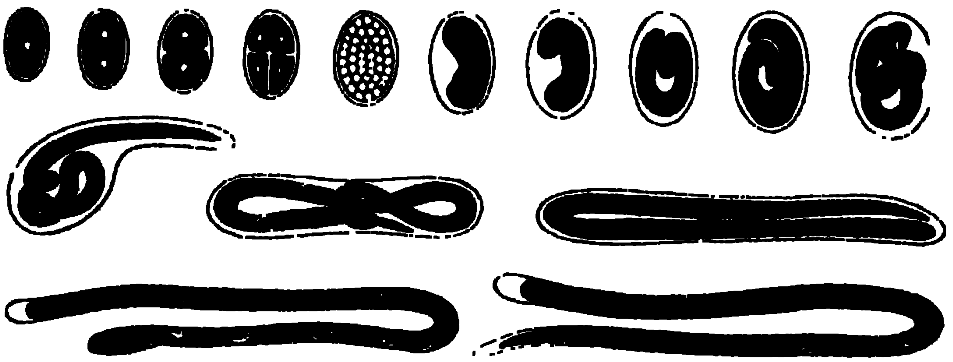


FIG. 268.—DIAGRAM OF THE DEVELOPMENT OF A MICROFILARIA (*Loa loa* STILES).

(After Penel.)

Leiper points out that these areas are not peculiar to the Filaria embryos, but occur also in other forms. The V-spot is the excretory vesicle and the tail-spot the proctodæum. The morphology of the worm has been studied in detail by Fülleborn, whose diagram is reproduced on p. 637.

These *Microfilariæ* occur in the peripheral blood at night, as has just been stated, beginning about 5 to 7 p.m., and increasing in numbers till midnight, and then diminishing till about 7 to 8 a.m., when only a stray one may be met with, as, indeed, can be observed all through the day until the evening increase begins. There is, therefore, a definite periodicity—at night the *Microfilariæ* abound in the blood, while in the day-time they do not.

In the day it appears that they live mostly in the lungs and in the large vessels of the thorax. This was shown by Manson by the careful examination of films and sections taken from the different organs of a man who had *Microfilaria bancrofti* in his peripheral blood, as well as a lymph scrotum and varicose groin glands. The post-mortem was made six hours after death, which took place almost instantaneously at 8.30 a.m., being due to drinking hydrocyanic acid. By far the largest number of parasites were to be found in the lungs and carotid artery, and then in the heart muscle, while a few were found elsewhere, especially in the kidney.

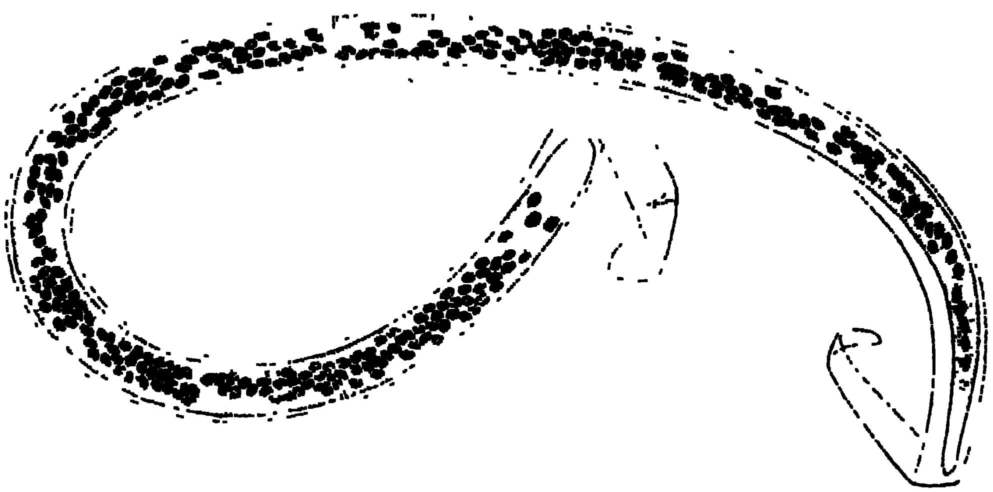


Fig. 269.—*Microfilaria bancrofti* Cobbold.

These facts have been confirmed, but the question as to what induces the parasites to live in the peripheral blood in the night and the thoracic organs in the day is not clear. True, it enables the *Microfilaria* to enter the mosquito, but that does not explain the problem. Neither variations in atmospheric temperature nor in pressure, in light, or in darkness seem to have any effect. Nor does the pulse-rate or the individual's temperature make much difference; but there is one factor, first shown by Mackenzie and since confirmed by Manson and others, that it is in some way connected with sleep; for if a person with *Microfilariæ* in his blood stays awake all night and sleeps during the day, the parasites will abound in his blood in the day, and not at night. Penel remarks that the problem of the periodicity of the *Microfilaria* and the periodicity of sleep in man are connected, and that when one is properly solved the other will also be elucidated.

Recently Bahr has shown that the microfilaria of *F. bancrofti*

in Fiji does not develop so well in *Culex fatigans* as it does in *Stegomyia pseudoscutellaris* Theobald, 1910.

This latter mosquito feeds only by day, and in Fiji Bahr has found that the microfilaria occur in the peripheral blood both during the day and during the night, and believes that the periodicity usually observed in the microfilaria is dependent upon the habits of the insect host.

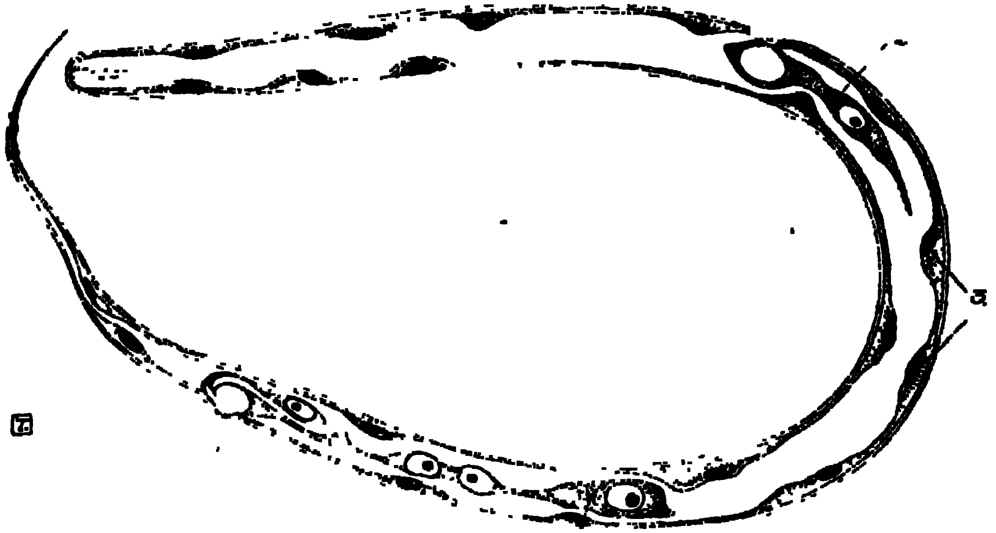


FIG. 270.—SCHEME OF THE STRUCTURE OF A MICROFILARIA, SHOWING (1) THE EXCRETORY PORE, (2) THE CELLS, WHICH WILL FORM THE EXCRETORY APPARATUS, (3) THE SUBCUTICULAR CELLS, (4) THE GENITAL CELLS; (5) ANUS.

(After Fulleborn.)

The number of *Microfilariæ* in the blood varies from very few up to quite considerable numbers, reaching, according to Manson, up to 500 in a single film, which gives some 40,000,000 to 50,000,000 in an average-sized man. This naturally raises the question of, How many adults do these come from? How long does an adult live? How long does a *Microfilaria* live? What finally happens to the *Microfilaria*?

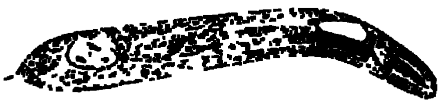


FIG. 271.- EARLY STAGE OF THE DEVELOPMENT OF *Filaria bancrofti* COBBOLD IN THE MUSCLES OF *Culex fatigans*.

(After Looss, from Mense's 'Tropenkrankheiten.)

It would seem probable that a given *Filaria* can live several years in the human body, and, of course, give rise to many embryos. Further, numbers of *Filaria* can be met with in one individual.

Fülleborn has shown that *Microfilariæ* can live in the blood for several months, and observers have thought that they may be destroyed by leucocytes and endothelial cells. It is, however, evident that they develop no further in the human body, and require to be taken into the body of a mosquito before further development is possible.

In the Mosquito.—Abounding as they do in the peripheral blood at night, there is no difficulty for the *Microfilariæ* to reach the stomach of a mosquito in the tropics, and here and in its thorax development proceeds.

The mosquitoes known to be capable of serving as efficient hosts for this development are: *Culex fatigans* Wied in the West Indies, *Myzomyia rossii* Giles in India, *Pyretophorus costalis* Loew in Nigeria, *Panoplites africanus* in Central Africa

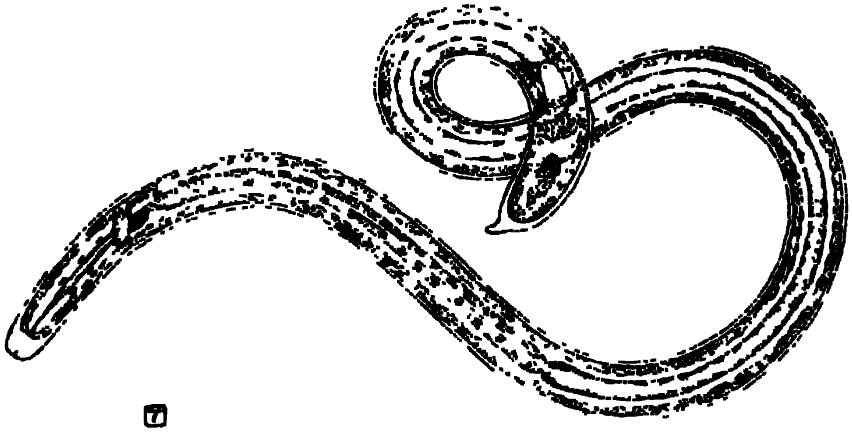


FIG. 272.—LATE STAGE OF THE DEVELOPMENT OF *Filaria bancrofti* COBBOLD IN *Culex fatigans*.

(After Looss from Mense's 'Tropenkrankheiten.')

Incomplete results have been obtained with *Culex microannulatus*, *C. albopictus*, *C. teniatus*, *Cellia albimana*, and negative results in *C. notoscriptus*, *C. annulirostris*, *C. hispidosus*, *C. vigilax*, *C. nigrithorax*, *C. procax*, *A. musivus*, *Myzomyia funesta*, *A. maculipennis*, *Pulex serraticeps*, *Stomoxys* (?), *Clinocoris lectularius*.

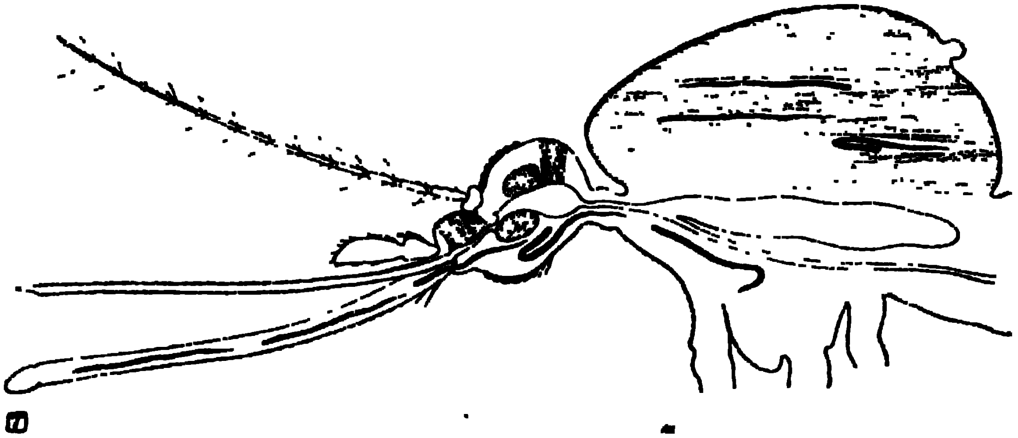


FIG. 273.—DIAGRAM OF THE DEVELOPMENT OF *Filaria bancrofti* COBBOLD IN THE THORAX, HEAD, AND LABIUM OF A MOSQUITO.

The *Microfilaria* enter with the blood into the mosquito's stomach, and there escape from the sheath by rupturing it at the anterior extremity.

They then pierce the wall of the stomach, and find their way into the muscles of the thorax, where they grow considerably till 1·5 millimetres long and 0·25 millimetre broad.

They also undergo development, obtaining an alimentary canal and a three-lobed tail. When so far developed, they leave the thorax and pass through the prothorax and head into the labium, where they remain until the mosquito bites a man, when they escape into the skin by making their way through Dutton's membrane, which is a thin membrane between the labella and the chitinous skeleton of the labium, as was demonstrated by Lebredo. (For further details see Chapter LXVI.)

Their further development in man is not known, but in due course they become adults.

Pathogenicity.—Usually non-pathogenic, these worms under certain circumstances can cause elephantoid fever, elephantiasis, lymph scrotum, etc., or, in other words, filariasis.

Filaria taniguchi Penel, 1905.

This *Filaria* was found in a lymphatic gland from a person living in Aida Kusha in Japan. Only the female and the microfilaria are known.

The former measured 68 millimetres in length and 0·2 millimetre in breadth, and had a non-striated cuticle, a terminal mouth with two pairs of papillae, an anus 0·25 millimetre in front of the posterior extremity, and a vulva 1·5 millimetres behind the mouth.

The latter measured 104 μ long by 8 μ broad, possessed a sheath and a truncated tail, and showed a nocturnal periodicity. Leiper regards this species as the same as *F. bancrofti*.

Life-History.—Not known.

Pathogenicity.—Not known.

Filaria ozzardi Manson, 1897.

Synonyms.—*Filaria ozzardi* Manson, 1897; *F. juncea* Railliet, 1908.

In 1895 Manson discovered a microfilaria in blood-films from natives of St. Vincent in the West Indies, which he named *Filaria demarquayi*, after the discoverer of the microfilaria of *F. bancrofti*. In 1897 he found in blood films from Carib Indians of British Guiana another microfilaria, which is the same as that called *F. demarquayi*, but which he provisionally considered to be a different species, and called *F. ozzardi*. The name *demarquayi* is preoccupied

Lately Penel and Manson have come to regard them as identical. Galgey found the adult females in the West Indies.

It is found in St. Vincent, Dominica, Trinidad, St. Lucia, in the West Indies, and in British Guiana, where it is found in jungly districts. The adults live in the connective tissue at the root of the mesentery and elsewhere.

Morphology.—The male has not yet been described, and only a fragment of a posterior end has been found. The female measures 65 to 80 millimetres in length and 0·21 to 0·25 millimetre in breadth, with a bulbous cuticular expansion at the tip of the tail. Anus 0·25 millimetre in front of the posterior extremity, vulva 0·71 millimetre behind the anterior end.

Life-History.—The egg develops into a microfilaria which has no sheath, shows no periodicity, and measures 200 μ by 5 μ. Its tail is tapering and sharp pointed, and it moves actively. Nothing further is known as to the life-history.

Pathogenicity.—Nil.

Filaria inermis Grassi.

Synonyms.—(?) *Hamularia lymphatica* Treutler; (?) ***Filaria palpebralis*** Pace, 1867; (?) *Filaria labialis*, etc.

Several female filaria worms have been described from Southern Europe as occurring in subcutaneous swellings in various parts of the body in man and horses. These resemble the forms recorded by Addario and Alessandrini under the name *Filaria conjunctivæ*, but differ, however, in the position of the vulva.

(Microfilaria) Le Dantec, 1904.

A collective group of the larvæ of unknown adult Filariidæ found in the blood of man and other vertebrates.

(Microfilaria) powelli Penel, 1905.

This microfilaria was found by Powell in 1903 in the blood of a Bombay policeman.

It showed a nocturnal periodicity (?), was provided with a sheath, measured 131 μ by 5·3 μ, and had a truncated tail.

(Microfilaria) philippinensis Ashburn and Craig, 1906.

Ashburn and Craig described this blood filaria in May, 1906. It measures 0·29 to 0·335 millimetre in length, has no periodicity, is actively and progressively motile, and is enclosed in a tight fitting sheath, within which it cannot slip backwards and forwards, and which is only clearly seen at the extremities. The anterior extremity is broad, with a serrated prepuce, and supports a small retractile spicule. The body has an outer striated musculo cutaneous coat and an inner clear portion, with an anterior **V**-spot situate 0·105 millimetre from the anterior end, and piercing the outer coat by its apex, and opening on the surface.

The central viscus is seen as a convoluted or spiral tube in the posterior part of the middle third of the body. The tail-spot is in the centre of the posterior third of the body, and opens by the apex of its **V** on the surface, where there is a distinct papilla. The tail begins to taper at a point midway between the tail-spot and the posterior end, and ends in a fine threadlike point. It is thought that this end disappears during later development.

The column of nuclei runs the whole length of the worm, being broken by unstained areas here and there. In stained species the **V**-spots and central viscus are not seen.

Life-History.—This microfilaria develops in *Culex fatigans* Wied. On entering the stomach of the mosquito it escapes from its sheath within twenty-four hours, and has pierced the stomach-wall and appeared free in the cœlom, where many die, but others develop rapidly, and complete their mosquito cycle. Generally by the third day they have left this position and travelled into the thoracic muscles, where they develop. At first there is a decrease in length from 0·32 to 0·21 millimetre, but an increase in breadth from 0·0065 to 0·01 millimetre.

By the eighth day the *Filaria* has increased in length and breadth, and shows an alimentary canal along its whole length.

From this till the eleventh day the development is rapid, and the worm now measures from 1·2 to 1·6 millimetres in length by 0·04 to 0·02 millimetre in breadth, and has a mouth, œsophagus, chyle intestine, and an anus, and the tail has three well-defined papillæ.

From the eleventh to twelfth day the worms are found in the head, and by the fourteenth to fifteenth day in the labium, lying side by side, with their heads pointing forwards.

Remarks.—There appears to be every reason to consider this microfilaria as merely the microfilaria of *F. bancrofti* Cobbold, 1877, because, as Low and Bahr have pointed out, they are morphologically identical, while both nematodes live in the tissues and are associated with the same pathological signs. Finally, the same mosquito, *Stegomyia pseudoscutellaris* Theobald, 1910, is an efficient host for both. Bahr suggests that the loss of periodicity is, probably, a partial adaptation to the habits of the intermediary host, *S. pseudoscutellaris*, which only feeds by day. This correlationship between parasite and host Sambon has long insisted upon.

(Agamofilaria) Stiles, 1906.

A purely collective group, made to contain agamic forms of Filariidæ which have not yet reached a stage in their development permitting their generic determination.

Species.—(*Agamofilaria*) *conjunctivæ* Addario, 1885; (*A.*) *labialis* Pane, 1864; (*A.*) *georgiana* Stiles, 1906; (*A.*) *oculi* Diesing, 1851; (*A.*) *palpebralis* Pace, 1867.

(Agamofilaria) conjunctivæ Addario, 1885.

Synonyms.—*F. peritonei hominis* Babès, 1880, *F. inermis* Grassi, 1887, *F. apapillocephala* Condorelli Francaviglia, 1892.

Remarks.—This worm was first discovered by Dubini in the eye of a man in Milan, then by Babès in the gastro-splenic omentum of a woman in Budapest, then by Vadela in the conjunctiva of a woman in Sicily. Perhaps *F. palpebralis* Pace, 1867, and *F. oculi humani* van Nordmann belong to this group. It is possible that the *F. loa* described in India was one of these parasites.

Morphology.—Several females are known. It is white in colour and measures 16 to 20 centimetres in length and 0·5 millimetre in breadth. The cuticle is striated except just around the mouth, but there are neither papillæ nor lips. The anus is subterminal, and the vulva close behind the mouth. There is a single vagina and a double uterus containing eggs and embryos.

Graham Forbes has recently recorded a male specimen from a soldier in Macedonia.

Life-History and Pathogenicity.—Intermediary is unknown. The worms produce subcutaneous tumours.

(Agamofilaria) labialis Pane, 1864.

This parasite was extracted from a small pustule on the inner surface of the upper lip of a person in Naples in 1864, and was not again described until Pierantoni, in 1908, again found it occurring in Naples. In both cases the female has been found, varying from 130 to 30 millimetres in length, with a whitish-yellow body, and a pointed anterior extremity, on which the terminal mouth, guarded by four papillæ, opens. The anus opens 150 µ anterior to the posterior end, and the vulva opens 3 millimetres behind the anterior extremity. The uterus bifurcates into two branches.

(Agamofilaria) georgiana Stiles, 1906.

These immature *Filariæ* were obtained by Graham from a sore on the leg of a negress at Darien.

They were cylindrical in shape, with a more or less uniform diameter, gradually attenuating towards both extremities. Mouth terminal, central, circular, small, unarmed, and surrounded by six papillæ, four of which were prominent and sub-median; two were smaller and latero-median. Anus a transverse slit, situated from 64 to 128 µ from the posterior end. Tip of the tail, with conical projections, 8 to 13 µ in length by 4 µ in breadth. Excretory pore 0·432 to 0·520 millimetre from anterior end.

Cuticle without striation, except some very fine transverse lines near the anus. Median lines visible in glycerine specimens. Lateral bands rather prominent, with longitudinal, sinuous ridges hanging into the body cavity, and with longitudinal canal emptying into excretory pore. Œsophagus simple, 2·5 to 2·9 millimetres in length, triradiate on section. Chyle intestine straight. Rectum 200 µ long. Body-cavity almost completely occupied by the intestine, lateral longitudinal glands, and reticular formation, which is probably the primordium (*Anlage*) of the genital apparatus.

(Agamofilaria) oculi von Nordmann, 1832.

Synonyms.—*Filaria oculi humani* von Nordmann, 1882; *F. lentis* Diesing, 1851.

These are immature filarial worms, found in cataracts by von Nordmann, Gescheidt, and Kuhnt. Braun rejects those by Quadri, Fano, Schoeler, and Everbusch. The common error here appears to be to mistake the remains of the hyaloid artery for a parasite. The worms measured from 0·38 millimetre up to 12·0 millimetres in length.

(Agamofilaria) palpebralis Pace, 1867, nec Wilson, 1844.

This *Filaria* was removed from a tumour in the upper eyelid of a boy.

Acanthocheilonema Cobbold, 1870.

Filariidæ with thin filiform bodies provided with smooth cuticle, which is only striated longitudinally. Mouth unarmed. Posterior extremity in both sexes provided with two short conical cuticular terminal appendages situate near the terminal point. Males with four pairs of pre-anal and one pair of post-anal papillæ and two unequal rod-like spicules. Female viviparous; vulva situate in the œsophageal region. Parasites in serous cavities of Carnivora and Primates. Embryos in general circulation.

Type.—*Acanthocheilonema dracunculoides* Cobbold, 1870.

Other species are *A. perstans* Manson, 1891 (*A. recondita* Grassi, 1890; and *A. grassii* Noè, 1907.)

Acanthocheilonema perstans Manson, 1891.

Synonyms.—*Filaria perstans* Manson, 1891; *F. sanguinis hominis minor* Manson, 1891; *F. sanguinis hominis perstans* Manson, 1891; *F. ozzardi* (variety truncated) Manson, 1897.

History.—The microfilaria was first found by Manson in the blood of negroes from the Congo. Daniels found the adults in British Guiana. The geographical distribution known at present is Tropical Africa and British Guiana.

Morphology.—The adults are found, as a rule, free in the connective tissue at the base of the mesentery, around the pancreas, behind the pericardium, and behind the abdominal aorta and the suprarenal capsules. The body is cylindrical, uniform, except towards both ends, when it tapers a little.

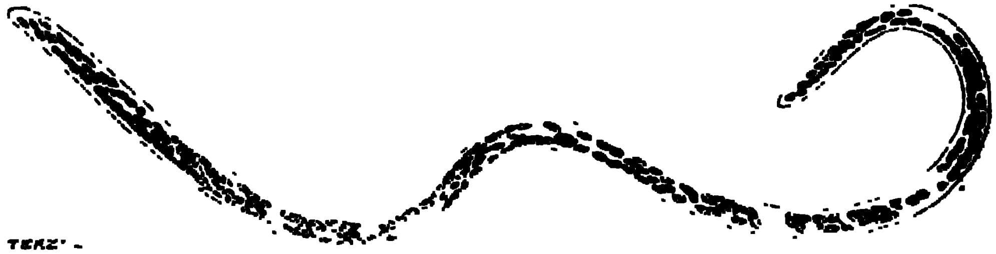


Fig. 274.—Embryo of *Acanthocheilonema perstans* Manson.

The male, rarely met with, is 45 millimetres in length by 0·6 millimetre broad, with a greatly curved tail, which ends in a bifid prolongation of the cuticle. Low describes two unequal spicules and four pairs of pre-anal and one of post-anal papillæ, all of which are very small. According to Leiper there are two pairs of post-anals.

The female is 70 to 80 millimetres in length and 0·12 millimetre in breadth, with a rounded head and a long neck. The incurved tail ends in two triangular cuticular lobes. The mouth is simple and small, and the alimentary canal shows no differentiation into œsophagus or intestine. The anus opens upon a papilla 0·145 millimetre in front of the tip of the tail. The uterus is double, and, when full of eggs and embryos in various stages of development, nearly fills the body. The vulva is 0·6 millimetre behind the anterior extremity.

Life-History.—The egg undergoes its development in the uterus, and the microfilaria escapes from its egg membrane and appears in the peripheral circulation without a sheath, and, consequently, can move about on a slide. It measures 190 to 210 μ in length and 4·5 to 5 μ in breadth. It is covered with a finely striated cuticle, and has a retractile spine, situated (apparently) upon a papilla at the anterior end of the body. The posterior two-thirds of the body tapers to the tip of the tail, which is abruptly rounded off.

It does not appear to have the central viscus seen in microfilaria of *F. bancrofti*. In stained specimens there is an area free from nuclei anteriorly, a transverse break at 34 μ, a V-spot at 49 μ, and the tail-spot at 125 μ.

A short type, measuring 90 to 100 μ, has been noted. There is no periodicity in its appearance in the peripheral blood. It never occurs in large numbers, but it is always there day and night.

Many unsuccessful attempts have been made to trace its life-history. Its larvæ are said to have been found in the thorax in *Panoplites (africanus ?)*, *Stegomyia fasciata*, and *Tæniorhynchus fuscopennatus*. It will not develop in a large number of blood-suckers, e.g., species of *Anopheles*, *Culex*, *Pulex*, *Pediculus*, and *Uranotænia*. Wellman and Feldham claim to have found its development in a tick (*Ornithodoros moubata*), as first suggested by Christy. According to Leiper, however, these are spermatophores!

It is to be noted that it only occurs in areas covered with dense forest and possessing swamps, which indicates that the host probably requires shade in the day and water to lay its eggs in.

Pathogenicity. Nil.

Dirofilaria Railliet and Henry, 1911.

Filariidæ with very long filiform body, with a striated cuticle unprovided with bosses, mouth unarmed, with six cephalic papillæ. Males with a spiral tail. Female with vulva in anterior hundredth of body. Viviparous.

Type. -*Dirofilaria immitis* Leidy, 1856.

Dirofilaria magalhæsi Blanchard, 1895.

Synonym. *F. bancrofti* Magalhæs, 1892, *nec* Cobbold, 1877.

In 1887 Magalhæs described male and female forms of a *Filaria* found by Figueira de Saboia in the left ventricle of the heart of a child in Rio de Janeiro.

For a time it was mistaken for *F. bancrofti*, but in 1894 Manson pointed out that it was a different species, and in 1895 Blanchard gave it the present name.

Morphology.- The worms were white, opalescent, and transversely striated, the head club shaped and simple, mouth terminal, œsophagus with a bulb, and there was a rounded tail. The male measured 83 millimetres in length and 0·28 to 0·4 millimetre in breadth, and possessed a rounded tail, with a cloaca 0·11 millimetre from its tip, with two spicules and four pre-anal and three post-anal pairs of papillæ.

The female was 155 millimetres in length, and 0·6 to 0·8 millimetre in breadth, with a vulval opening 2·56 millimetres behind the mouth, and an anal opening 0·13 millimetre in front of the tip of the tail.

Life-History and Pathogenicity.--Unknown.

Dirofilaria immitis Leidy, 1856.

This worm lives in the right heart and in the veins of the dog, and also of the wolf and the fox, in Europe and tropical regions. It is very common in China and Japan.

Bowlby is commonly reported to have found it in the portal vein, kidneys, bladder, ureters, and lungs of an Arab, and also in a rectal tumour in a youth, but this is quite erroneous, as he never made any such statement, for the eggs in the bladder and rectum, and the parasites in the portal vein of the Arab, were *Schistosoma hæmatobium*, as he carefully reported, never mentioning *D. immitis*. Braun, however, seems to think it possible that this worm may occur in man.

Morphology.—The worm is long, measuring 12 to 18 centimetres by 0·7 to 0·9 millimetre in the male and 25 to 30 centimetres by 1·0 to 1·3 millimetres in the female, and filiform, with a smooth rounded cuticle and a rounded anterior extremity, on which is situated the terminal mouth with six small papillæ. The anus is subterminal, and the posterior extremity pointed.

The male has a twisted tail with a cuticular fold on each side, and four pre-anal and post-anal papillæ. In the female the vulva is 7 millimetres from the anterior extremity. Viviparous.

Life-History.—The young larvæ 285 to 295 μ by 5 μ, are not enclosed in an egg case, and have a tapering posterior extremity. They appear in the peripheral blood particularly at night, when they may enter a mosquito if it bites the dog.

They enter the Malpighian tubules or their epithelial cells, where they moult and grow, eventually passing via the body cavity to the labium.

They escape through Dutton's membrane on to the skin when the mosquito bites, and so enter the dog.

Loa Stiles, 1905.

Filariidæ with bosses on the cuticle and with large caudal papillæ.

Species.—*Loa loa* Guiyot, 1778.

Loa loa Guyot, 1778.

Synonyms.—*Filaria oculi* Gervais and van Beneden, 1859; *Dracunculus oculi* Diesing, 1860, *D. loa* Cobbold, 1864, *F. subconjunctivalis* Guyon, 1864.

The larval names are: *F. sanguinis hominis* var. *major* Manson, 1891; *F. diurna* Manson, 1891.

History.—That a *Filaria* occurred in the eye appears to have been known since the end of the sixteenth century in Europe, and probably in Africa, especially in Angola, where it was called 'loa.' That knowledge must have been very ancient. Mongin in 1770 appears to have been the first person to record the presence of a worm in the eye. Guyot, in 1778 and 1805, thought it was a *Strongylus*, and used the term 'loa' for the first time in European literature. In 1891 Manson found a microfilaria in the blood of several negroes from the Congo which differed from those already described, and which he named *Filaria diurna*, and further suggested that it might be the larva of *L. loa*. Since then this hypothesis has been proved to be correct by the observations of Penel, Prout, Henly, Brumpt, Wurtz, and Kerr. *L. loa* and *Microfilaria diurna* are, therefore, simply different stages in the life-history of the same parasite.

L. loa is a parasite of the superficial connective tissue—the conjunctiva, the subcutaneous fat, and the superficial aponeuroses, in all parts of the body. It probably only occurs in man, for its alleged existence in sheep and goats in the Cameroons requires further investigation. Its endemic area is on the West Coast of Africa from Sierra Leone to Benguela, being most common in Old Calabar, the Cameroons, and the Ogowé River. It is, however, by no means confined to the coast, for it is known to penetrate at least 600 miles into the interior of Africa.

The cases reported from India are of doubtful validity, and the cases from the West Indies and South America appear to have all been imported from the West Coast of Africa.

The parasite appears to have never become endemic outside a given area, which means that the animal by which it is spread has a restricted geographical range.

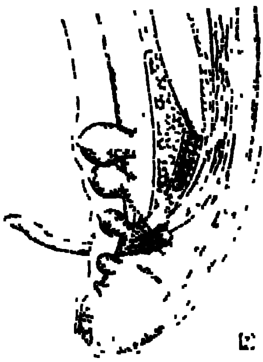


FIG. 275.—*Loa loa* COBBOLD. POSTERIOR EXTREMITY OF THE MALE.

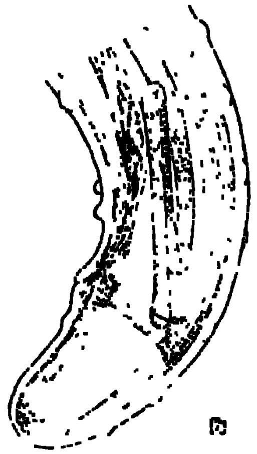


FIG. 276.—*Loa loa* COBBOLD. POSTERIOR EXTREMITY OF THE FEMALE.

(After Looss.)

Morphology. The male is a thin, white, almost transparent worm, with a body tapering to each extremity, and measuring 25 to 34 millimetres in length and 0·273 to 0·430 millimetre in breadth. The head is like a truncated cone; the neck is but feebly indicated. The tail, more or less incurved, has a rounded tip, from which the anus is distant 74 to 82 μ. There are three pairs of well marked pre-anal and two pairs of post anal papillæ, with sometimes a little tubercle on each side of the middle line far posteriorly.

The spicules are two in number and unequal, and are usually stated to differ but little in length. Penel says that the larger is traversed by a fine canal, opening laterally a little distance from the free extremity.

The cuticle consists of a superficial, thin, translucent layer and a deeper perpendicularly striated layer. Scattered over this cuticle there are rounded thickenings, or bosses, the smaller being 9 to 11 μ and the larger 14 to 16 μ in height. The thickness at the posterior extremity is variable, as also is the constriction corresponding to the neck. The viscera are enclosed in a cylindrical musculo-cutaneous tube. The mouth is terminal, small, unarmed, and surrounded by a powerful muscular cone; the œsophagus is short, and without a bulb; the intestine opens via the rectum at the anus, near the posterior extremity. The excretory pore is 0·65 millimetre from the anterior end of the body.

The genital apparatus consists of a tubular testis and vas deferens, filled with spherical spermatozoa, which terminates in a vesicula seminalis situate in the neighbourhood of the bases of the spicules.

The female is larger and thicker than the male, measuring in the fresh condition 44 to 63 millimetres (may be from 32 to 57 millimetres in different conditions of preservation) in length, and from 0·38 to 0·49 millimetre in thickness. The cuticle and anterior extremity resemble those of the male.

The genital system consists of a vulva situated on a little elevation 23 μ in height, and distant some 2·5 millimetres from the anterior extremity. This vulva leads into a thick-walled canal—the vagina—from which the two uterine tubes full of embryos and eggs diverge, and end in the ovaries.

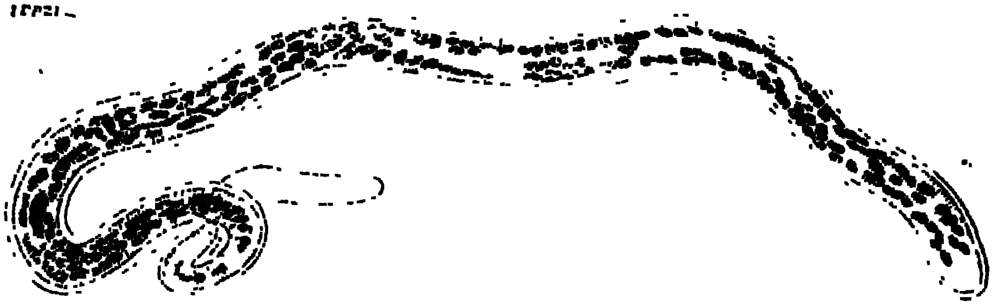


FIG. 277.—EMBRYO OF *Loa loa* GUYOT.

Life-History.—The life-history, unfortunately, is not well known. The unsegmented egg, starting in the uterus with a length of 32 μ and a breadth of 17 μ, grows into 40 by 25 μ in the morula stage, and 50 by 25 μ in the stage when a twisted and rolled-up embryo can be seen. It now approaches the vulva, and the embryo unrolls and elongates itself inside the egg membrane, which is now considerably lengthened, measuring 250 to 260 μ in length by 5·5 to 6·6 μ in breadth. The embryo now escapes from the mother, and passes via the lymph-stream into the blood, where it is known as *Microfilaria diurna*, and is noticed to have increased somewhat in size, which Penel considers is due to imbibition of fluid by osmosis, and now measures 298 by 7·5 μ. It will be noted, however, that it does not quite fill up its sheath, which is generally empty in front and behind for a short space. These embryos are only to be found in the peripheral blood during the day, and not at night, but they have no relation to sleep in the host like *M. bancrofti*, as they are unaffected by altering the habits of the host, and making him sleep in the day and work at night. When examined under the microscope, they can be seen in irregular curves, which are different from the graceful curves of *M. bancrofti*. The anterior **V**-spot can be seen, and probably opens at the apex to the exterior, as Penel has observed that the stain penetrated easily at that spot; probably there is also an opening at the tail-spot. In stained specimens the first 8 μ is clear, without nuclei; at 62 μ the column of nuclei is broken by an irregular transverse spot; at 99 μ by a triangular spot; at 253 μ by a large and at 207 μ by a small spot. The last nuclei are arranged in single file. One noticeable thing about these embryos is the scarcity with which they are met with in the peripheral blood as compared with those of *F. bancrofti*. No explanation of this is forthcoming at present.

It has been thought by Manson that the further stages of the life-history will be found in a mango-fly (*Chrysops dimidiatus*), and this has been shown to be the case by Leiper, who also finds a development in *C. silacea*, but the method of infection of man is unknown.

After entering the human body, it would appear probable that the worm takes some three to four years to reach sexual maturity, and that it is long lived—*i.e.* fifteen or more years. The reason for believing this is the fact that immature forms may be noted in children and the fully grown worm found in the adult. When the worm dies, it may become cretified.

TABLE SHOWING THE DIFFERENCES BETWEEN THE EMBRYOS OF *Filaria bancrofti* AND *Loa loa*. (MODIFIED FROM DR. G. C. LOW.)

	Filaria bancrofti Embryos	*Loa loa Embryos.*
Average length	0·317 millimetre	0·245 millimetre
Average breadth ..	0·0081-0·0075 millimetre	0·0075-0·0070 millimetre
Break in cells from head	0·050 millimetre	0·042 millimetre
V-spot from head ..	0·060 millimetre	0·060 millimetre
Eggs (average)	0·050 × 0·033 millimetre	0·042 × 0·033 millimetre
Character of curves in dried specimens on slides	Spiral coils	In wavy lines
Periodicity .. .	In blood at night (or in equal numbers in blood by day and night, Fiji, etc.)	In blood by day
Periodicity when habits of sleeping and waking changed	Inverted	No change

Pathogenicity.—It may be noted under the skin of the finger, the back, the breast, the scrotum and penis, the eyelid, under the conjunctiva, the mucosa of the tongue. It moves quickly, and may cause itching, creeping sensations, so-called Calabar swellings, irritation of the eyes and of the glottis (see Chapter LXXXVIII.).

Setaria Viborg, 1795.

Synonyms.—*Hamularia* Treutzler, 1793; *Tentacularia* Zeder, 1800, *nec* Bosc, 1797.

Definition. *Filariidæ* with chitinous ring (and papillæ around the mouth) which is deeply notched laterally and less so dorsally and ventrally. Tail in both sexes with caudal appendages. Parasitic in serous cavities of ruminants.

Setaria equi Gmelin, 1789.

Synonyms.—*Gordius equinus* Abbild, 1789; *Filaria equi* Gmelin, 1789; *Hamularia lymphatica* Treutzler; *Tentacularia subcompressa* Zeder, 1800; *Filaria papillosa* Rudolphi, 1802; *F. hominis bronchialis* Rudolphi, 1829; *F. hominis* Diesing, 1851; *Strongylus bronchialis* Cobbold, 1879.

History.—*Setaria equi* is frequently found in horses and asses, generally in the abdominal cavity, but also in the liver, female genitalia, and cranium.

It is doubtful whether the immature *Filariæ*, so commonly met with in horses' eyes in India and Ceylon, belong to this species. Railliet has recently put forth the view that they are due to the cattle filaria *F. labiato-papillosa*. Other cases have been noticed by Blanchard, Brera, and von Linstow.

Morphology.—Whitish filiform body, pointed posteriorly. Cuticle with delicate transverse striata, and mouth small, round, with chitinous ring and two lips, and papilliform processes dorsally and ventrally and two submedian papillæ.

Male 6 to 8 centimetres in length, with posterior extremity spiral, with four pre-anal and four post-anal papillæ, and two unequal spicules.

Female 9 to 12 centimetres.

Pathogenicity.—Nil.

SUBFAMILY ONCHOCERCINÆ Leiper, 1911.

Onchocerca Diesing, 1841.

Synonym. *Oncocerca* Creplin, 1846.

Filariidæ with thick cuticle possessing spiroid thickenings. Male with always four pre-anal papilla; female very long, with vulva situated anteriorly. Viviparous. Name derived from ὄγκος ('a hook') and κέρκος ('a tail').

Species.—*Onchocerca volvulus* Leuckart, 1893.

Other species are common in cattle, *e.g.*, *O. gibsoni* Cleland and Johnston, 1910, in Australia, *O. gutturosa* Neumann, 1910, in Algeria and Tunis. They cause onchocerciasis. Cleland and Johnston suspect that *O. gibsoni* is spread by lice, especially *Hæmatopinus vituli*. They report finding a Protozoal parasite somewhat like a Herpetomonas or a Crithidia in *O. gibsoni*.

Onchocerca volvulus Leuckart, 1893.

This worm was discovered by a German medical missionary in two tumours on the scalp and chest of negroes in the Gold Coast Colony, West Africa. Labadie, Lagrave, and Deguy found another specimen in a small swelling in the arm of a soldier from Dahomey. Prout next described two cases in Sierra Leone, and Brumpt a number of cases in his tour in West Africa, and Fulleborn has thoroughly studied the condition.

It is found in Sierra Leone, Gold Coast, and Dahomey; but on the Welle, between Dongon and M'Bini, it is said to occur in 5 per cent., and on the Itimbiri, between Bonta and Idembo, in 1 per cent. of the population. It has not been recorded as far south as the Congo. Thèze has recorded three cases from Dutch Guiana, and Leiper has recently confirmed its occurrence in Guatemala, where, according to Robles, the infection is very common.

Morphology.—The male worm has a white filiform body, slightly attenuated at the ends, covered with a transversely striated cuticle, measuring 30 to 35 millimetres in length and 0·14 millimetre in breadth.

The head is rounded, the mouth unarmed, the alimentary canal straight and undifferentiated, the anus subterminal 0·049 millimetre in front of the posterior end. Other canals are reported, which probably belong to the generative and excretory systems.

The tail is strongly recurved, and somewhat flattened on its concave aspect. Brumpt reports three pairs of papillæ on each side of the anus and three pairs of post-anal papillæ. There are two unequal spicules, the larger 177 μ and the smaller 82 μ in length.

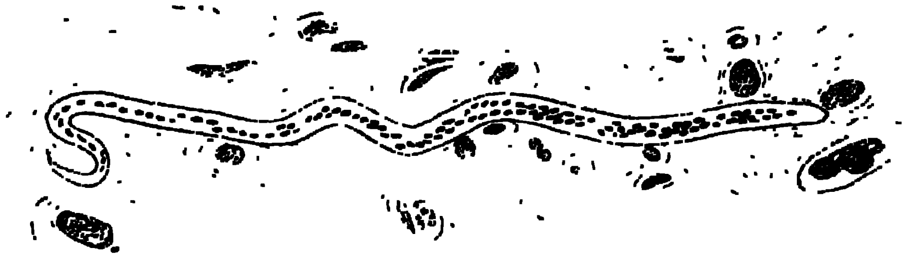


FIG. 278.—MICROFILARIA OF *Onchocerca volvulus* LEUCKART.
(After Fülleborn.)

The female is longer and thicker than the male, measuring 60 to 70 millimetres in length and 0·30 millimetre in breadth. The cuticular striations are ring-like and well marked. The tail is recurved. The uterus is seen full of eggs and larvæ, and the vulva is 0·70 millimetre from the anterior end.

Life-History.—The worm is said to lie in a lymphatic, which becomes inflamed, and a perilymphangitis causes a condensation of connective tissue, in which males and females are embedded, leaving the posterior end of the male and the anterior end of the female free in the lymph space. The embryos pass out of the uterus into this space, where they can be found 250 to 300 μ in length, and 5 to 6 μ in breadth, with a rounded head and a body which tapers during the last fifth, and terminates in a pointed tail. There is no sheath. The anterior V spot is clearly seen. The microfilaria have not been seen in the blood, and their further development is quite unknown.

The embryos have recently been found in the blood, and Brumpt is inclined to think that the further development will be in a tsetse-fly. The adults live for years in the human body.

Pathogenicity.—Lymphangitis, perilymphangitis, sometimes acute and with fever, and resulting in small tumours, are their pathological signs.

FAMILY 7. DRACUNCULIDÆ Leiper, 1912.

Dracunculus Kniphoff, 1759.

Nematodes with small males and long females. In the latter a vagina is wholly absent; the embryos being discharged by rupture of the gravid female.

Dracunculus medinensis (Linnæus, 1758).

Synonyms.—*Dracunculus veterum* Velsch, 1674; *Vena medinensis* Velsch, 1674; *Dracunculus persarum* Kämpfer, 1691, *Gordius medinensis* Linnæus, 1758; *Filaria dracunculus* Bremser, 1819; *F. æthiopica* Valenciennes, 1856; *Dracunculus medinensis* Cobbold, 1864.

Dracunculus medinensis, commonly called the guinea-worm, the dracunculus, Beinwurm, Brachwa-serwurm, tankworm, or dragonneau, is endemic in tropical Africa, India, Persia, Turkestan, Arabia, and some places in South America, to which it was imported from Africa.

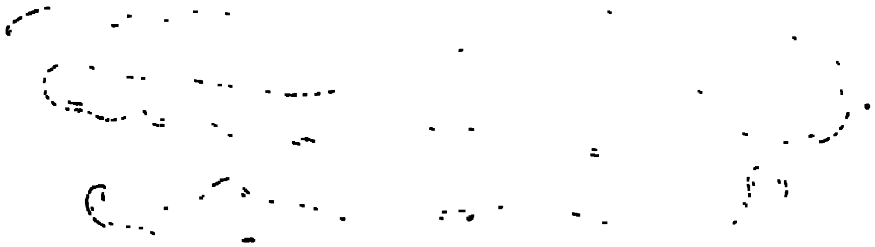


FIG 279.—*Dracunculus medinensis* LINNÆUS.

It has been known since the most remote periods, and it was probably the fiery serpent mentioned by Moses who apparently knew the method of twisting the worm out on a stick, as he appears to have made a model of this method of extraction. Galen called the disease caused by these worms dracontiasis.

The anatomy of the worm was carefully studied by Bastian in 1863, and the infection of *Cyclops* with the larva was observed by Fedschenko in 1870, and confirmed later by Manson. Charles found a calcified guinea worm in 1892, which he described as the male.

Leiper, 1907, has repeated these experiments, and has further proved that when monkeys are fed on infected *Cyclops* the males and females can be found.

Morphology.—The female is a long white filiform worm 50 to 80 centimetres in length and 0·5 to 1·7 millimetres in diameter.

The anterior end is bluntly rounded, and carries the small terminal mouth, which has two lips and two lateral and four submedian papillæ. It leads into a straight alimentary canal, which atrophies considerably in the fully developed condition. The large uterus, which occupies the whole length of the body when filled with embryos, evacuates its contents by a rupture close to the mouth and just external to the papillæ. The tail is rounded off, and carries a small bent chitinous hook.

Leiper states that the male is only 22 millimetres in length, and has five pairs of papillæ.

Life-History.—The males and females live in the connective tissue about the mesentery, and after copulation probably the males die off. When the female is gravid, she moves, head first, apparently in search of water, usually downwards towards the leg or foot; more rarely she moves to the hand or arm, and very rarely to the head. Arrived under the epidermis, she bores her way through the deep layers, while a little bulla on the surface marks her presence.

When this bulla bursts, a small hole is seen, at the bottom of which lies the vulva, through which the tube of the uterus has prolapsed, bending the head to one side. Clear fluid can be seen escaping from this tube, which, when examined, is found to be full of embryos.

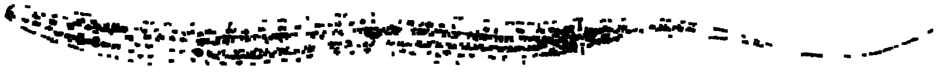


FIG. 280.—LARVA OF *Dracunculus medinensis* LINNÆUS.
(After Looss, from Mense's 'Tropenkrankheiten.')

The segmentation of the egg takes place in the uterus, and the embryos are born alive. They are flat, pointed little bodies, 0·6 millimetre in length and 17·5 μ in breadth, with a narrow, very pointed tail. The mouth is at the anterior end, and leads into an alimentary canal with an anus. There is a little sac on each side of the root of the tail. According to Leiper, these little larvæ cannot swim, but either die or are swallowed by a *Cyclops*. In this crustacean they pass from the stomach into the cœlom, where they develop for four weeks. Leiper describes the first ecdysis as taking place about the seventh to ninth day, and the second between the tenth and eleventh day, after which progressive histological changes occur. After the fourth week no further change takes place, though they can live for forty-one days in the *Cyclops*. When placed in 0·22 per cent. solution of hydrochloric acid, the *Cyclops* is promptly killed, while the larva appears to be stimulated, undergoing ecdysis, and escaping from the *Cyclops* by boring its way through the chitinous cuticle. In a monkey fed with infected *Cyclops*, three females and two males were found. It is, therefore, correct to assume that man is infected by ingesting infected *Cyclops* with his drinking-water, and it is probable that, set free in the stomach, the larvæ enter the connective tissue by boring their way through the stomach-wall.

Pathogenicity.—The worm causes dracontiasis (see Chapter LXXXVIII.).

FAMILY 8. MERMITHIDÆ.

Nematoda with a diagonal fibre system in the cuticle, without anus, and with six mouth papillæ.

The male has two spicules and three rows of numerous papillæ.

Genus.—*Mermis* Dujardin.

Mermis Dujardin, 1845.

Mermithidæ possessing the characters of the family.

Subgenus (Agamomermis) Stiles, 1903.

A purely collective group, which contains forms sexually immature and not capable of being definitely placed.

(Agamomermis) restiformis Leidy, 1880.

Synonym.—*Filaria restiformis* Leidy, 1880.

In 1880 Leidy received from Woodward a worm which was supposed to have come from the urethra of a man living in America. Stiles has re-examined this specimen, and concludes that it is an Agamomermis.

The cuticle is 32 to 48 μ thick, with a diagonal fibre system. The head end is attenuated, and possesses a very small terminal mouth without lips, behind which are six papillæ. The excretory pore (?) is 0·112 millimetre behind the mouth. The pharynx is straight, and opens into the cylindrical intestine, which is a dark cæcal structure; but there is no anus and no caudal papillæ. The tail is curved ventrally and bluntly rounded.

On one side of the œsophagus there is a blind sac, which probably represents the fat body.

Filaria (?) hominis oris Leidy, 1850. Perhaps this worm ought to be classified here instead of under Filaria.

FAMILY 9. ASCARIDÆ Cobbold, 1864.

Definition. Nematoda with three lips, one median dorsal and two submedian ventral, touching one another in ventral median line; œsophagus with a bulb. Male with (one or) two spicules; female with two ovaries. Oviparous. Development believed to be direct.

Genera.—*Ascaris*, *Toxascaris*, *Belascaris*, and *Lagochilascaris*.

Ascaris Linnæus, 1758.

Synonyms. *Stomachida* Pereboom, 1870; *Fusaria* Zeder, 1800.

Definition.—Ascaridæ in which the oral cavity is surrounded by three large lips provided generally with denticulated borders, one placed dorsally and two ventrally. Male with two equal spicules and numerous pre-anal and post-anal papillæ. Vulva in front of the middle of the body. Shell of egg thick, with outer albuminous layer often raised into numerous projections.

Species.—*Ascaris lumbricoides*, *A. texana*, *A. maritima*.

Ascaris lumbricoides Linnæus, 1758.

Definition.—*Ascaris* with reddish-yellow colour in fresh condition. Oral papillæ finely toothed, without interlabia.

Remarks.—This is one of the most common parasites in the tropics. It is, however, possible that other species escape recognition by being casually considered to be *Ascaris lumbricoides*. It is usually met with in the small bowel, but may be found post mortem in the stomach, œsophagus, mouth, nose, larynx, trachea, or bronchi. It may also be found escaping from the anus. More rarely it has been seen in the liver, causing abscesses, in the pancreatic duct, and in the vermiform appendix, and in worm abscesses in the body-wall. Usually it gives rise to no symptoms, but at times, when in large numbers, it may cause pathological effects.

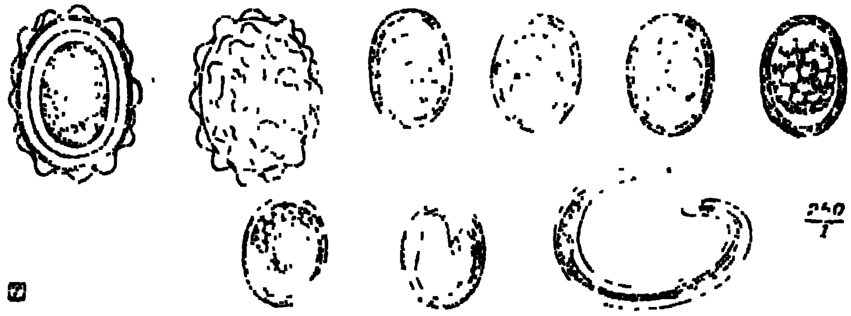


FIG. 281.—DEVELOPMENT OF *Ascaris lumbricoides*. (After Stiles.)

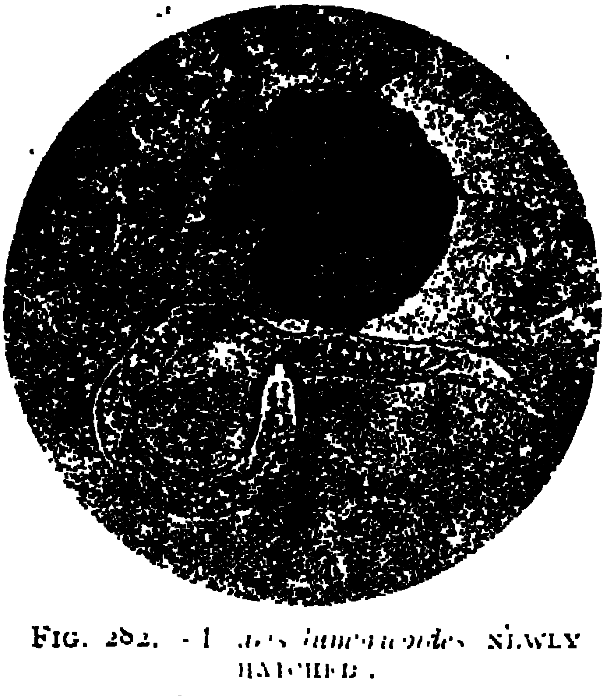


FIG. 282.—*Ascaris lumbricoides* NEWLY HATCHED.
(Microphotograph by J. J. Bell.)

Morphology.—It is yellowish in colour, with often a faint trace of a reddish tinge. In form it is spindle-shaped. Male is 15 to 25 centimetres in length and 3 millimetres in diameter. The posterior extremity is conical, and bent ventrally, with two spicules 2 millimetres in length, and broader at the tips. On each side of the cloaca there are seventy to seventy-five papillæ, of which seven pairs are post-anal. Female [illegible] 20 to 40 centimetres in length by 5 millimetres in breadth. The vulva is at the junction of the anterior and middle thirds of the body.

Life-History.—The eggs are laid in the small intestine, and appear unsegmented in the fæces. They measure 50 to 70 μ in length by 40 to 50 μ in breadth, surrounded by a thick transparent shell, which has an externally irregular coating of albumin, which is stained brownish-yellow by the stercobilin of the fæces. These eggs can stand alteration in temperature and moisture. In warm, moist earth the embryo appears in about a month in the form of a spiral roll, but does not hatch until it reaches the interior of man, when it develops into an adult, as was shown by the experiments of Davaine, Grassi, Calandruccio, Lutz, and Epstein.

Leuckart and von Linstow believed that an intermediate host was necessary. Stewart has shown that the larval forms after hatching from the eggs pass into the liver and thence by the blood-stream to the lungs, whence they reach the stomach by migrating up the bronchii and trachea.

Stiles found that the house-fly could carry the egg, which passed through its alimentary canal unaltered. The worm matures, and deposits ova in one month from entering the body.

Pathogenicity. It is only pathogenic in large numbers, or when it invades the liver, causing abscess, or the appendix, causing appendicitis. The larvæ in the lungs apparently cause bronchitic symptoms.

Animals.—Monkeys, dogs, and perhaps pigs.

Ascaris (?) **maritima** Leuckart, 1870.

An immature worm, possibly accidentally swallowed in food, was vomited by a child in North Greenland in 1865, and was supposed to be an immature female *Ascaris*.

Ascaris (?) **texana** Smith and Goethe, 1904.

Stiles appears very doubtful as to whether this worm is an *Ascaris*. The female only is known, measuring 58 to 60 millimetres in length. Uterine eggs 60 by 50 μ. It was found in a man in Texas.

Toxascaris Leiper, 1907.

Definition. Ascaridæ with the anterior end of the body bent dorsally, cuticle finely striated, œsophagus simple, without a bulbous portion. Palpi of lips club-shaped. Male with a tapering, acicular tail, and without ventral protuberance behind anus. Six pairs of post-anal papillæ in two groups, the ventral pairs continuous, with a pre-anal row on each side of the body, and three lateral pairs on the outer aspect of the tail. Testis lies in the anterior part of the posterior half of the body. Seminal vesicle long and tubular. Ejaculatory duct short. Female with vulva about the centre of the body. Egg oval and smooth.

Species.—Of the species belonging to this genus, only one, *Toxascaris canis* Werner, 1782, is known in man.

Toxascaris canis Werner, 1782.

Synonyms.—*Lumbricus canis* Werner, 1782; *Ascaris canis* Gmelin, 1789; *A. marginata* Rudolphi, 1802; *Toxascaris limbata* Railliet and Henry, 1911.

Remarks. — *Toxascaris canis* is the common *Ascaris* of dogs, which used to be called *A. canis*, but recently Leiper, when examining a number of specimens of *A. lumbricoides* in Egypt, found among them several smaller and apparently younger forms. On examining these he found that they had winged expansions on either side of the head, which indicated that they were not *A. lumbricoides*. On further examination they proved to be the same species as that found in dogs, but differed from that found in cats. Up to that time *A. canis* in the dog and *A. mystax* in the cat were supposed to be identical. Finally, on careful anatomical examination, it was found that the two not merely differed considerably from one another, but also from *A. lumbricoides*. He therefore formed two new genera—*Toxascaris* and *Belascaris*. So far, *Toxascaris* has only been recorded once in man.

Morphology. Body white or reddish, head curved dorsally, with two membranous lateral expansions, broader behind than in front. Male 5 to 10 centimetres in length, with curved tail, possessing two small lateral membranous wings and twenty-six papillæ. Female 9 to 12 centimetres in length, with an obtuse tail. Eggs 75 to 80 μ in diameter.

Life-History. Development is similar to *A. lumbricoides*.

Pathogenicity. It often causes intestinal and nerve symptoms in dogs. Post mortem the mucosa of the intestine is tumefied and catarrhal.

Belascaris Leiper, 1907.

Definition. Ascaridæ with the anterior end of the body bent ventrally, cuticle coarsely striated, œsophagus with a distinct bulbous portion. Male with a probular tail, *i.e.*, like a closed fist, with forefinger semi-extended. Immediately behind the anus there is a protuberance, with a pair of papillæ. On the tail there are two ventral and two lateral pairs of papillæ, the tips of which support a slight expansion of the cuticle. The testis is situate in the anterior half of the body. The vesicula seminalis is remarkably long, and there is a short ejaculatory duct. Female with vulva situated in the anterior part of the body. Egg with a honeycombed shell.

Type. *Belascaris cati* Schrank, 1788.

Belascaris cati Schrank, 1788.

Synonyms.— *Fusaria mystax* Zeder, 1800; *Ascaris alata* Bellingham, 1839.

This *Ascaris* is common in cats, and has been recorded nine times in man.

Morphology. Head curved ventrally, with two membranous lateral expansions. Male 4 to 6 centimetres in length; female 4 to 10 centimetres in length.

Life-History.—Similar to *A. lumbricoides*.

Pathogenicity.—It rarely causes any symptoms.

Genus Lagochilascaris Leiper, 1909.

Definition.—*Ascaridæ* with dense cuticular lips and interlabia surrounded by a ridge and furrow, separating the lips from the rest of the body. Œsophagus simple. Shallow ledge-like cuticular alæ extend along either side of the body to near the tail. Eggs mosaic.

Type Species.—*Lagochilascaris major* Leiper, 1909, in the lion.

Lagochilascaris minor Leiper, 1910.

This species has been found in the pus of subcutaneous abscess in man in Trinidad.

Morphology.—Males 9 millimetres in length by 0·5 millimetre in breadth, with bent posterior part of body. Female 15 millimetres in length, straight posteriorly. The vulva, with two projecting lips, opens 6 millimetres from the anterior end.

Hosts.—Possibly one of the Carnivora. Man is an accidental host.

Habitat.—Probably intestinal in its normal host. The specimens were found in abscesses under the skin in man. An allied species, *A. major*, occurs in the intestine of the lion in East Africa.

FAMILY 10. OXYURIDÆ Dujardin.

Genus Oxyuris Rudolphi, 1803.

Definition.—*Nematoda* in which the three labial papillæ are not very distinct. Œsophagus long, with a double dilatation. Skin markedly striated. Male with curved posterior end, one spicule, and two pairs of pre-anal papillæ. Female with straight posterior end, which tapers to a point. Vulva in the anterior part of the body.

Type.—*Oxyuris vermicularis* Linnæus, 1767.

Oxyuris vermicularis Linnæus, 1767.

Synonyms.—*Ascaris vermicularis* Linnæus, 1767; *Fusiaria vermicularis* Zeder, 1803.

Remarks.—*Oxyuris vermicularis* is the pin or thread worm, and occurs, as far as is known, only in man and all over the world. It is believed to live in the lower part of the small intestine at first, and then the gravid females travel to the large bowel. It has been known from the earliest times.

Morphology.—It is a minute white round worm, with transversally striated cuticle, which forms two ridges along the ventral and dorsal surfaces corresponding to the lateral ridges.

Male is 3 to 5 millimetres in length, with a spirally rolled posterior extremity, with one spicule and six papillæ. Female is 10 millimetres in length and 0·6 millimetre in breadth, with a long pointed tail.

Life-History.—The egg, when deposited from the uterus, measures 50 to 52 μ by 16 to 24 μ, with a thin shell and a fairly well-developed embryo. The dorsal surface of the egg is more convex than the ventral. These eggs escape in the fæces. They are then reintro-

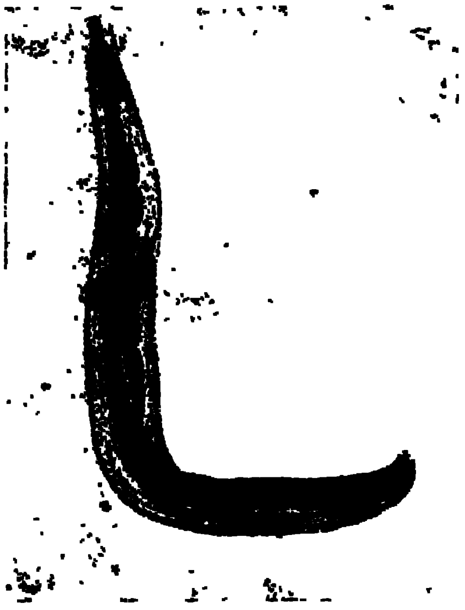


FIG. 283.—*Oxyuris vermicularis* (LINNÆUS, 1767): MALE.

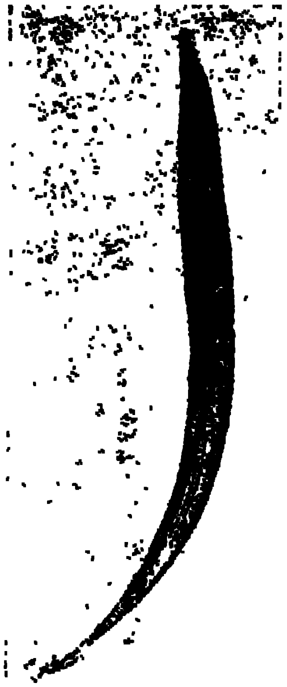


FIG. 284.—*Oxyuris vermicularis* (LINNÆUS, 1767): FEMALE.

(From a photograph by J. J. Bell.)

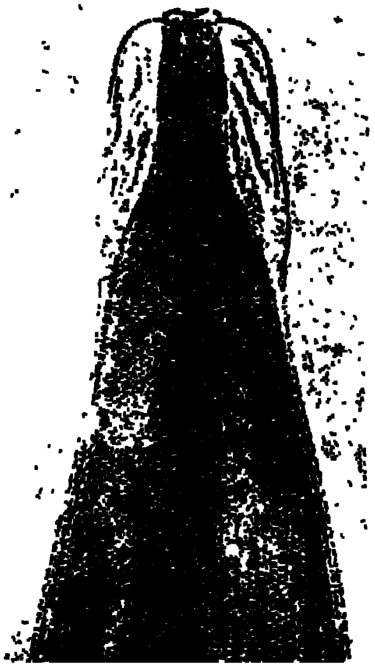


FIG. 285.—*Oxyuris vermicularis* (LINNÆUS, 1767): HEAD. (From a photograph by J. J. Bell.)

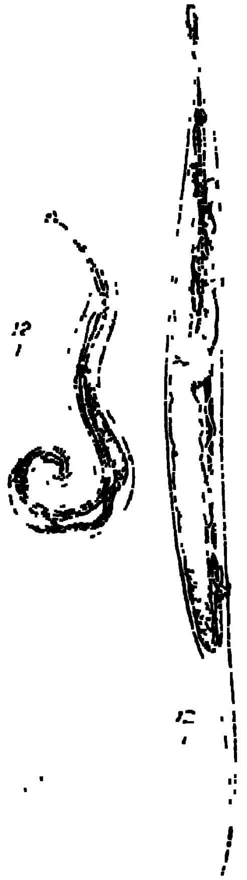


FIG. 286.—*Oxyuris vermicularis*. The male is to the left, the female to the right. (After Claus.)

duced into the mouth or nose by self-infection, fruits, vegetables, etc., hatch, and grow in the small intestine into male and females.

After fertilization the males die off and the females travel into the caecum, and later into the colon, and have a great tendency to wander through the anus to the outside. The duration of life of *O. vermicularis* in the human body is not known.

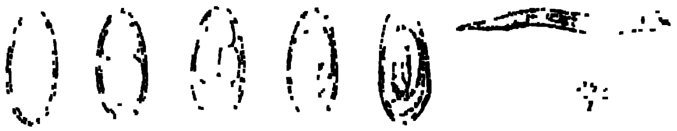


FIG. 287. DEVELOPMENT OF *Oxyuris vermicularis*
(After Leuckart, from Stiles.)

Pathogenicity. In large numbers may set up enterocolitis, in small numbers it causes only irritation.

DIVISION BURSATA.

Definition. Nematoda with true cuticular bursa in the male.

Classification. Leiper gives the following table for the differentiation of the various bursate families represented by species in man:

A. Mouth with simple pore, no buccal capsule:
  (a) Male with large bursa and elongated rays; female oviparous, uteri divergent, ovijectors present. Intestinal parasites. *Trichostrongylidæ.*
  (b) Male with short bursa and stunted rays; female oviparous, uteri convergent, ovijectors absent. Lung parasites. *Metastrongylidæ.*

B. Mouth a simple opening, leading into a large buccal capsule guarded by chitinous structures:
  (a) Mouth capsule bent dorsally and guarded by paired bilaterally arranged plates. *Ancylostomidæ.*
    Plates with smooth edge. *Necator.*
    Plates with toothed edge. *Ancylostoma.*
  (b) Mouth capsule terminal guarded by ring of setæ. *Strongylidæ.*

BURSATA.

FAMILY II. STRONGYLIDÆ Cobbold, 1864.

Nematoda with cylindroid, rarely filiform bodies, mouth usually with wide buccal capsule, with ring of chitinous armature, and an œsophagus more or less enlarged posteriorly. Male with a bursa copulatrix and two equal spicules. Female with two ovaries; vulva situated medially or posteriorly. As a rule, the species are small. Oviparous.

Type Genus.—*Strongylus* Mueller, 1780.

Other Genera.—*Triodontophorus* Looss, 1901; *Œsophagostomum* Molin, 1860.

Triodontophorus Looss, 1901.

Synonyms.—*Triodontus* Looss, 1901, *nec* Westwood, 1845; *Ternidens* Railliet and Henry, 1909.

Strongylidæ with small, almost spherical, thick-walled oral cavity, arising from the floor of which three teeth are found, each of which consists of two surfaces joined together at an acute angle. Male bursa is finely serrated at the edge. The female genital orifice is situate a short distance in front of the tip of the tail.

Found in horses and men.

Triodontophorus deminutus Railliet and Henry, 1905.

Synonym.—*Ternidens deminutus* (Railliet and Henry, 1905).

Railliet and Henry in 1905 discovered that a male and female parasite presented in 1865 by Monestier to the Paris Natural History Museum, and collected post-mortem from an American negro who died in Mayotte, were not ankylostomes, but belonged to Looss's genus *Triodontophorus*. They named them *deminutus* because of their small size. Leiper also met with some specimens of the same species collected in Nyasaland and Lorenço Marques. It has now been recorded in a number of cases. It is also found in monkeys. Their normal habitat is the large intestine.

Morphology.—To the naked eye their size and general appearance resemble those of ankylostomes. The body is white, cylindrical, tapering towards the end. Cuticle transversely striated, and forms an overhanging transverse fold across the ventral surface of the body at the level of the excretory pore.

The mouth-collar is moderately developed, with a depth of 0·04 millimetre. The anterior surface carries four small knob-like submedian papillæ, and the edge surrounds the entrance to the mouth with a double series of delicate fringes composed of cuticle. These two rows constitute the external and internal crowns of the corona radiata.

The buccal capsule is a barrel-shaped chitinous structure capped and covered in by the mouth-collar and the corona radiata. Posteriorly it touches the dilated end of the œsophagus, whose chitinous lining expands into a funnel uniting with the cuticle on the outside of the œsophagus, and coming near the cuticle of the buccal cavity. It shows three cuticular edges projecting into the lumen, which are continued forwards as three stout chitinous prongs or teeth, one dorsal and two ventral. The characters of these teeth are specifically important. They are formed of two plates curved longitudinally and meet to form a keel. The œsophagus is muscular, 0·8 millimetre long, with three fleshy valves guarding its entrance into the chyle intestine. The rectum is short and ends in the anus, which is 0·24 millimetre from the tip of the tail. The excretory system opens on the ventral surface halfway between the posterior limit of the buccal cavity and the nerve ring.

The male is 9·5 millimetres long by 0·56 millimetre in breadth, with a spicule 0·9 millimetre long. Female is 14 to 16 millimetres in length, and 0·73 millimetre in breadth, with a tapering posterior extremity. The vulva is nearly 0·48 millimetre from the hinder end. The vagina is short, and opens into two uterine tubules. The uterine eggs are 60 to 80 μ by 40 μ, with a delicate shell and often a morula.

Life-History and Pathogenicity.—Unknown.

Œsophagostomum Molin, 1861.

Strongylidæ in which the mouth is small and circular, with a chitinous ring, which carries a fold and six papillæ. There is a marked swelling just behind the anterior extremity. Male bursa with two equal spicules; female with two ovaries, and the vulva opening situate near the anus.

Type Species.—*Œ. subulatum* Molin, 1861; *Œ. dentatum* (Rudolphi, 1803).

Species.—*Œsophagostomum apiostomum* and *Œ. stephanostomum*, var. *thomasi* Railliet and Henry, 1909, are known in man, but other species are found in the gorilla, chimpanzee, and other monkeys.

Œsophagostomum apiostomum Willach.

Synonym.—*Œsophagostomum brumpti* Railliet and Henry 1905.

This worm was found by Brumpt in cyst-like nodules in the cæcum and colon of a negro on the Omo River near Rudolph's Sea in East Africa. Found also in monkeys.

According to Leiper, this parasite occurs in 5 per cent. of the natives of Northern Nigeria.

Morphology.—Female 8·5 to 10·2 millimetres long by 0·295 to 0·325 millimetre broad, white and cylindrical, tapering towards the posterior end. Cuticle transversely striated. There is a distension behind the oral cavity which is formed of a cuticular band with a crown with twelve spines; on the front and inner side lamellæ; six head papillæ (two lateral, four submedian). Posterior end rounded off with three broad undulations.

Life-History.—Outside the body similar to that of the Ankylostomes.

Pathogenicity.—The young form cyst-like nodules in the large intestine.

Œsophagostomum stephanostomum var. thomasi Railliet and Henry, 1909.

This species was found by Wolferston Thomas in tumours, numbering 187, in the large and small intestines of a man in Brazil. The tumours were in some instances large enough to diminish the lumen of the bowel. Each tumour contained a male and a female worm. The species *Œ. stephanostomum* Stossich 1904, was found in the large intestine of the gorilla, and a variety *Œ. stephanostomum* var. *dentigera* Railliet and Henry, 1909, is found in the chimpanzee.

Morphology.—Body cylindrical, thick, only attenuated towards the extremities. Buccal capsule with an external crown of 38 lamellæ. Male 17 to 22 millimetres in length and 0·75 millimetre broad. Bursa thick at the sides, with one spicule 1·38 to 1·475 millimetres long. Female 10 to 20 millimetres long by 0·9 millimetre broad. Vulva in front of the anus, 0·5 to 0·525 millimetre from the posterior end.

Life-History.—Not known.

Pathogenicity.—Forms tumours in the wall of the small and large intestines.

FAMILY 12: METASTRONGYLIDÆ Leiper, 1912.

Nematoda with simple mouth, very small cavity, and not enlarged to form a buccal capsule, and a bursa in the male with true but stunted rays. Two spicules.

This family includes a number of genera, parasitic in the lungs of domesticated animals.

Metastrongylinæ Leiper, 1908

Metastrongylus Molin, 1861.

Metastrongylidæ with mouth surrounded by six small papillæ. Male with a bursa copulatrix and two spicules. Female with two ovaries and a tapering posterior end, vulva situate in the hinder half of the body. Embryos without teeth, and with slightly developed œsophageal bulb.

Metastrongylus apri Gmelin, 1789.

Synonyms. *Gordius pulmonalis apri* Ebel, 1777; *Ascaris apri* Gmelin, 1789; *Strongylus suis* Rudolphi, 1809; *S. paradoxus* Mehlis, 1831; *S. elongatus* Dujardin, 1845; *S. longevaginatus* Diesing, 1851.

Metastrongylus apri is not uncommonly found in the bronchial tubes of pigs in Germany (60 per cent. Berlin; 15 to 52 per cent. Leipzig), occasionally it infects other animals including man. (*Filaria trachealis* Rainey, 1855, found by Rainey and by Bristowe, may be infection of man with this parasite.) Diesing recognized the worm in the lungs of a boy aged six in Klausenburg in 1845. It is said to also occur in the intestine, but this is looked upon as accidental, as its usual habitat is the lungs, where it may cause pneumonia and bronchitis.

Morphology.—Body relatively short, colour white or brown; mouth with six lips, of which the two lateral are the largest. Male: 12 to 25 millimetres in length, with bilobed bursa with five ribs in each lobe, and thin spicules about 4 millimetres in length. Female: 20 to 50 millimetres in length, with a curved posterior end, close in front of which is the anus, while the vulva opens on a papilla just in front of this. Eggs elliptical, 50 to 100 μ by 39 to 72 μ; when oviposited, they already contain an embryo.

Life-History. Only the embryonic and larval development appear to have been studied. From analogy with Ankylostoma a skin infection would be presumed nowadays, and further the fact that the worms have been noted in the alimentary canal bears quite a different significance from what it did years ago, as it may be natural for the worms at times to travel from the lungs to the bowel like the Ankylostoma. It is interesting to note that Leuckart failed to infect sheep by feeding them with bronchial mucus full of embryos.

Pathogenicity.—This subject has recently been studied by Santiocchi, and consists essentially of bronchitis, broncho-pneumonia, and pneumonia.

FAMILY 13: TRICHOSTRONGYLIDÆ Leiper, 1912.

Nematoda with filiform bodies; cuticle markedly striated transversely or longitudinally; mouth without buccal capsule or tooth armature; bursa large, with well developed rays; genital pore in posterior half of body; ovejectors present; oviparous. Intestinal parasites.

Nematodirus Ransom, 1907.

Trichostrongylidæ with bursa provided with double ventral median ribs, two dorsal ribs, spicules long and filiform, without accessory piece. Head 50 microns in diameter; cuticle with eighteen distinct longitudinal ridges. Cervical papillæ absent.

Type Species.—*Nematodirus filicollis* Rudolphi, 1802.

Remarks.—The subgenus *Mecistocirrus* Railliet, 1912, with distinct cervical papillæ and cuticular ridges little apparent, contains the human parasite.

Mecistocirrus fordi Daniels, 1908.

Synonym.—*Nematodirus gibsoni* Stephens, 1909.

This worm was discovered by Bell in the fæces of a Chinaman in Hong Kong, and described by Stephens

Morphology.—The male measures 21 millimetres by 0·4 millimetre, and possesses an attenuated head with two cervical papillæ, and a mouth with two lateral papillæ. The bursa shows two well marked lobes, continued dorsally on to the body as a **V**-shaped slit. There is one pair of ventral rays and six pairs of dorsal rays an anterior, two middle, and two posterior, which last arise from a common stem. The spicules are very long (7 millimetres) and delicate.

The female measures 25 millimetres long and possesses a pointed tail, on which the anus opens 0·2 millimetre from the tip, while the genital pore is 0·5 millimetre from the same extremity The uterine egg measures 110 μ by 53 μ.

Life-History.—Nothing is known as to the life history.

Pathogenicity. It is not stated whether it is or is not pathogenic.

Hæmonchus Cobb, 1898.

Synonyms. *Hæmonchus* Stiles, 1903, *Strongylus* O. F. Muller, *pro parte.*

Strongylidæ with unarmed mouth Male bursa trilobed, with median lobe asymmetrical, spicules short with an accessory piece, female with vulva situate posteriorly and protected by some tegumentary appendages.

Type Species.—*Hæmonchus contortus* Rudolphi, 1803.

Hæmonchus contortus Rudolphi, 1803.

Synonyms.—*Strongylus contortus* Rudolphi 1803; *S. filicollis* Molin, 1861; *S. placei* Place, 1893.

This worm was found by de Magalhães in a case of anæmia supposed to be due to *Ankylostoma duodenale*, and from which the specimens were obtained by treatment with thymol, after which treatment the patient rapidly recovered.

Morphology.—Body red or white, filiform, with attenuated extremities Anterior extremity with two cervical papillæ in the form of teeth directed backwards. Cuticle finely striated Male: 10 to 20 millimetres in length, with bursa provided with two lobes of which the right carries an asymmetrical median lobe. The two spicules measure 0·3 to 0·[illegible] millimetre in length and are each furnished with an accessory portion Female: 20 to 30 millimetres in length, with caudal extremity pointed Vulva situated in the posterior fifth of the body. Eggs are ellipsoidal, 70 to 95 μ long by 43 to 54 μ broad.

Life-History.—The eggs quickly develop when placed in pure or muddy water, producing rhabditic embryos; the latter undergo ecdysis.

Habitat.—The intestine of the goat, sheep, etc.

Pathogenicity.—Produces anæmia, resembling that of ankylostomiasis, and has a hæmolytic toxin.

Trichostrongylus Looss, 1905.

Trichostrongylidæ with body tapering gradually from the genital opening anteriorly. Head with three small lips and blunt or pointed papillæ, without cuticular protuberances or neck papillæ. Cuticle transversely striated; œsophagus long. Male with the bursa closed round by large side flaps, without evident median folds; spicules spoon-like, with a boat-shaped accessory piece. Female with the genital opening in the posterior half of the body. Tail short, with two small papillæ near the tip. Egg thin-shelled.

Type Species. -*Trichostrongylus retortæformis* Zeder.

Four species of interest in tropical pathology: *Trichostrongylus colubriformis*, *T. probolurus*, *T. vitrinus*, and *T. orientalis*.

Trichostrongylus colubriformis Giles, 1892.

Synonyms.- -*Strongylus colubriformis* Giles, 1892; *S. instabilis* Railliet, 1893; *S. subtilis* Looss, 1895.

This species was found by Looss in post-mortems on fellahs in Alexandria and Cairo, and also by Ijima in a woman in Japan. In man, however, it is only an accidental parasite, being usually found in the duodenum, rarely in the stomach, of sheep, antelopes, dromedaries in Egypt, monkeys in North America, and sheep in India.

Morphology.- Male 4 to 5 millimetres in length, and 0·08 millimetre in thickness just in front of the bursa. Spicule 1.35 to 1.45 μ in length, and the accessory portion 70 μ in length, with a long muscular œsophagus. Bursa with two lateral semicircular wings connected by a cross bridge. Ribs arranged asymmetrically. Female 5 to 6 millimetres in length, and about 0·09 millimetre in breadth. Posterior extremity tapers to a pointed tail, in front of which the anus is situated, 0·055 to 0·07 millimetre, and the vulva 1·05 to 1·2 millimetres. Eggs 72 to 80 μ by 40 to 43 μ; when oviposited, generally contain eight to twelve celled embryo.

Life-History.- Resembles that of *Ancylostoma duodenale* outside the body, according to Leiper.

Pathogenicity. -Believed to be unimportant.

Trichostrongylus orientalis.

Synonym. *Trichostrongylus subtilis* Looss, 1895.

Trichostrongylus eggs have recently been found in the fæces of a considerable percentage of the agricultural population of certain districts in Japan, and is probably the same as that recorded previously from Japan by Ijima and Looss as *Trichostrongylus subtilis* (*vide T. colubriformis*, *supra*). This species differs slightly in details of ray-disposition in the bursa and in configuration of the spicules.

Trichostrongylus probolurus Railliet, 1896.

Synonym.- -*Strongylus probolurus* Railliet, 1896.

This parasite lives in the duodenum of sheep, antelopes, and dromedaries in Egypt, and has also been found in man in Egypt.

Morphology.—Male 4·5 to 5·5 millimetres in length, 0·08 millimetre in breadth just in front of the bursa. Spicule 126 to 134 μ, accessory piece 75 to 80 μ in length.

Female 4·5 to 6 millimetres in length, anus 0·04 to 0·05 millimetre, and vulva 1·08 to 1·25 millimetres in front of the tip of the tail, which is short. Egg 76 to 80 μ by 43 to 46 μ

Life-History.—This is unknown.

Pathogenicity.—Believed to be unimportant.

Trichostrongylus vitrinus Looss, 1905.

T. vitrinus is found in the duodenum of sheep and dromedaries, and also in man in Egypt.

Male 4 to 5·5 millimetres in length by 0·085 millimetre in breadth in front of the bursa, which is larger than in the other two species. Spicule 160 to 170 μ, accessory piece 85 to 95 μ in length.

Female 5 to 6·5 millimetres long; vulva 1·15 to 1·25 millimetres in front of the tip of the tail; egg 84 to 90 μ by 46 to 50 μ.

Life-History.—This is not known.

Pathogenicity.—Believed to be unimportant.

FAMILY 14: ANCYLOSTOMIDÆ LOOSS, 1911

Strongyles with armed mouth and bursa copulatrix provided with ribs.

Subfamilies.—Ancylostominæ and Bunostominæ.

SUBFAMILY ANCYLOSTOMINÆ, LOOSS, 1911.

Ankylostomidæ with more or less funnel shaped mouth capsule, its walls on the ventral side, and, especially towards the anterior edge, provided on each side with two longitudinal thickenings projecting outwards like ridges. In the gutter-like depressions between the ridges lie the terminations of the dorsal and lateral papillary nerves. Floor of the mouth cavity with one pair of inner ventral teeth, otherwise free from tooth like structures. Aperture of the dorsal œsophageal gland situated in the wall of the mouth capsule. Bursa of the male closed all round. Only one third of the dorsal ray is cleft. The course of the genital tubes is longitudinal.

Type Genus.—*Ancylostoma* Dubini, 1843. Other genus: *Uncinaria* Frölich, 1789.

Ancylostoma Dubini, 1843.

Synonym.—*Dochmius* Dujardin, 1845, *pro parte*.

Ancylostominæ with the head end, where the mouth is situated, abruptly truncated. Mouth large, round, with its ventral margin armed with two pairs of strong hook-like teeth, the points of which are bent backwards, while the bases are continuous posteriorly with longitudinal rib-like thickenings of the external surface of the capsule wall. The aperture of the dorsal œsophageal gland can be seen in the dorsal wall of the mouth capsule.

Male with a three-lobed bursa, broader than long, with two spicules. Female with vulva behind the middle of the body.

Species.—A number of species are known in man, dogs, bears, civet cats, and other carnivora.

Ancylostoma duodenale Dubini, 1843.

Synonyms.—*Strongylus quadridentatus* von Siebold, 1851; *Dochmius ancylostomum* Molin, 1860; *Sclerostoma duodenale* Cobbold; *Strongylus duodenale* Schneider, 1866; *Dochmius duodenalis* Leuckart, 1876, *pro parte*.

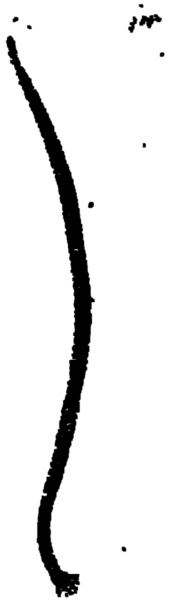


FIG. 2[illegible].—*Ancylostoma duodenale* DUBINI 1843. MALE.

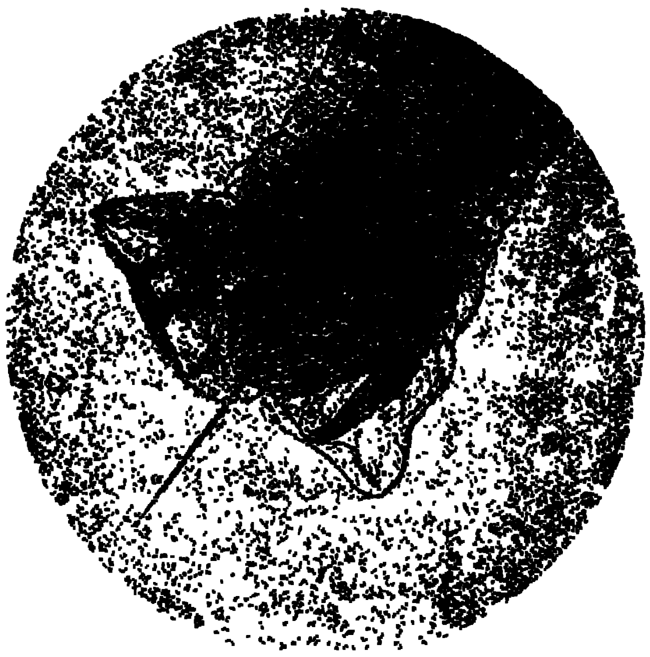


FIG. [illegible].—*Ancylostoma duodenale* DUBINI, MALE BURSA.

(From photographs by Bell.)

This worm, which is the great cause of tropical anæmia, was perhaps known to the ancient Egyptians under the term 'Heltu,' mentioned in the 'Ebers Papyrus,' which is supposed to have been written some 1550 years B.C., the disease being called A.A.A., and a remedy being advised. Perhaps the same anæmia is referred to in the 'Harita Samhita' under the term 'pandu roga,' which was said to be caused by swallowing clay. If this is correct, then knowledge of anæmia due to geophagy is very old indeed. If the ancients did really know about this worm, and the disease caused thereby, the knowledge was totally lost, and it was not till Dubini in 1838 discovered the worm in a peasant woman in Milan that modern medicine knew anything about its existence. Pruner, in 1846, found the parasites in Egypt, and Griesinger, in 1851, showed that it was the cause of Egyptian anæmia. Wucherer, in 1872, found that it was the cause of tropical anæmia in Brazil (called 'oppilação'). Perroncito found that it was the cause of the anæmia which badly affected the miners employed in the St. Gothard tunnel. Grassi and Parona in 1878 discovered the eggs in the fæces, thus enabling a diagnosis to be made during life. The wide geographical distribution of the parasite, and the amount of disease which it causes, is slowly being realized, and the deaths from anæmia, general dropsy, and so-called beri beri, etc., in different tropical regions are being found to be due to this animal.

The development and method of infection have been completely traced out by Looss in Egypt in a most masterly manner.

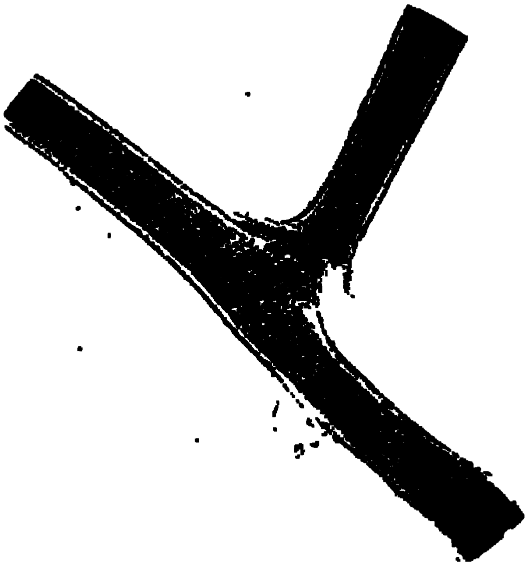


FIG. 290.—COPULATION OF AN[illegible]
(From a photograph by J. J. [illegible]

In 1902 Stiles found that under the term *Ancylostoma* two different parasites were being confused, one corresponding to Dubini's *Ancylostoma duodenale*, and the other new, which he named *Necator americanus*. Leiper has shown how widespread this latter parasite is in the Old World.

The geographical distribution is probably not fully known, because in many places it is confounded with *Necator*. It is supposed to be cosmopolitan in tropical regions, and in mines and tunnels in colder climates, in which, of course, the air-temperature is higher than that of the outside.

Morphology.—The body is cylindrical, tapering from back to front in both sexes. During life it is flesh-coloured. The cuticle is ringed. The mouth is terminal, with a chitinous wall, which ventrally carries two pairs of hook like teeth, and dorsally one pair. Close to the base of the outer ventral tooth opens the single-celled head gland, which runs through nearly half the length of the body. In the floor of the mouth there are two ventral chitinous plates, and the prominent opening of the dorsal head gland (often called a tooth).

Male measures about 10 millimetres in length by 0·4 to 0·5 millimetre in breadth, and possesses a bursa copulatrix at the posterior end, which is umbrella-shaped and supported by chitinous rods which are arranged as follows: In the median dorsal line is the costa dorsalis, which divides dorsally into two small branches, which are ramified at their tips. Postero-laterally there is one root on each side—the single costa dorsalis externa, in front of which is a single broad lateral root, which divides into the costa lateralis posterior, the costa lateralis media and the costa lateralis externa; while anteriorly also on each side is the costa ventralis. Through the opening of this bursa project the two spicules, unless they are retracted, which are long and slender, and measure about 2 millimetres in length. The male generative apparatus consists of a testis in the form of a tube, an oval vesicula seminalis, and a long cement gland, whose secretion fixes the male to the female during conjugation, and a spicule sac.

The female measures 12 to 18 millimetres in length, and has the vulva at the junction of the middle and hinder parts of the body, from which a short vagina opens into two tubes, which are divisible into ovijector, uterus, receptaculum seminis, and an ovary.

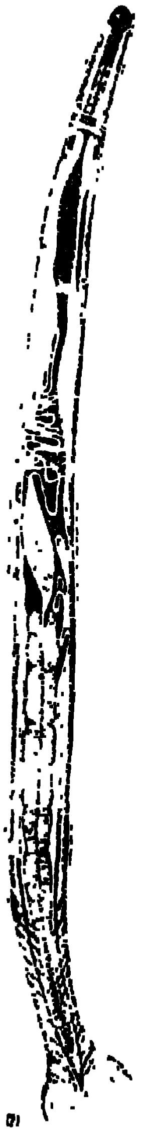


FIG. 291.—*Ancylostoma duodenale* DUBINI: MALE.

(After Looss.)

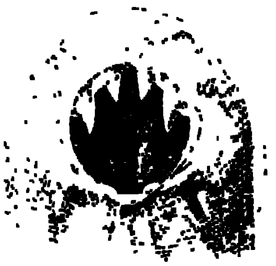


FIG. 292.—ANTERIOR END OF *Ancylostoma duodenale* DUBINI.

(After Looss, from Mense's 'Tropenkrankheiten.')

Life-History. The adult worms live chiefly in the jejunum of the host, where they feed upon the villi. Blood is only accidentally found in a worm. Here the females lay the eggs, which are oval in form, with broad rounded poles, surrounded by a colourless shell, which is really double, but looks single, inside which lies an oval granular mass separated from the shell by a considerable space. As the egg travels down the alimentary canal the granular mass divides into two, and finally into four segments, in which condition the egg is usually found in the fæces. Development proceeds in the fæces, depending upon the temperature of the atmospheric air. In twenty-four hours, if supplied with air, water, and heat, the embryo can be seen coiled up in the egg, from which it escapes as a larva, and feeds on the fæcal material. The larva is needle-shaped, pointed posteriorly, and measures 200 to 250 μ in length by 15 to 17 μ in breadth, and is rhabdite in form, with a long cylindrical terminal mouth, opening into an œsophagus, which, after narrowing, swells out into a bulb with three valves. The straight intestine surrounded by granular material opens into an anus situate some distance in front of the tip of the tail. This larva undergoes a first ecdysis when it becomes narrower, and the œsophagus and mouth lose their characteristic appearance, while it forms a new skin inside the chitinous cuticle, so that (at the end of five days in the tropics) it now ceases to grow and feed, and takes to water or moist earth, where it can remain unchanged for months, living on the food material enclosed in its own cells (stage of encystment). During this condition it may be quite active, and can swim and climb up any surface which is wet. This is an important factor in explaining the production of certain kinds of skin eruptions. It is now ready to infect man, which it does through the hair-follicles of the skin causing eruptions or sores—e.g., ground itch.

From the hair follicles it forces its way via the subcutaneous tissue into the venous bloodvessels and lymphatics. In the former it reaches the right heart and the lungs easily; in the

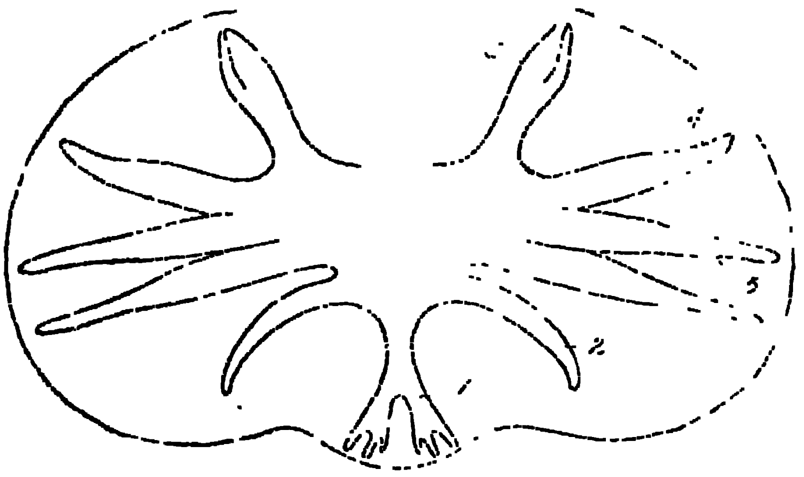


FIG. 293.—THE MEDIAN AND EXTERNAL CAUDAL BURSA OF *Ancylostoma duodenale* DUBINI.

1, Costa dorsalis; 2, costa dorsalis externa; 3, costa lateralis posterior et externa; 4, costa lateralis media; 5, costa ventralis.

(After Railliet from Stiles's Report.)

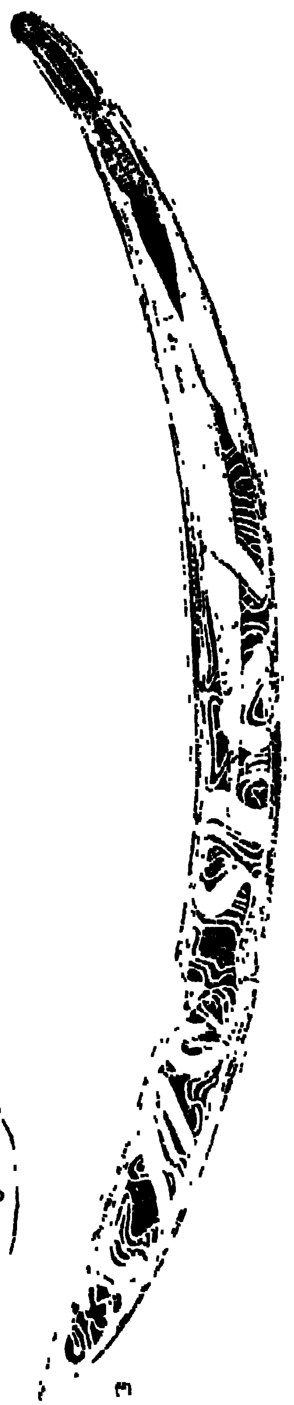


FIG. 294.—*Ancylostoma duodenale* DUBINI. FEMALE. (After Looss.)

latter many are killed in the lymphatic glands, but some get through to the blood, and in this way are carried to the lungs. They now work their way out of the capillaries into the lumen of the air cells, and travel up the bronchi, trachea, and larynx into the œsophagus (they might by chance get into the mouth), and so through the stomach to the intestine. The time occupied by this journey is believed to be from seven to ten days. In the skin they undergo their second ecdysis, and later a third and fourth ecdysis takes place in the alimentary canal, the third in four to five days and the fourth from four to six days after their arrival. They now measure 3 to 5 millimetres in length, and eight days later the generative organs begin to attain maturity, and the first copulations take place, and a few days later the first eggs appear in the faeces, thus completing the cycle of development, of which the portion after infection occupies four to six weeks.

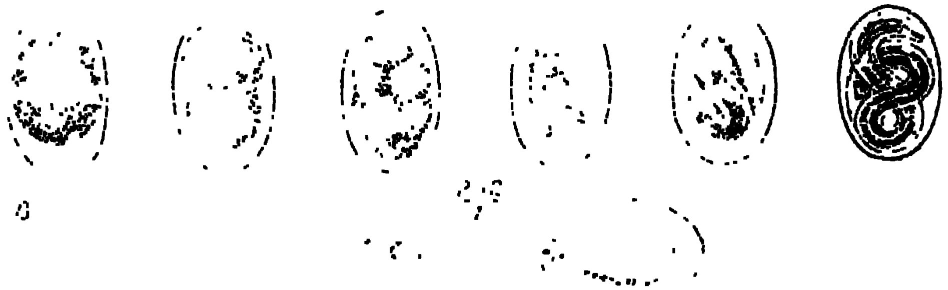


FIG. 295.—*Ancylostoma duodenale* DUBINI: DEVELOPMENT OF THE EXTRA-UTERINE EMBRYO.
(After Looss except the last figure which is after Perroncito.)

FIG. 296.—HATCHING OF EGG OF *Ancylostoma duodenale* DUBINI, 1843.
(From a photograph by [illegible])

The more important morphological changes which take place in the human body may be briefly recapitulated.

On entering the skin the third stage of development begins, during which the provisional buccal capsule is formed. A third ecdysis ushers in the fourth stage characterized by the provisional buccal capsule armed with a dorsal and a ventral pair of teeth. During this stage the sexes become differentiated and the permanent buccal capsule is formed. The fourth ecdysis results in the appearance of the adult worms.

The number of females can be calculated from the number of eggs in the fæces by the formula $X = \frac{A}{47}$, where X is the number of females and A the number of eggs in a gramme of fæces.

This history has been pieced together by Looss from observations on the infection of *Ancylostoma duodenale* in man and *A. caninum* in dogs.

These discoveries of Looss have been confirmed by Lambinet. Sambon, while agreeing with the view that the worms penetrate the skin and work their way to the lungs, considers that they pass from the pulmonary artery to the pulmonary veins, and in this way reach the general blood stream, and in due course the jejunum, the mucosa of which they pierce, and enter the lumen of the bowel. He believes that the worms seen in the trachea, larynx, and stomach by Looss are merely stray specimens which have escaped in the air cells from the vessels of the lungs. His reasons for this belief are:—

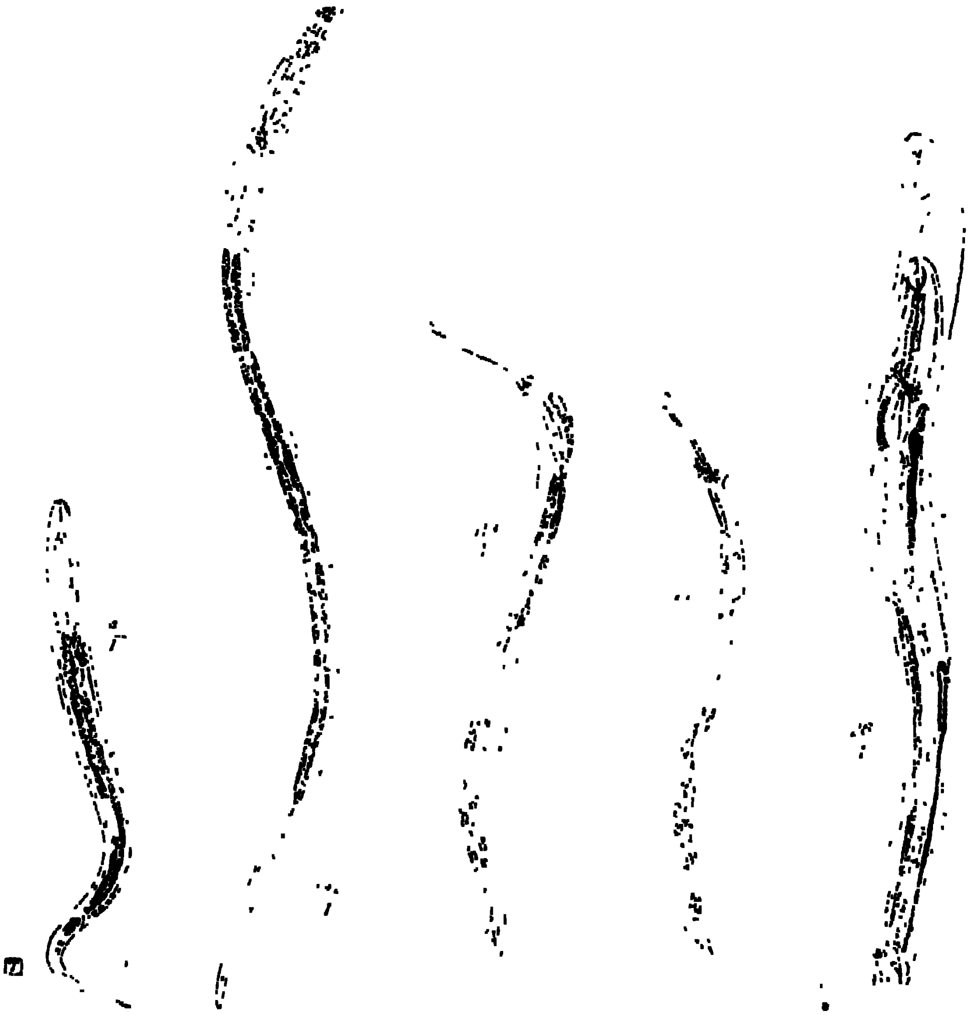


FIG. 297. FIG. 298. FIG. 299. FIG. 300. FIG. 301.

FIGS. 297-301.—DEVELOPMENT OF *Ancylostoma duodenale* DUBINI. (After Looss from Mense.)

1. The larval forms of *A. duodenale* have seldom been found in the stomach and when found in this organ are lodged beneath the epithelium.
2. They are invariably absent from the duodenum.
3. They have been found in the left heart, in the pulmonary and azygos veins, in the thoracic duct, in the peritoneum, in the kidneys, in the lymph glands, and in the connective tissue of various regions.
4. At the beginning of the infection there is always an intense hæmorrhagic inflammation of the jejunum, which entirely subsides later on, notwithstanding the presence of enormous numbers of parasites in the intestine.

5. Immature forms have been found again and again in blood-filled spaces beneath the intestinal mucosa by Bilharz, Griesinger, Sonsino, Grassi, and many other competent investigators.

6. A number of other worms which inhabit the intestinal cavity at maturity, such as *Œsophagostomum Sclerostomum*, *Ascaris*, *Gnathostoma*, etc., in an earlier developmental stage are usually found either free or encysted beneath the intestinal mucosa

He also considers that when the larvæ are taken in by way of the mouth they probably pierce through the walls of the œsophagus like the larvæ of *Hypoderma bovis* (see Chapter XXXIII.) and reach their intestinal habitat by way of the vessels in exactly the same way as those which penetrate the hair follicle.

Fülleborn and von Schilling-Torgau have re-investigated the subject by tracheotomizing dogs and inserting a cannula in such a way that the larvæ could not pass from the lungs to the œsophagus, but only to the exterior. The dogs were then infected with *Ancylostoma caninum* (Ercolani 1859), and after some time the secretion from the cannula in the trachea swarmed with larvæ. In other dogs the œsophagus, not the trachea, was cut across and its ends separately stitched to the skin, and after a time the secretion from the upper cut end contained larvæ. In both sets of experiments the dogs became infected intestinally with only a very small number of parasites.

It is thus seen that Sambon's hypothesis is theoretically correct, but Looss's route is the one by which the vast majority of the larvæ enter the body.

Pathogenicity.—It causes ankylostomiasis in man.

SUBFAMILY BUNOSTOMINÆ LOOSS, 1911.

Ancylostomidæ with small mouth capsule, with aperture narrowed anteriorly by plates with cutting edges springing from the sides, and more or less covering the ventral half of the aperture. At the base of the cone which carries the opening of the dorsal œsophageal gland there is on each side one tooth-like plate with smooth edges. Coils of the genital tubes very numerous and close. Externo-dorsal ray thin, more especially at the root. Spicule of the male barbed at the end.

Type Genus.—*Necator* Stiles, 1903.

There are seven genera in the subfamily—viz., *Bunostomum* Railliet, 1902; *Necator* Stiles, 1902; *Brachycionus* Railliet and Henry, 1910; *Gaigeria* Railliet and Henry, 1910; *Eumonodontus* Molin *emend.* Railliet and Henry; *Bathmostomum* Railliet and Henry, 1909; and *Grammocephalus* Railliet and Henry, 1910; but only *Necator* Stiles, 1903, concerns us.

Necator Stiles, 1903.

Bunostominæ closely resembling *Ancylostoma*, but distinguished therefrom by the small mouth capsule, which is armed only by semilunar plates. The head is strongly bent dorsally. In the male the bursa is bilobed. In the female the vulva lies in the anterior part of the body.

Type Species.—*Necator americanus* Stiles, 1902. Other species: *N. africanus* Looss, 1911, in the chimpanzee.

Necator americanus Stiles, 1902.

Synonyms.—*Dochmius duodenalis* R. Leuckart, *pro parte*; *Uncinaria americana* Stiles, 1902; *Ancylostoma americanum* von Linstow, 1903, *pro parte*.

In 1902 Stiles discovered that two distinct genera were being confused under the term *Ancylostoma*, and eventually called the new genus *Necator*. Leiper has recently shown that this new genus is very widely distributed over the world, and is the common cause of ankylostomiasis in Ceylon; while it occurs in India, Assam, Burma, the Philippine Islands, Fiji, Japan, America, and has been found in West and Central Africa and in North-West Rhodesia. In due course, no doubt, it will be reported in other places.

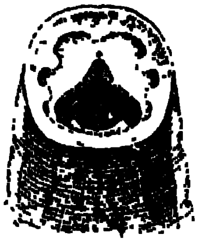


FIG. 302. — THE MOUTH CAPSULE OF *Necator americanus* STILES (After Looss, from Mense)

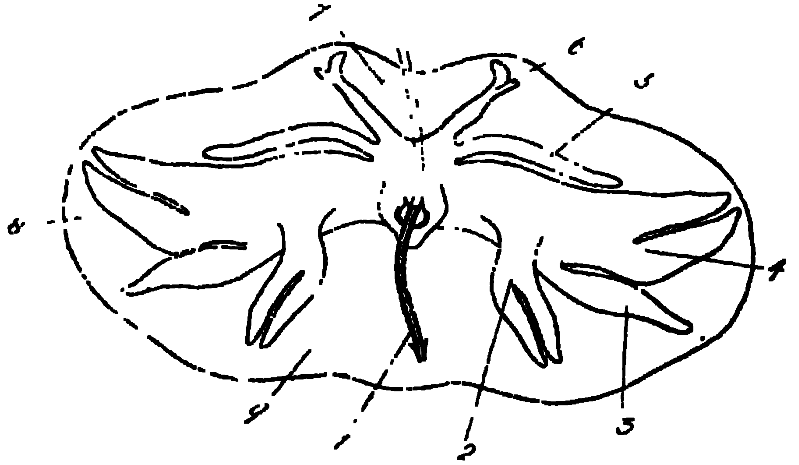


FIG. 303.—THE BURSA COPULATRIX OF A MALE *Necator americanus* STILES.

1, Spicules; 2, costa ventralis; 3, costa lateralis posterior; 4, costa lateralis externa et costa lateralis media; 5, costa dorsalis externa; 6 costa dorsalis; 7, dorsal lobe, 8 lateral lobe; 9, ventral lobe.

(After Stiles.)

Morphology.—The body is cylindrical, and somewhat attenuated anteriorly. Head acutely bent dorsally. Mouth with a ventral pair of prominent semilunar chitinous plates and a dorsal pair of slightly developed plates. Into the floor of the mouth projects the opening of the dorsal head gland, which appears like a dorsal conical tooth, while deep in the cavity appear one pair of dorsal and one pair of ventral submedian lancets. Excretory pore 0·5 millimetre behind the mouth, with cervical papillæ on either side.

Male 7 to 9 millimetres in length and 0·3 to 0·35 millimetre in breadth. The bursa consists of two large lateral lobes joined to a dorsal median lobe, which appears as if divided into two, and to an indistinct ventral lobe. There is a slight ventral enlargement just posterior to the point at which the bursa joins the body-wall. The costa dorsalis is divided at its base into two diverging branches, which are bipartite. The common base of the costa dorsalis and costa dorsalis externa is very short, while the latter ray is long, slender, and clavate. The costa lateralis externa is closely joined to the costa lateralis media. Two small precaudal papillæ can be seen anterior to the ventral rays. The spicules are long and slender, 0·92 millimetre in length, and terminate in barbed points.

Female is 9 to 12·6 millimetres in length; vulva in the anterior half of the body, but near the equator. Eggs 57·7 to 80 μ by 35 to 52·5 μ; average, 60 by 40 μ.

Life-History. This is the same as *Ancylostoma duodenale*.

Zoological Distribution.—Man and the gorilla.

Pathogenicity. It causes ankylostomiasis in certain regions.

Ancylostoma ceylanicum Looss, 1911.

Synonym. (?) *Ancylostoma braziliense* Gomez de Faria, 1910.

Definition. Ancylostoma with one large tooth at the anterior edge of the mouth capsule and below and behind this a very small tooth towards the middle line. Lobes of bursa almost as broad as long.

Remarks. This worm was found in cats and dogs in India, and is the same as that found in the civet cat in Ceylon, and in man in Bengal by Clayton-Lane, and called *A. ceylanicum*.

It has also been found by Darling in a Tamil and a Chinese in Kuala Lumpur, and also in dogs, in which they were frequently found.

Clayton-Lane suggests that the genus Ancylostoma should be divided into two subgenera—viz.:

$$\text{Subgenus } \textit{Ancylostoma} \begin{cases} \textit{A. duodenale.} \\ \textit{A. caninum.} \end{cases}$$

$$\text{Subgenus } \textit{Ceylancylostoma} \begin{cases} \textit{A. ceylanicum.} \\ \textit{A. malayanum.} \end{cases}$$

G. de Faria maintains that *A. braziliense* and *A. ceylanicum* are probably not the same, because of the character of the oral capsule and bursal rays.

PSEUDOSTRONGYLES Leiper, 1912.

Nematoda with simple mouth, and a cuticular bursa in the male without rays. One spicule.

FAMILY 15: EUSTRONGYLIDIDÆ Leiper, 1912.

SUBFAMILY DIOCTOPHYMINÆ Railliet.

Eustrongylidæ with unarmed mouth; bursa copulatrix without ribs or bands. Genus: *Dioctophyme* Collet-Megret, 1802.

Dioctophyme Collet-Megret, 1802.

Very large Strongylidæ with cylindrical bodies, mouth with six papillæ. Male with collar-like bursa and one spicule. Female with one ovary; vulva in the anterior half of the body.

Dioctophyme renale (Goeze, 1782).

Synonyms.—*Ascaris canis et martis* Schrenk, 1788; *A. visceralis et renalis* Gmelin, 1789; *Strongylus gigas* Rudolphi, 1802; *Eustrongylus gigas* Diesing, 1851; *Strongylus renalis* Moquin-Tandon, 1860; *Eustrongylus visceralis* Railliet, 1885.

This worm lives in South America in the pelvis of the kidney in the dog, seal, otter and wolf. It has been recorded twelve times in man if the records really refer to this worm.

Morphology.—The worm is blood-red in colour, but otherwise very like a large *Ascaris lumbricoides*. Along the lateral lines there are about 150 papillæ. The submedian ridges are well developed, and the anterior extremity somewhat attenuated. Cuticle finely striated transversely.

Male 40 centimetres long by 4 to 6 millimetres broad, bursa without rays, and with one very long, slender spicule 5 to 6 millimetres in length. Female 100 centimetres in length and 12 millimetres in thickness, with an obtuse, slightly curved posterior end, a single ovary, and a vulva situate 50 to 70 millimetres behind the anterior extremity. Eggs ovoid, with thick, brownish shell 68 to 80 μ by 40 to 43 μ, with numerous depressions.

Life-History.—Development begins in the uterus of the female, but stops at a certain stage and does not continue (Balbiani) until brought into contact with water or damp soil, when the egg hatches. The embryo is 240 μ by 14 μ, cylindrical, and gradually tapering posteriorly. The head is pointed, with a terminal mouth without papillæ, but which is thought to be provided with a small protractile dart. The further development is not known; it has been thought that it takes place in fish, but experiments have failed to justify this view.

Pathogenicity.—It is usually found in the kidney, which it destroys. In animals it has also been found in mammary and perineal tumours. Symptoms appear to be hæmaturia, and the diagnosis is made by the discovery of the eggs.

FAMILY 16. TRICHOSOMIDÆ.

Nematoda with the anterior portion of the body thin and whip-like; posterior portion thick with genitalia. Mouth small, without papillæ. Œsophagus very long, traversing a peculiar strand of cells.

Trichinellinæ Ransom, 1911.

Male without spicule. Female producing embryos.

Trichurinæ.

Male with spicule. Female producing barrel-shaped eggs.

Genus Trichinella Railliet, 1895.

Trichinella Railliet, 1895.

Synonym.—*Trichina* Owen, 1835, *nec* Meigen, 1830.

Very small Trichinellidæ, with thin, hair-like bodies. Posterior end of the male with two cone-like appendages, between which the cloaca is situate. Vulva placed far forwards.

Trichinella spiralis Owen, 1835.

Synonym.—*Trichina spiralis* Owen, 1835.

T. spiralis, though discovered by Paget in 1835 and described by Owen, had been previously seen by Peacock in 1828 and by Hilton in 1833.

It is really a parasite of the black rat (*Epimys rattus*) and the sewer rat (*E. norvegicus*), in which the rate of infection is placed from 8·3 to 100 per cent., according to the locality, but it spreads from the rat to pigs, dogs, cats, and many other animals.

Man becomes infected from the pig as a rule, for that animal is particularly liable to the disease, because it is apt to be fed upon scraps of raw meat. Further, the larva in the flesh of the pig is very difficult to kill, for it will resist a temperature of 80° C., pickling, smoking, and freezing. Hence, though ham be well boiled, it does not follow that the larvæ in its centre are killed. Sausages, however, are the greatest danger, for in them the larvæ can live well protected.

In order to infect man, there must be a source of infection for the pig, and this, in the first instance, can come from the rat, and afterwards be kept up in the pig, and then the transmission to man is easy.

As rats, pigs, and men are cosmopolitan, so trichiniasis is also cosmopolitan. It is not uncommon in certain parts of India, and is known in China. In considering the endemicity of the disease, it must not be forgotten that the wild boar (*Sus scrofa ferox*) is susceptible. The disease is supposed to have been introduced into Europe from Asia either by *Epimys norvegicus* at the end of the eighteenth century, or by the Chinese pig from 1820 to 1830. At present it is common also in America.

Morphology and Life-History.—It is usually found in human or pig's muscles, where it appears as minute white specks, which when magnified, are found to be encysted larvæ. These cysts are oval with their long axis in the same direction as that of the muscular fibres, measuring 400 by 250 μ. The cyst membrane is formed from inflamed connective tissue, which has invaded the infected muscular fibre. Inside the cyst is the coiled-up worm. In this condition the larvæ may live for years, but may be killed by calcification. They are mostly found in the diaphragm, the larynx, tongue, abdominal and intercostal muscles.

When these cysts reach the stomach of a man or animal, the gastric juice dissolves the cyst-wall, and the parasites escape, and, entering the duodenum and jejunum, they grow into adult males 3 to 4 millimetres long by 60 μ in diameter, and females 1·4 to 1·6 millimetres long by 40 μ in diameter, which copulate. The males now die off, and the females, increasing in size, penetrate the mucosa of the bowel until they reach a lymph-channel, where they deposit their larvæ, which are born alive. Leuckart says one female gives rise to 1,500 larvæ, which are carried by the lymph and blood streams all over the body. The larvæ now leave the capillaries and work their way into the tissues, and in about nine to ten days encapsule in the muscles, the attacked fibres of which degenerate and become inflamed, and the cyst already described is formed.

Pathogenicity.—When the female pierces the mucosa, and during the wandering through the lymph and blood of the larvæ, very severe symptoms called trichinosis or trichiniasis are produced.

SUBFAMILY TRICHURINÆ Ransom, 1911.

Type Genus.—*Trichuris*; also *Capillaria* Zeder, 1800.

Trichuris Roederer and Wagler, 1761.

Trichosomidæ, with the anterior part of the body very long and thread-like, and the posterior thicker portion sharply truncated, with a terminal anus. Male with a spirally rolled posterior end and one spicule; female with one ovary, and the vulva situated at the junction of the thinner and thicker parts of the body.

Species in man: *Trichuris trichiura* Linnæus, 1761.

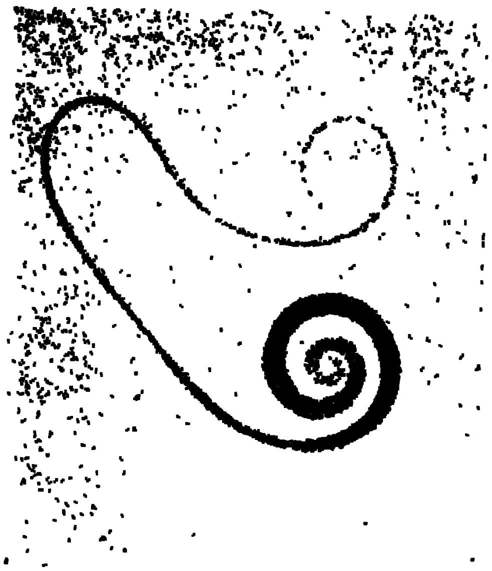


FIG. 304.—*Trichuris trichiura* (LINNÆUS, 1761): MALE.

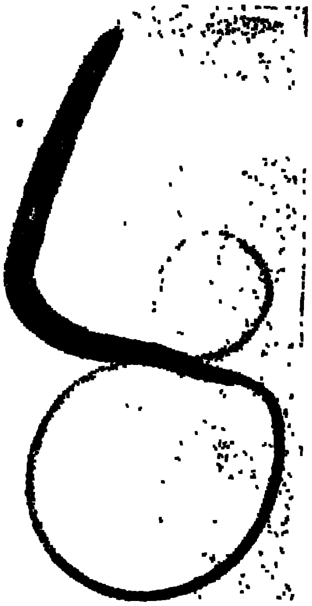


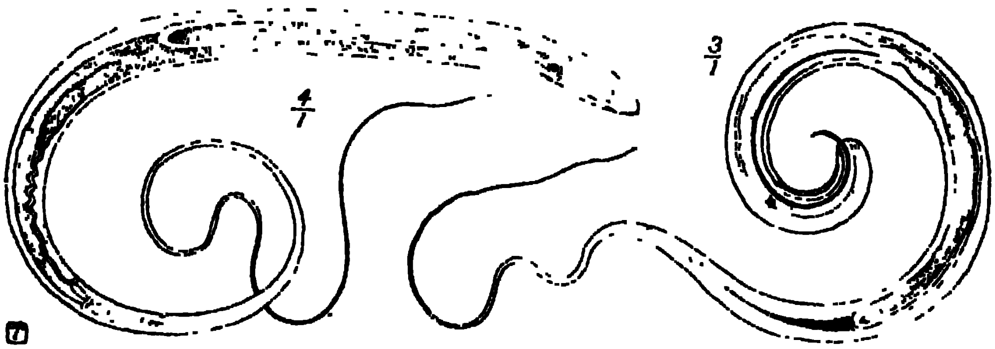
FIG. 305.—*Trichuris trichiura* (LINNÆUS, 1761): FEMALE.

(From a photograph by J. J. Bell.)

Trichuris trichiura Linnæus, 1761.

Synonyms.—*Ascaris trichiura* L., 1771; *Trichocephalus hominis* Schrank, 1788; *T. dispar* Rudolphi, 1801.

This worm is very commonly met with in the tropics. Its eggs appear in the fæces, and it is met with in the cæcum and sometimes in the vermiform appendix during post-mortems. Its anterior end is frequently found buried in the mucous membrane, and while in this position it is possible for bacteria to enter and cause disease —*e.g.*, appendicitis.



FIGS. 306 AND 307.—*Trichuris trichiura* LINNÆUS: FEMALE AND MALE. (After Claus.)

It is commonly called the whip-worm, and is cosmopolitan in its distribution.

Morphology.—The male measures 40 to 45 millimetres in length, and is easily recognized by the spirally coiled posterior end. Its spicule, which lies in a retractile pouch, measures 2·5 millimetres. The female measures 45 to 50 millimetres in length. The ova are oval, brown, thick-shelled, with a pale, clear body at each pole, where the shell is deficient. They measure 50 to 54 by 23 μ.

Life-History.—When the egg appears in the faeces, it is unsegmented, and is said to take eighteen months before the embryo is fully developed. The egg with the enclosed embryo is then taken in through the mouth in contaminated food or water, there being no intermediate host. The shell is dissolved by the gastric juice, and the embryo reaches maturity in the intestine in about four to five weeks.

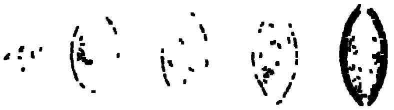


FIG. 308.—DEVELOPMENT OF THE EGG OF *Trichuris trichiura*. (After Stiles.)

Pathogenicity.—Usually harmless, but may give rise to intestinal disturbance and at times appendicitis.

Syngamus von Siebold, 1836.

Strongyles with broad head, mouth with a chitinous capsule. Male with two spicules. Female with two ovaries and a vulva situate in the anterior part of the body.

Syngamus kingi Leiper, 1913.

King forwarded quite recently a pair of specimens to Leiper purporting to come from a woman living in St. Lucia who suffered from chronic cough, when the worms were expectorated with blood. Leiper thinks that this may be an accidental infection of man with a parasite which is harboured possibly by a carnivore. It differs from *S. trachealis*, the common nematode of poultry, in the buccal capsules, these in the male and female are on the same level, whereas in *S. trachealis* that of the male is more anterior. Mouth capsules terminal. Tail of female bluntly pointed.

ORDER II. GORDIACEA.

Nemathelminthes with the intestinal canal always atrophied anteriorly in the adult, head without papillae, two testes, but never spicules in the male; vulva always united with the posterior portion of the intestine to form a cloaca; rare in man, only accidental parasites.

These worms are popularly known as horsehairs, and are supposed to cause serious and even fatal disease in man or animals if swallowed. Their pathogenicity has recently been studied by Stiles, who is unable to support the popular belief as to the serious nature of these parasites in man. They are very long, thin worms, like *Filaria*, which can be found in ditch-water swimming freely or twining round water plants.

The body is covered with a well-developed two layered cuticle. The mouth and the anterior part of the intestine is obliterated. The posterior end of the male is lobed, and without spicules. In the female there are two ovaries and the egg-sacs, which open by means of oviducts into a uterus. The males are often blackish brown, and the females light clay brown.

The life-history of *Parachordodes tolosanus* is very complicated: the first larva enters the larva of the alder-fly (*Sialis lutaria* L.), where it lives during the winter, and passes over to the imago of the same insect, which is eaten by a beetle (*Pterostichus niger*). The first larva changes, becoming a second larva, which lives in the beetle during the second winter, and finally escapes into the water about twenty months after hatching. In the water it soon becomes adult Gordiidæ.

The Gordiacea includes the family Gordiidæ, which is divided by Camerano into four genera: *Gordius* Linnæus, 1758; *Paragordius* Camerano, 1879; *Parachordodes* Camerano, 1897; *Chordodes*.

Without going into details, it may be said that the following species have been reported as parasitic in man:—

Gordius aquaticus L., 1758. Four recorded cases in Europe with abdominal symptoms, pain, vomiting, etc. and nervous symptoms, hysteria, and neuralgia.

G. chilensis E. Blanchard, 1849.—This is simply based on the legends of Chilian Indians, who fear the worm.

Paragordius varius Leidy, 1851.—Four cases of infection in North America. Worms were expelled *per anum* or by vomiting. Symptoms: unimportant.

P. tricuspidatus Dufour, 1828. One case in France. Symptoms: slight colic. Worm extracted from the throat.

P. cinctus von Linstow, 1900. From a man in Leydenburg in the Transvaal.

Parachordodes tolosanus Dujardin, 1842. Four cases, in one of which it is accused of causing epileptiform fits. Cases occurred in France and Italy.

P. pustulosus Baird, 1853. One case in Italy caused anal pruritus and discharge.

P. violaceus Baird, 1853. One case in France; it lodged in the throat before expulsion.

P. alpestris Villot, 1884. One case in France.

Undetermined.—Ward, in 1903, published the account of a case in which the genus of the worm was not determined.

CLASS II.

ORDER III. ACANTHOCEPHALA Rudolphi.

Nemathelminthes with a retractile proboscis armed with several rows of spines or hooks; intestine absent; parasitic in the intestine of vertebrates.

The Acanthocephala are elongated cylindrical worms, in which the body can be divided into proboscis, neck, and trunk. The proboscis is a hollow, finger-shaped, retractile process, covered with a thin cuticle, and armed with rings of hooks arranged in longitudinal rows. The neck is not always discernible. The trunk has a rounded posterior end, and consists of a body-wall with muscular layers, covered by a thin cuticle, enclosing the excretory and reproductive organs. The sexes are separate. The male organs are two oval testes, whose vasa efferentia unite into a vas deferens, which opens into a cirrus contained in a pouch or bursa, and provided with a prostate gland.

The female organs consist of two ovaries, which break down into masses of cells which escape into the cœlom. Here the ova are fertilized and the embryo is formed, and escapes through a funnel-shaped structure called 'the bell' into the uterus, and so through the vagina and the genital orifice at the posterior end of the body into the lumen of the host's intestine.

The embryo leaves the host with the fæces, and, getting into water, enters the alimentary canal of a crustacean, water-insect, or fish, inside which it hatches. It now bores its way through the intestinal wall into the cœlom, where it develops all its organs except the reproductive.

The crustacean, water-insect, or fish must now be eaten by a vertebrate, when the acanthocephalid becomes sexually mature in the intestine. They are very rarely found in man.

Classification.—The Acanthocephala are divided into four families by Hamann and Shipley:—Echinorhynchidæ, Gigantorhynchidæ, Neorhynchidæ, and Arhynchidæ. Human parasites, which are very rare, are only found in the first two families.

ECHINORHYNCHIDÆ.

Acanthocephala with elongated, smooth body; proboscis can be retracted into a sheath with double walls.

Genus.—*Echinorhynchus* Müller, 1776.

Echinorhynchus (Müller, 1776).

Echinorhynchus hominis Lambl, 1859.

This parasite was found in the intestine of a boy who died of leukæmia; it was 5·6 millimetres long. There appears to be much doubt as to whether this really was *Echinorhynchus*.

GIGANTORHYNCHIDÆ.

Gigantorhynchus Hamann, 1892.

Large Acanthocephala with ringed, flat, tæniform bodies.

Gigantorhynchus gigas (Goeze, 1782).

This parasite was alleged by Lindemann to occur in man in South Russia, where Schneider says Melolontha is eaten raw. It is 10 to 15 centimetres long; eggs 80 to 100 μ long, with three shells. Its usual life history is that the adult is found in pigs, and the larva in *Melolontha vulgaris*, *Cetonia aurata*, or *Lachnosterna arenata*.

Gigantorhynchus moniliformis (Bremser, 1911).

Synonym.— *Echinorhynchus moniliformis* Bremser, 1911.

Leiper records a parasite found in a Sudanese by Christopherson as probably belonging to this species. It has also been seen in man by Grassi and Calandruccio. The worm is found in Europe, Africa, and Brazil.

Morphology.—White body with attenuated ends with many rings, making it closely resemble a Porocephalus. Male 4 to 5 centimetres in length, with a bursa visible to the naked eye. Female 7 to 10 centimetres long. Eggs ellipsoidal, 85 μ by 45 μ.

Life-History.—The intermediate host is *Blaps mucronata*. Calandruccio has shown experimentally that it can develop in the human body.

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CHAPTER XXVII

ANNULATA AND HIRUDINEA

Annulata—Hirudinea—Classification—Gnathobdellidæ—Hirudinæ—Hæmadipsinæ—Remaining orders—References

PHYLUM ANNULATA AUCTORES.

METAZOA with elongated bodies divided externally into a number of rings which represent a division of the internal parts into segments or somites (metameres), usually with an extensive cœlom. Nervous system consists of a cerebral ganglion, with double commissure and ventral nerve cord. Organs of excretion in the form of metamerically arranged pairs of nephridia.

The only class of this phylum which contains animals of importance in tropical medicine is the Hirudinea or Discophora—*i.e.*, the leeches.

CLASS HIRUDINEA SAVIGNY, 1817

Annulata with oval bodies, showing a dorso-ventral flattening and two suckers, one at each end.

Remarks.—Leeches are of interest in the tropics, first because they may be a considerable nuisance as ectoparasites—*e.g.*, land leeches or *Hæmadipsa*; and, secondly, they may be of considerable danger to the health and even the life of a person as endoparasites—*e.g.*, the water leeches, particularly *Limnatis*.

As ectoparasites they are apt to fasten on the legs of persons going through grass or jungle. In fact, in Ceylon, while standing on a piece of grass in certain parts of the low country, the leeches can be watched converging from all quarters of the compass towards the observer.

Very often the bite is not noticed, and the leech or leeches may have sucked a considerable amount of blood before any attention is paid to them, and tales are told of persons feeling faint before noticing that they were being attacked by these creatures.

They are apt to get into the nose, naso-pharynx, or larynx with drinking-water, and in this endoparasitic condition they may suck blood and cause epistaxis or hæmoptysis, and this may go on to such an extent that anæmia and even death may result.

It is hardly possible to believe that they can live in the stomach, for it is much more likely that they are at once killed by the gastric juice and digested.

A great many tropical countries appear to be plagued with leeches which affect men and animals as indicated above, but it is probable that Algeria, Palestine, and Ceylon are the most infested. Among the other places in which they are troublesome may be mentioned the Philippines, Java, Sumatra, Australia, Japan, and Chili. In Algeria and Palestine the leech lives in the pools of drinking-water, and here the endoparasitic form may be met with; whereas in Ceylon it is usually a land leech which attacks the individual, and therefore the ectoparasitic condition is common, while the endoparasitic is more rare, being due to ***Hirudo multistriata***.

Morphology.—Leeches have an elongated, more or less oval body, which is very retractile and extensile, and is marked by annuli or rings, of which several—usually five—form a somite. The number of rings to a somite is, however, reduced anteriorly and posteriorly, being abbreviated. At the anterior extremity is the oral sucker, and at the posterior the acetabulum. The skin possesses many unicellular dermal glands. The mouth-opening is situate in the anterior sucker, and the anus either in or just in front of the constriction which separates the posterior sucker from the body.

The male genital opening is placed on the twenty fourth annulus, and the female five annuli behind it in *H. medicinalis*; but the female orifice may vary with regard to the male in other genera. A number of nephridial orifices can be seen as paired openings on the posterior annuli of many of the somites. Eyes exist as small, dark dots on the dorsum of the body, behind the anterior sucker. The mouth may be armed or unarmed. In the former condition it possesses three jaws—one dorsal and two ventro-lateral—each with a thickened free edge notched with teeth. In the latter there may be only a proboscis. Into the mouth open the salivary glands, which secrete a fluid which prevents the coagulation of the blood. The pharynx is an oval sac, with strong muscular walls and radial muscles, which can alternately contract and dilate the cavity, thus forming a sucking-pump. From the pharynx an œsophagus leads to the crop, which is a straight, thin-walled tube with lateral diverticula.

Behind the crop comes the small stomach, which opens into a narrow straight tube—the intestine—which runs to the anus. The cœlom consists of a series of tubes containing red blood. The excretory system consists of the nephridia. There is a supra-œsophageal ganglion, a nerve collar, and a ventral nerve chain. The male reproductive organs are a number of testes, with vasa efferentia opening into two vasa deferentia, which, after coiling into epididymis run to the single penis. The female organs are a pair of ovaries and oviducts opening into a single vagina.

Biology.—Leeches appear to be essentially water animals, and though certain genera can live on land, still, they require a great deal of moisture. Hence land leeches retire into moist places under stones, earth, etc., and only come out when requiring food. In dry weather not a leech can be seen, while in damp weather they may be very abundant.

Any disturbance of the air appears to affect them. Hence they are quickly aroused from their retreats when a human being or animal approaches, and set forth at once, often with considerable speed, to the attack.

The bite is not always painful at first, and may not be noted until the flow of blood is observed. The leech, while biting, keeps itself and the skin of the victim moist by liquid excreted by the nephridia and the dermal glands. When it has gorged itself with blood it drops off, but its salivary secretion prevents the coagulation of the blood, and hence the site of the leech-bite bleeds considerably for some time. The blood is stored up in the crop and its cæcal diverticula, and only a little is used day by day for food.

Pathogenicity.—Leeches are hosts of trypanosomes and other parasites, and their bite may possibly introduce these parasites into the skin of the human victim as well as into that of animals.

The marked feature of the pathogenesis is loss of blood, not merely caused by the sucking of the leech, but also by the bleeding from the wound caused by the bite. Further, the punctures caused by *Hæmadipsa zeylanica* are extremely liable to become ulcers, which, according to Marshall and Davy, caused a high rate of mortality among the Madras sepoys and coolies during the Kandyan rebellion of 1818 in Ceylon. Short of death, amputation of the limb was necessary in those days. We are not inclined to consider these old statements as erroneous, because it is quite possible that some organism is often introduced into the affected part by the leech-bite. For a further discussion of the pathogenicity, see the chapters on Diseases of the Respiratory Organs and of the Skin.

Classification.—The class Hirudinea may be divided into several orders.—

Order I.: Rhynchobdellida.—Hirudinea without jaws, with an extensile proboscis and with colourless blood, living in salt and fresh water.

The Rhynchobdellida are divided into two families:

Family 1 Ichthyobdellidæ.—Rhynchobdellida with the anterior narrower part of the body distinct from the posterior and with both suckers distinct from the body.

To this family belong the genera *Piscicola* de Blainville 1818, and *Pontobdella* Leach, 1815, mentioned in the chapter on Protozoa.

Family 2 Glossiphoniidæ.—Rhynchobdella with the anterior sucker fused to the body, while the posterior is distinct.

Among the genera of this family is *Hæmentaria* de Filippi, 1849, of which *H. officinalis* de Filippi is found in Mexico, and is alleged to cause drowsiness, buzzing in the ears, and a painful rash, when it bites a person. The causation of these symptoms is obscure. Another species is *H. ghilianii* de Filippi, 1849.

Other genera are *Glossiphonia* Johnson 1816, *Hemiclepsis* Vejdovsky, 1883; and *Placobdella* R. Blanchard, 1893.

Order II.: Arhynchobdellida.—Hirudinea usually with jaws, without a proboscis, and with red blood, living in fresh water or on land. There are two families, Gnathobdellidæ and Herpobdellidæ, of which only the first concerns us.

FAMILY GNATHOBDELLIDÆ.

Arhynchobdellidæ with five or more, rarely four, pairs of eyes, and, except in the Semiscolinæ, with three denticulate jaws. Eggs enclosed in a spongy cocoon, which is deposited above water-line.

The Gnathobdellidæ are classified into the following subfamilies: Hirudininæ, Hæmadipsinæ, and Semiscoleeinæ, which last is not of interest to us.

SUBFAMILY HIRUDININÆ R. Blanchard, 1894.

Aquatic Gnathobdellidæ with ten eyes, and with an eyeless ring between the third and fourth pair of eyes, with denticulate jaws. Complete somite formed of five rings. The nephridial pores open near the margins of the body on the ventral surface.

In 1896 Blanchard divided this subfamily into two series: (1) Monostichodonta—jaws armed with one row of teeth; (2) Distichodonta—jaws armed with two rows of teeth.

The genera are: *Hirudo, Limnatis, Hæmopis, Hirudinaria, Limnobdella, Macrobdella,* and *Whitmania,* which are divided into two series.

Series 1: Monostichodonta.

Hirudininæ with jaws with or without papillæ, and armed with a single row of numerous sharp teeth.

Hirudo Linnæus, 1758

Synonyms. *Sanguisuga* Savigny, 1822, *Iatrobdella* de Blainville, 1827.

Hirudininæ with twenty-six somites of which the 1st and 2nd have each one ring; 3rd two rings, 4th, 5th, and 6th, each three rings; 7th to 22nd, each five rings, 23rd three rings, 24th 25th, and 26th, each two rings, making in all 102 rings.

Eyes are carried on the 1st, 2nd, 3rd, 5th, and 8th rings. The buccals are the 5th and 6th, and the post buccals the 7th and 8th. The first pair of nephridia is on the 13th and the last (the 17th) pair on the 93rd ring.

The male orifice is between the 30th and 31st rings which are the 2nd and 3rd of the 10th somite.

FIG. 300. *Hirudo multistriata* SCHMARDA.
The common water leech of Ceylon.

The female orifice is five rings behind that of the male—*i.e.*, between the 35th and 36th rings. The anus is situate on the 102nd ring, or between the 101st and 102nd.

Hirudo medicinalis Linnæus 1758, is found principally in Hungary. Variety *officinalis*.

H. troctina Johnston, 1816 is the medicinal leech of England, France, Spain and Algeria.

H. nipponia Whitman, 1886. Japan.
H. sinica de Blainville, 1827. China.
H. quinquestriata Schmarda. Australia.
H. saigonensis. Cochin-China.
H. asiatica R. Blanchard. Afghanistan and Persia.
H. timorensis R. Blanchard. Timor.
H. septemstriata Grube. South Africa.
H. hildebrandti R. Blanchard. East Africa, Victoria Nyanza.
H. multistriata Schmarda. Ceylon.

Series 2: Distichodonta.

Hirudininæ with jaws without papillæ, and armed with two rows of infrequent blunt, irregular teeth.

Hæmopis Savigny, 1817.

Synonym.—*Aulastoma* Moquin-Tandon, 1826.

Hirudininæ with 3 rings on the 23rd somite, and two rings to the 24th, 25th, and 26th somites. Crop with one pair of elongate lateral cæca reflected posteriorly. Genital openings usually separated by five rings. Upper lip of anterior sucker not divided inferiorly by a longitudinal groove. *H. sanguisuga* Linnæus, 1758 found in Europe, and *H. lacustre* Leidy in America.

Limnatis Moquin-Tandon, 1826.

Hirudininæ with a longitudinal groove on the inner surface of the upper lip of the anterior sucker. Jaws with more than 100 teeth.

Limnatis nilotica Savigny, 1820. This leech is 8 to 10 centimetres in length, and is common in North Africa, the Canaries, South Europe, and Asia Minor while it, or some other species, is found on the West Coast of Africa.

Limnatis mysomelas Serulias and Virey, 1829, is found in Senegambia, and *L. granulosa* Savigny, 1820, in India.

These leeches are of importance, because they are apt to get into the nose, naso-pharynx, pharynx, and larynx of persons drinking at pools of water, and to cause serious symptoms. Other species are *L. africana* R. Blanchard in Senegal and the Congo, *L. maculosa* Grube, 1859, in Singapore, *L. mysomelas* in Senegal, and *L. granulosa* in India.

Hirudinaria Whitman, 1886.

Hirudininæ with the sexual pores separated by several rings. Acetabulum very large.

H. javanica Wahlberg, 1855. In Batavia, Sumatra, and Burma.

Limnobdella R. Blanchard

Hirudininæ with 103 to 104 rings. Jaws without papillæ. The 6th somite with three rings, the 23rd with five rings.

L. grandis R. Blanchard. Timor, Sumatra, and Ceylon.
L. australis Bosisto, 1859. Sydney and New South Wales.
L. mexicana R. Blanchard. Mexico.

Macrobdella Verrill, 1872.

Hirudininæ, jaws without sensory papillæ, teeth not numerous, 103 body rings. Both genital openings on the 11th somite.

M. sestertia Whitman, 1886. America.

Whitmania R. Blanchard, 1884.

Hirudininæ with 105 to 107 rings; 6th segment with five rings; 23rd has always more than three rings. Teeth more or less rudimentary.

W. ferox R. Blanchard, 1886. London Zoological Gardens and in Asia.

SUBFAMILY HÆMADIPSINÆ R. Blanchard, 1894.

Gnathobdellidæ, small leeches, living on land, with ten eyes and no eyeless ring between the 3rd and 4th eyes. The three last body somites (twenty-three to twenty-six) with only one ring each. Dentition simple and complete.

Remarks.—The Hæmadipsinæ were monographed by Blanchard in July, 1917, in his usual masterly style.

Type Genus.—*Hæmadipsa* Tennent, 1861.

Hæmadipsa Tennent, 1861.

Synonyms.—*Hæmopis* Schmarda, 1861; *Chthonobdella* Grube, 1865.

Hæmadipsinæ, terrestrial in habit, 2 to 3 centimetres in length; subcylindrical, tapering slightly forwards, cephalic lobe, rounded when at rest, but pointed in extension; acetabulum moderately large, round, or oval, centrally attached, separated from the body only by a feeble constriction.

Eyes in five pairs, the rings bearing the 3rd and 4th pair, not separated by an intervening ring; the rings bearing the 4th and 5th pairs, separated by two rings. Œsophagus with three plications—one dorsal and two lateroventral. The three maxillæ covered with teeth, which increase in size towards the converging anterior ends of the jaws. Clitellum includes three somites and fifteen rings. Genital orifices separated by five rings, nephridial pores at the margin of the body, the last pair opening in the constriction between the body and the acetabulum.

Remarks.—The land leeches of Ceylon were separated from the genus *Hirudo* by Tennent in 1861, under the name of *Hæmadipsa*; and those of

Australia by Whitman in 1886, under the term *Geobdella*, altered to *Moquinia* by Blanchard.

Land leeches are mostly tropical, living in the area defined by the parallels 40° N. and 40° S. of the Equator, for they appear to prefer a warm, moist climate. In the Himalayas they ascend to a height of 11,000 feet; but in Ceylon they diminish in numbers above 4,000 feet. They are to be found in Ceylon, India, Java, Sumatra, Luzon, Mindanao, Pelew Islands, Japan, New Guinea, Celebes, New South Wales, Queensland, and the southern provinces of Chili and Trinidad. They live under damp leaves and loose rubbish, and appear when the air is disturbed by the approach of man or beast, and so quickly do they rush to the attack that they have earned the name of the 'jumping leech.' As a rule they bite gently, but make a deep wound the scar of which may take months to disappear. They fill themselves with blood in about thirty minutes and then drop off.

Classification.—Some of the species are as follows:

H. zeylanica de Blainville, 1827. Ceylon.
H. limbata Grube. Sydney.
H. fallax R. Blanchard. Madagascar.
H. morsitans R. Blanchard.
H. vagans R. Blanchard. Madagascar.
H. javanica Wahlberg. Java.
H. talagalla Meyen. Philippines.
H. japonica Whitman. Japan.

Other Genera.

Mesobdella R. Blanchard, 1893. With three rings to a somite.
M. gemmata R. Blanchard, 1894.
Philaemon R. Blanchard, 1893. With four rings to a somite.
P. pungens R. Blanchard. Java and Australia.
P. grandidieri R. Blanchard. Madagascar.
Phytobdella R. Blanchard, 1893.—With six rings to a somite.
P. meyeri R. Blanchard. Luzon.
P. moluccensis R. Blanchard. Salawati.
Planobdella R. Blanchard, 1894.—With seven rings to a somite.
P. quoyi R. Blanchard. North Celebes.
P. molesta R. Blanchard. Celebes.
Moquinia R. Blanchard, 1881.—With seven and a half rings between genital apertures.

Remaining Orders.

The remaining orders, Ichthyobdellida, Acanthobdellida, and Branchiobdellida, do not concern us.

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CHAPTER XXVIII

ARTHROPODA

Arthropoda—Diplopoda—Acarina—Gamasoidea—Ixodoidea—Trombidoidea—Eupodoidea—Sarcoptoidea—Vermiformia—Linguatulida—Crustacea—Chilopoda—References.

PHYLUM ARTHROPODA v. Siebold and Stannius, 1845.

BILATERALLY symmetrical metazoa, with well-developed body cavity and heteronomously segmented body with hollow segmental appendages, moved by intrinsic muscles and penetrated by blood spaces. One or more pairs of appendages behind the mouth are densely chitinized and turned inwards so as to act as jaws.

The phylum Arthropoda is divided into the following grades and classes by Ray Lankester:—

GRADE A: PROTARTHROPODA.

Class I. Onchophora.

GRADE B: EUARTHROPODA Lankester.

Class II. Diplopoda.
Class III. Arachnida.
Class IV. Crustacea.
Class V. Chilopoda.
Class VI. Hexapoda.

The Onchophora, which includes the genus *Peripatus*, does not concern us, but the other classes all contain species of importance in medicine.

CLASS II. DIPLOPODA RAY LANKESTER, 1904.

Synonym.—*Chilognatha.*

Euarthropoda, in which the somites generally fuse after early development, forming double somites, with two pairs of appendages, or present legless and leg-bearing somites alternately. They are terrestrial, breathing by tracheæ.

The following orders are recognized:—(1) Juliformia; (2) Symphyla; and (3) Pauropoda. We shall only consider the first.

Order I. Juliformia—*Diplopoda with two pairs of appendages on each somite.*—Two families of the Juliformia need be mentioned:—

FAMILY JULIDÆ.—*Juliformia with large free head, without broad dorsal plates.*—Two species of Julus—viz., *J. terrestris* L. and *J. londinensis* Leach—have been found as occasional parasites (accidental) in the human alimentary canal in Europe.

FAMILY POLYDESMIDÆ.—*Juliformia with large free head and laterally extended dorsal plates.*—*Polydesmus complanatus* has once been recorded as an accidental parasite in the human alimentary canal in Europe.

Pathogenicity.—These parasites give rise to symptoms both direct and reflex.

CLASS III. ARACHNIDA Lamarck, 1815.

Euarthropoda with two pre-oral segments, the first bearing typical eyes, and the second antennæ or chelicerae, and six post-oral appendages, modified so as to function as jaws, but possessing also a well-developed ramus, which may be a leg, palpus, or chela. The primitive forms have branchial respiratory processes, and the higher pulmonary organs.

The Arachnida are classified by Lankester into:-

- Grade A: Anomomeristica.
- Grade B: Nomomeristica.
  - Subclass I. Pantapoda.
  - Subclass II. Euarachnida.
    - Grade *a*. Hydropneusta.
    - Grade *b*. Aeropneusta.
      - Section A. Pectinifera.
        - Order Scorpionidea.
      - Section B. Epectinata.
        - Order I. Pedipalpi.
        - Order II. Aranea.
        - Order III. Palpigrada.
        - Order IV. Solifuga.
        - Order V. Pseudoscorpiones.
        - Order VI. Podogona.
        - Order VII. Opiliones.
        - Order VIII. Acarina.
        - Order IX. Linguatulida (Incertæ sedis).

Details with regard to this classification may be obtained by reference to Ray Lankester's paper in the *Quarterly Journal of Microscopical Science*, 1904, vol. xlviii., p. 165.

We have already considered the effects of the bites of the Scorpionidea, the Aranea, and some of the Acarina, and now it is necessary to consider more particularly those which are parasitic, and cause or spread disease.

Two orders must be dealt with in some detail—viz., the Acarina and the Linguatulida.

ORDER ACARINA Nitzsch, 1818.

Synonym.—Rhynchostomi.

Definition.—Degenerate Arachnida with the basal segments of the second pair of appendages united in the middle line behind the mouth, while those of the third, fourth, fifth, and sixth appendages are widely separated, and take no part in mastication. The respiratory stigmata usually belong to the prosoma, and the primitive segmentation of the opisthosoma has either entirely or almost entirely disappeared.

Remarks.—The Acarina include the mites and ticks which have long been known to be human parasites, but it is only recently that the latter have come into notice as carriers of disease.

It is true that a mite, or rather its larva, has long been suspected to be the cause of Tsutsugamushi disease, but it is probable that at present we are not fully aware of the disease-carrying and producing effects of these small arachnids.

The Acarina are cosmopolitan in their distribution, and are said to be most numerous in temperate regions. They are abundant at high altitudes. Banks remarks that the parasites follow the distribution of the host—*i.e.*, of the food—a remark the importance of which has already been appreciated. The observer will find that a parasitic disease is often bounded by the distribution of the food of the insect, which spreads the real cause of the disease.

Morphology.—The morphology is described under the heading Ixodoidea.

Life-History. The female lays eggs covered by a shell and an inner membrane called the deutovum. A six-legged larva hatches out from the egg, and after a time, during which it may be active or quiescent, moults and produces the nympha, which is eight-legged, and resembles the adult, except in the non-development of the sexual organs and apertures. The leg which is added to the nympha is the fourth, or posterior. The nymph is usually energetic, and feeds on some host; eventually passing into a quiescent stage and undergoing considerable histological changes, it moults and becomes the adult male or female. The males are usually smaller and more active than the females. Both sexes suck fluid nourishment from the host, whether animal or plant. Their life-history will be found to vary with the different families and species.

Pathogenicity. The Acarina are important in the dissemination of disease both among men and animals. In men they are responsible for the spread of such fevers as Dutton's relapsing fever, the tick fever of the Rocky Mountains, Tsutsugamushi disease, and the disease associated with the Miana bug in Persia; also they are responsible for a number of skin diseases, among which may be mentioned scabies. In animals they are responsible for the spread of the Babesiases, and of some Spirochaetiases, as well as causing some forms of dermatitis. Incidentally it may be mentioned that they also cause disease in plants, producing galls, etc.

Enemies.—Hurtful as they are themselves, they are not, however, free from persecution on the part of other animals. Blood-sucking insects, particularly the Reduviidae, prey on some arachnids, sucking their blood. Wellman has reported that he has caught *Phonergates bicoloripes* Stal in the act of sucking the juices of *Ornithodoros moubata*, the tick responsible for the spread of Dutton's relapsing fever.

Classification.—The order Acarina is divided into the following suborders:—

SUBORDER NOTOSTIGMATA.—Acarina in which the opisthosoma is segmented by ten integumental grooves, of which the anterior four are furnished with a single pair of dorsally placed spiracles. (Family: Opilioacaridæ.) This suborder does not concern us.

SUBORDER II. CRYPTOSTIGMATA.—Acarina with a hard integument strengthened by chitinized dorsal and ventral sclerites. Stigmata on the acetabula of the third, fourth, fifth, and sixth pairs of appendages (Family: Oribatidæ.) This also does not concern us.

SUBORDER III. METASTIGMATA.—Acarina with a hard integument like the Cryptostigmata. One pair of stigmata above and behind the base of the fourth, fifth, or sixth pair of appendages.

Superfamily A: Gamasoidea.
Superfamily B: Ixodoidea.

SUBORDER IV. PROSTIGMATA.—Acarina with soft integument strengthened by special sclerites, those on the ventral surface of the prosoma apparently representing the basal segments of the legs embedded in the skin. Except in the aquatic species, there is a pair of stigmata close to or above the first pair of appendages.

Superfamily A: Trombidoidea.
Superfamily B: Eupodoidea.

SUBORDER V. ASTIGMATA.—Degenerate Acarina, mostly parasitic, like Prostigmata in the development of integumental sclerites and the softness of the skin, but with the respiratory system absent. (Superfamily: Sarcoptoidea.)

SUBORDER VI. VERMIFORMIA.—Degenerate parasitic Acarina without respiratory system, and with the body produced posteriorly into an annulated caudal prolongation. With the third, fourth, fifth, and sixth pairs of appendages short, and only three jointed. (Family: Demodicidæ.)

SUBORDER VII. TETRAPODA.—Degenerate attacheate Acarina with body as in the Vermiformia, but with the third and fourth pairs of appendages long and normally segmented, and the fifth and sixth entirely absent. (Family: Eriophyidæ.) This suborder, however, need not concern us.

SUBORDER III. METASTIGMATA.

The parasites included in this suborder would in popular language all be called ticks.

It is divided into two superfamilies:—

A. GAMASOIDEA.—With a small hypostome without teeth.

B. IXODOIDEA.—With a large hypostome armed with many recurved teeth.

SUPERFAMILY A: GAMASOIDEA.

The superfamily Gamasoidea is divided into three families: (1) Dermanyssidæ, (2) Uropodidæ, (3) Gamasidæ.

FAMILY 1: DERMANYSSIDÆ.

Gamasoidea parasitic on vertebrates, with mandibles fitted for piercing, with the body sometimes constricted, with soft integuments finely striated.

The Dermanyssidæ are divided into two subfamilies:—Dermanyssinæ, with an anal plate; Halarachninæ, without an anal plate.

SUBFAMILY DERMANYSSINÆ.

Dermanyssus Dugès, 1834.

Dermanyssinæ with a long body not distinctly constricted; peritreme on the venter, with chelate mandibles in the male and long styliform mandibles in the female. Parasitic on birds.

Dermanyssus gallinæ Redi, 1674.

Synonyms. *Pulex gallinæ* Redi, 1674; *Acarus gallinæ* de Geer, 1778; *Dermanyssus avium* Dugès, 1836.

This parasite lives in cracks, etc., in the hen house during the day, and attacks the fowls at night, sucking the blood. It is also found on many other birds and mammals, and occasionally on man, generally on poultry men, in whom it produces a papular eczematous dermatitis on the back of the hands and forearms. *D. hirundinis* Hermann, 1804, which is probably only a variety of this species, can also be found on man.

Morphology. Body egg-shaped, posterior end wider than anterior, abdomen with short, marginal, widely separated bristles.

Male, 0·6 millimetre by 0·32 millimetre; female, 0·7 millimetre by 0·4 millimetre.

Holothyrus Gervais, 1842.

Holothyrus coccinella Gervais, 1842.

This arachnid is found on ducks and geese in Mauritius, and is said to attack human beings, causing swelling of the affected part, which, if the lips or tongue of a child, may be dangerous. Some authorities consider that this arachnid should form a separate family of its own—Holothyridæ.

FAMILY 2: GAMASIDÆ.

In this family comes the genus *Lælaps* Koch, 1842, with its species *L. echidninus* Berlese, mentioned in the chapter on Protozoa, because Miller has traced the life-cycle of *Hæmogregarina muris* Balfour, 1905, in it and in the rat *Mus decumanus*.

SUPERFAMILY B: IXODOIDEA BANKS, 1894.

Synonyms. *Acarus* Linnæus, 1746, *pro parte*; *Ricinia* Latreille, 1804, *pro parte*; *Ixodides* Leach, 1815; *Ixodea* Burmeister, 1837; *Ricini* Koch, 1844 and 1847; *Ixodes* Gervais, 1844; *Ixodida* Küchenmeister, 1855; *Ixodidæ* Leach, 1863; *Ixodides* Donnadieu, 1875, and Mégnin, 1876; *Ixodæ* Wagner, 1876; *Metastigmata* Canestrini, 1892; *Cynorhæstea* Marx, 1892; *Arpagostoma* Lahille, 1905.

The term *Cynorhæstea* is derived from Aristotle, who speaks of these arachnids as κυνοραίστης (the dog-tormentors), because ticks were well known in his day to attack hunting dogs.

The Ixodoidea are the ticks, which have become of importance in tropical medicine not merely because of their unpleasant bite, but because of the spread of disease by their agency—as, for example, the tick fever of Africa, Tsutsugamushi disease, the tick fever of the Rocky Mountains, etc. They are parasitic on mammals, birds, and reptiles, but are not strictly confined to one host. The Argasidæ, one of the two families included in the superfamily, are now nocturnal in habits, and do not become greatly distended with blood; while the other family, Ixodidæ, or true ticks, are very common in tropical countries.

Morphology.—A tick is divisible into a head, rostrum, or capitulum, and a body. The capitulum is the small anterior structure with the mouth parts, and is easily visible from above in the Ixodidæ (*vide* Fig. 313), but must be viewed from below in the Argasidæ (Fig. 321). It joins the rest of the body at the camerostome. The capitulum consists of the following parts:—

1. *Neck.*—This is the junction of the rostrum with the rest of the body.

2. *Base.* This is the hard basal portion, and is usually quadrangular, but its outline varies.

In females of the Ixodidæ there are two porose areas on the upper surface (*vide* Fig. 311). Attached behind the base is the neck; in front, in the middle line, is the haustellum, composed of the hypostome and the mandibles and their sheaths, on each side of which lie the palpi.

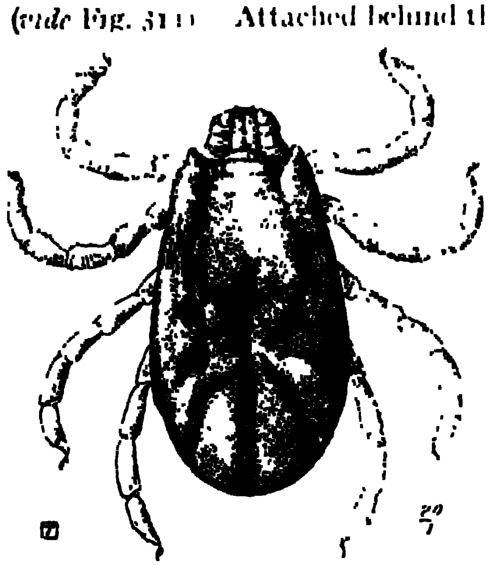


FIG. 310.—*Margaropus annulatus* VAR. *australis* SAY: DORSAL VIEW OF THE MALE.

3. The hypostome is an elongated structure composed of two symmetrical halves, with numerous minute teeth, called denticles, on its ventral surface.

4. The chelicera or mandibles, are two in number—one on each side of the median line, lying dorsal to the hypostome. The posterior portion enclosed in the body is swollen for the attachment of muscles, while the anterior is flat and narrow, and terminated by a hook-like digit, which has two or three processes—the apophyses—an internal, an external, and a middle, with hook-like teeth.

5. The mandibular sheath lies dorsal to the mandibles.

6. The palpi are composed of four segments or articles—basal, antepenultimate, penultimate, and apical. They are of importance in classification into genera, as they possess hairs, bristles, edges, angles, and spines, varying in different species. There is sometimes a group of long hairs on the internal aspect of the palpi, which are probably sensory.

The body varies greatly in form, colour, outline, and structure. It is divided into (1) Dorsal surface, (2) ventral surface; (3) to (5) anterior, posterior, and lateral margins.

1. *Dorsal Surface.* On the dorsal surface may be noted (Figs. 313 and 318):—

(*a*) The scutum, found in the *Ixodidæ* and well marked in the adult male but much smaller in the adult female. It is a hard, chitinous plate, with two longitudinal grooves (cervical grooves).

(*b*) The eyes, only sometimes present on each lateral margin of the scutum in Ixodidæ or near the first coxa in Argasidæ.

(*c*) The dorso-submedian porose plates are small, circular, or oval chitinous structures on each side of the median line, near the third and fourth legs.

(*d*) The postero-marginal festoons, when present, are eleven areas marked out by grooves lying along the posterior margin of the body between the stigmata.

(*e*) The dorsal grooves are usually longitudinal, and not always distinct, as they are due to muscular contractions.

(*f*) Pits, hairs, spines, etc., may be visible on the dorsal surface.

2. *Ventral Surface.*—The ventral surface exhibits (Fig. 324):—

(*a*) The genital pore, situated in the ventro-median line, between the coxæ of the first three pairs of legs.

(*b*) The anus, situate in the ventro-median line, behind the posterior pair of legs. It is surrounded by a valve, and in the male of certain genera has laterally the clypea or anal valves.

(*c*) The ventral shields of chitin are small sclerites covering the surface in the male.

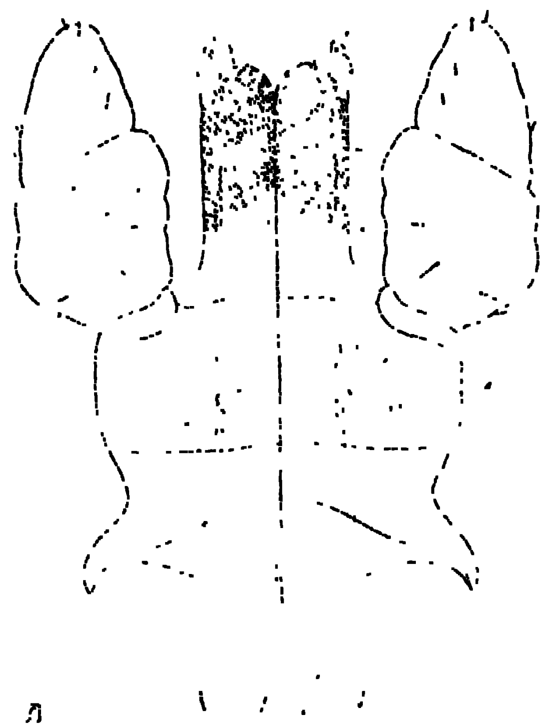


FIG. 311.—DORSAL VIEW OF THE CAPITULUM OF A TICK: FEMALE (*Haemaphysalis punctata* C. AND F.)

1, Cheliceræ; 2, hypostome; 3, palp; 4, porose area.

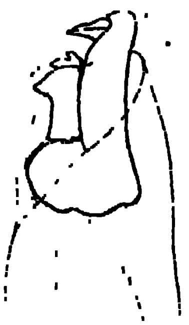


FIG. 312. CHELICERA OF *H. punctata*: MALE (C. AND F.).

(After Nuttall, Cooper, and Robinson, *Journal of Parasitology*)

(*d*) The stigmata lie one on each side of the body, between the 3rd and 4th pairs of legs in the Argasidæ, and behind the fourth in the Ixodidæ.

(*e*) There are often to be seen a pair of genital furrows and an anal furrow.

(*f*) Pits, pores, hairs, and punctations are to be found as on the dorsal surface.

3. *Anterior Margin.*—This varies as compared with the posterior, being sometimes straighter, sometimes emarginate, and receiving at the camerosome the rostrum.

4. *Posterior Margin.*—This is generally rounded, and often marked by the festoons already mentioned on the dorsal surface.

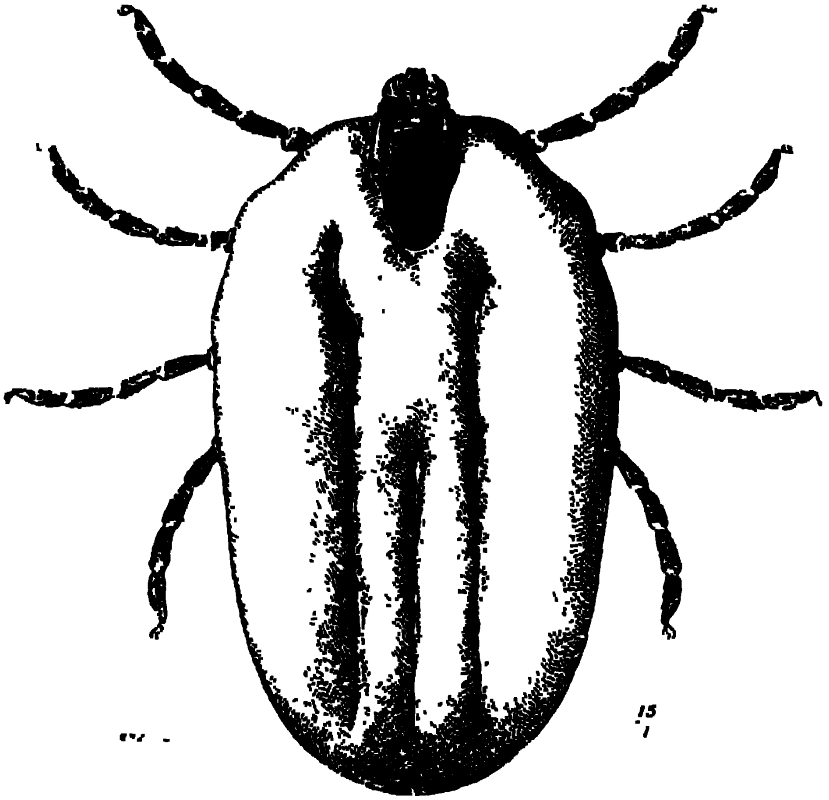
5. *Lateral Margins.*—They vary as to their straightness or degree of curvature.

The legs are segmented into the following articles: coxa, trochanter, femur, patella, tibia, and tarsus.

Internal Anatomy.—The internal anatomy has been studied by Christophers in *Ornithodoros savignyi*, and most elaborately by Bonnet in eight Ixodidæ and three Argasidæ, males and females.

The tegument consists of chitinous layers, under which lies the epidermis. On the surface are the openings of numerous glands. A large cephalic gland is present in some species, opening dorsally at the junction of the rostrum with the body.

The mouth, which is lined with chitin, is situated anteriorly between the mandibular sheath dorsally and the hypostome ventrally. In this position it is merely a horizontal slit, with open sides, but farther back these are closed by the junction of the hypostome with the mandibular sheaths. The cavity extends backwards some little distance, and ends blindly. Into its postero-lateral angles open the ducts of the salivary glands, two large racemose glands lying over the bases of the first pair of legs. The acini are globular, and their walls consist of large cells, as a rule laden with refractile granules staining deeply, or with indistinct granules staining less deeply.



Margaropus annulatus VAR *australis* SAY: DISTENDED FEMALE

In addition to the ordinary acini, there are groups of four or five cells, forming pear-shaped masses, which have a peculiar affinity for acid stains like eosin. These elements are really unicellular glands, which open into the principal salivary ducts, not into the small ductules. These glands, which are numerous in the Argasidæ, are probably poison glands.

On the floor of the mouth is a **V**-shaped opening, apex pointing forwards, which leads into the pharynx. This is a fusiform organ, narrow in front, where it turns upwards to open into the mouth, while behind it ends in the œsophagus. Its walls consist of chitinous plates arranged ventrally and laterally, so that the lumen is triradiate on transverse section. At the angles the chitinous plates are united together by double folds, allowing expansion and contraction, and brought about by the contraction and relaxation of muscles taking origin in the sclerites forming the endoskeleton of the head and inserted into these plates. It ends posteriorly in a narrow œsophagus which is without chitinous support, and therefore soft. This œsophagus runs backward, perforating a large ganglionic mass, and ends in the mid-gut. Its walls are composed of a layer of columnar cells internally and by muscular fibres externally. Just before it joins the mid-gut its wall thickens and forms a fold, the homologue of the proventriculus, which projects into that passage.

The œsophagus opens on the floor of the large central food reservoir or mid-gut, the main canal of which runs forward a little distance in front of this opening, and backwards to the neighbourhood of the rectum.

The central canal gives off diverticula, which may be classed into an anterior set, consisting of a single diverticulum; a lateral set, consisting of an antero-lateral diverticulum, subdivided into three branches a medio-lateral, into two or three, a postero-lateral, which is single, and a posterior set, which is also single.

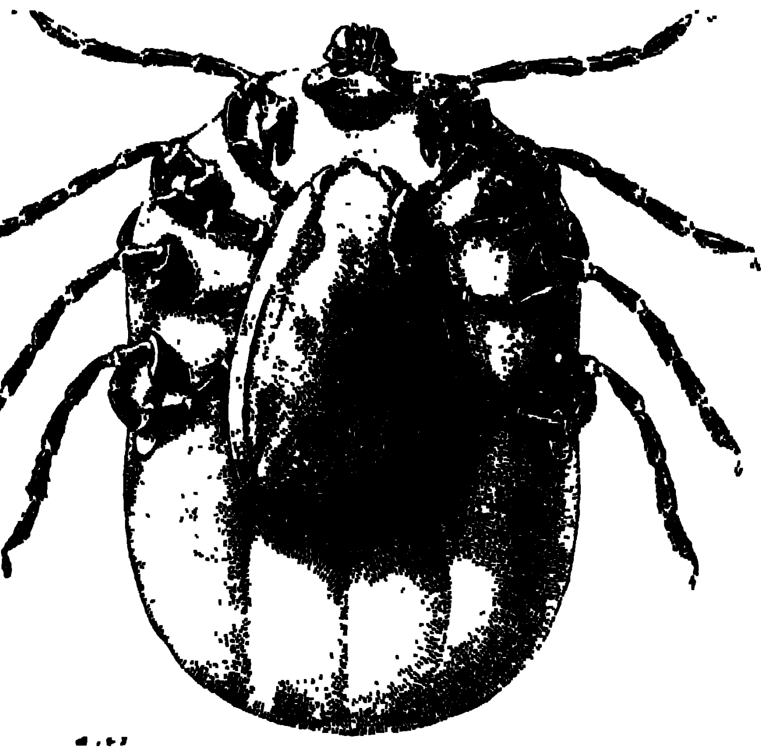


FIG. 314. COPULATION OF THE MALE AND FEMALE TICK
(After Sambon.)

The walls of the central tube and the diverticula consist of a single layer of large cells lying upon a thin basement membrane, external to which are large single muscular fibres arranged longitudinally and transversely in an open network. Digestion is assisted by free cells mingling with the coagulated blood filling the diverticula.

Posteriorly the central canal is connected with the rectum by means of a very fine canal, which appears to represent a functionless rudimentary intestine This communication is not admitted by Bonnet

Into the rectum open also two long, fine, much convoluted tubules -- the Malpighian tubes, which are composed of a single layer of large cells placed on a basement membrane. In females they may contain spherical corpuscles, which, though present in males, are much smaller. Berlese and Bonnet consider that these bodies are composed of guanine.

The rectum is a sacculated tube, with a wall composed of a single layer of flattened cells leading to the anus. Bonnet objects to the term 'anus, considering the tubules as renal, the rectum as a bladder, and the opening as an excretory pore; but this term must be kept for morphological reasons. Further, he states that this excretory matter is only expelled during moulting, collecting at other times in the rectum. The anus is a slit-like aperture, guarded by two lateral semicircular chitinous plates.

The male reproductive organs consist of a thin, transparent tubule—the testes—ending at either end in a vas deferens, which, after coiling upon itself, enters a lobulated structure—the white gland. The ejaculatory duct ends in the chitinous penis. The female reproductive organs consist of a single ovary, which lies across the abdomen just behind the central alimentary sac. This ends in two coiled oviducts, which open into a large spermatheca with thick walls, and from which a duct leads to the genital opening.

The tick breathes by a means of a system of tubes, lined by a spiral thread of chitin. These tubes are called tracheæ, and radiate, from the opening on the stigma called the 'spiracle,' all over the body. The circulatory system consists of a median heart and distributing vessels. The fat body is well marked.

There are a number of dermal glands, a coxal gland in the second coxal joints and opening on the first coxal joints by a minute pore, and a cephalic gland in the head.

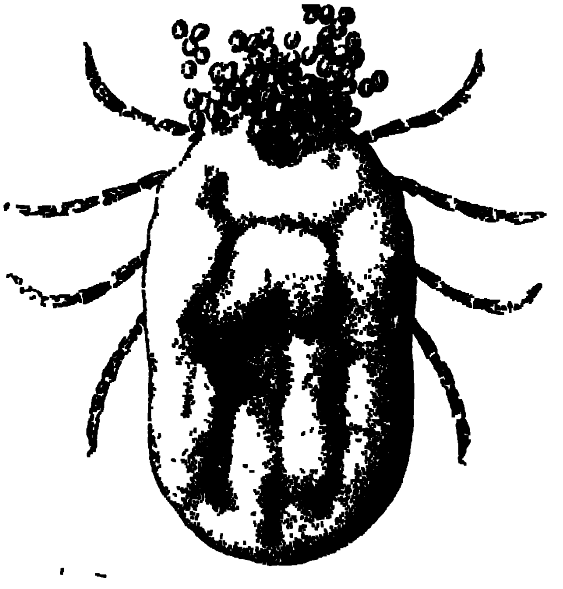


FIG. 315.—A TICK LAYING EGGS.
(After Sambon.)

Life-History.—While on the host sucking blood, the male and female parasites copulate, and the latter, growing to a large size, drops to the ground and lays a number of eggs. The egg consists of a shell with an inner membrane, enclosing food yolk and embryo, which eventually hatches as a six-legged larva, without sexual organs or stigmata. The digestive organs are, however, present, and the little larva, becoming parasitic on some animal, sucks its blood, drops off and moults, giving rise to the nympha. The nympha has eight legs and a pair of large stigmata, but is without reproductive openings or organs. The nymphæ now become parasitic, and feed, after which they drop off, moult, and become males or females with fully developed generative organs.

The adults now become parasitic and moult, and the young female, fixing itself to the host, grows considerably, but rarely changes her place: while the male, remaining small, wanders about looking for the female.

The life-history and the habits of the different divisions of the *Ixodidæ* are so various that they will be described under their separate heads. One example may, however, be mentioned here—viz., *Margaropus decoloratus*—whose life-history has been studied by Lounsbury. In this species the female, dropping off the host, completes oviposition in a time varying, according to the temperature of the air, from five days to four weeks, while the incubation of the egg varies from three weeks to three months. The larvæ, which are capable of remaining on grass without food for months, must obtain access to cattle, on which they feed, and grow for three days, after which they moult and form nymphs on the sixth day of their parasitic existence—*i.e.*, without leaving the host. The nymph sucks blood and grows till the eleventh day, and the adult is hatched on the thirteenth to sixteenth day without the nymph leaving the host.

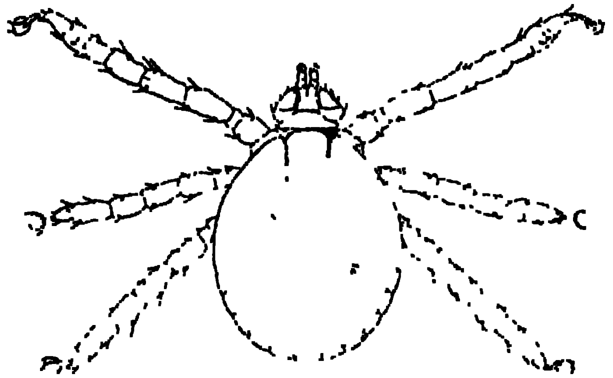


FIG. 316.—THE LARVA OF *Hæmaphysalis punctata* C. AND F. (× 10.)

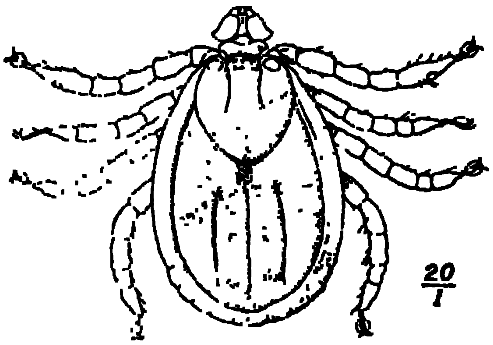


FIG. 317.—THE NYMPH OF *Hæmaphysalis punctata* C. AND F.

(After Nuttall, Cooper, and Robinson, *Journal of Parasitology*.)

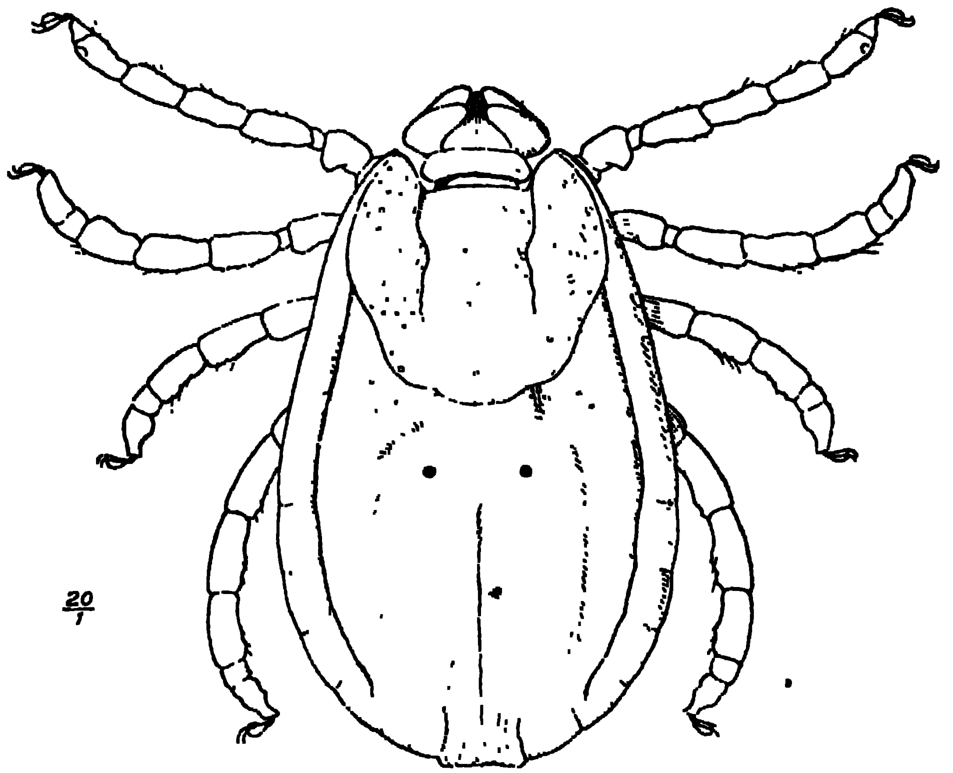


FIG. 318.—ADULT FEMALE OF *Hæmaphysalis punctata* C. AND F.
(After Nuttall, Cooper, and Robinson, *Journal of Parasitology*.)

Pairing takes place on the seventeenth to twentieth day, and the fertilized gorged female drops off the host on the twenty-fourth to thirty-first day. Thus, in this case the larva and nymph remain parasitic on the host, and do not drop off as described above.

Parasitic on Man.—The ticks known to be parasitic on man are:—(1) *Argas reflexus* Fabricius; (2) *A. persicus* Oken; (3) *Ornithodoros savignyi* Audouin; (4) *O. moubata* Murray; (5) *O. megnini* Dugès; (6) *O. turicata* Dugès; (7) *O. tholozani* Laboulbène and Mégnin; (8) *Alectorobius talaje* Guérin-Méneville; (9) *Eurhipicephalus sanguineus* Latreille; (10) *Margaropus annulatus* Say; (11) *Rhipicentor bicornis* Nuttall and Warburton; (12) *Dermacentor reticulatus* Fabricius; (13) *D. andersoni* Stiles; (14) *D. electus* Koch; (15) *D. modestus* Banks; (16) *Ixodes ricinus* Linnæus; (17) *I. hexagonus* Leach; (18) *Amblyomma americanum* Koch; (19) *A. dissimile* Koch; (20) *Hyalomma ægyptium* Linnæus.

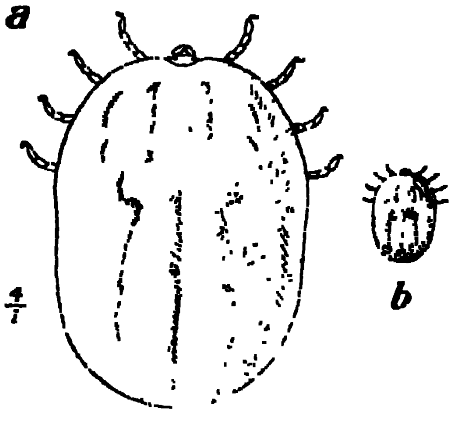


FIG. 319. FULLY REPLETE FEMALE OF *Hæmaphysalis punctata* C. AND F.

(After Nuttall, Cooper and Robinson, *Journal of Parasitology*.)

(*a*) Magnified, (*b*) natural size.

Pathogenicity. Ticks are spreaders of disease in man and animals. They may be classified into spreaders of *Spirochætidæ*, spreaders of *Babesia* and into spreaders of unknown germs.

1. Spreaders of Spirochætidæ.

1. *Ornithodoros moubata* carries *Spiroschaudinnia duttoni* Novy and Knapp, 1906, and causes African tick fever or Dutton's relapsing fever in man.

2. *Argas persicus* carries *Spiroschaudinnia marchouxi* Nuttall, 1904.

3. *Margaropus annulatus* carries *Spiroschaudinnia theileri* Laveran, 1904.

2. Spreaders of Piroplasma.

1. *Eurhipicephalus appendiculatus* carries *P. bigeminum.*
2. *E. simus* *P. bigeminum.*
3. *E. evertsi* *P. equi.*
4. *E. sanguineus* *P. canis.*
5. *E. bursa* *P. ovis.*
6. *Margaropus annulatus* *P. annulatum*
7. *Hæmaphysalis leachi* *P. canis.*

3. Spreaders of Unknown Germs.

1. *Argas persicus* causes a disease in Persia. 2. *Dermacentor venustus* (see *D. andersoni*) causes Rocky Mountain fever.

Experimentally, the nymphs of *D. marginatus* and *Amblyomma* *americanus* and the nymphs and adults of *D. variabilis* can transmit the virus of Rocky Mountain fever.

Enemies.—The enemies of ticks are numerous, and among them may be mentioned fowls and blackbirds.

Prophylaxis.—The prevention of ticks in cattle is a difficult proceeding. The following are some of the methods in use (from Balfour and Archibald):—

Cattle Washes and Dips.—Arsenic used to be employed (Cooper's Dip Powder), but was found to be dangerous. A useful oil is crude petroleum, 2 gallons; hard soap, ½ pound; and water, ½ gallon. The soap is dissolved in the hot water and the petroleum gradually added. Five days' spraying is advocated in place of the usual fortnightly dip.

Rotation of Crops. This is said to be useful in the United States.

Burning of Pastures.—Not a good plan.

Immunization.—Immunization by inoculation against babesia, etc. It is not very useful.

Quarantine. Quarantine of cattle and control over their movements is important.

There are, however, a good many practical points to be attended to in spraying or dipping cattle. Reference may be made to Cooper's paper in the *Journal of Agricultural Science*, vol. iii., or to Newstead's Report of Twenty-first Expedition of the Liverpool School of Tropical Medicine.

Classification.—The Ixodoidea are divided into two families:—

FAMILY 1: ARGASIDÆ Canestrini, 1890. Ixodoidea without a scutum; mouth parts of adult not prominent from above; no pulvillus attached to tarsus in adults.

FAMILY 2: IXODIDÆ Murray, 1877.—Ixodoidea with a scutum; mouth parts prominent from above; pulvillus present, attached to the tarsus in adults.

Remarks.—Neumann's classification is very different from the one used in this book. He recognizes Ixodidæ (= Ixodoidea) divided into Ixodinæ (= Argasidæ and Ixodidæ) and Spelæorhynchinæ, these last being parasites on bats. Other classifications are those by Lahille and by Banks.

FAMILY 1: ARGASIDÆ.

These arachnids are more like bugs than ticks in their habits. During the day they are concealed in cracks in walls or floors, or in gravel, but at night they come out and run about. Christophers says that if handled they sham death, and that when running about they have a curious habit of raising the first pair of legs as though to receive information about their surroundings. They can live for a long time (three to four years) without food. They generally feed after dark, being gorged in about fifteen minutes.

Donovan states that while feeding fluid is secreted by the coxal glands, and lies between the parasite and the skin of the host. This fluid is alkaline, and prevents coagulation of blood. After feeding, the tick drops to the ground, and, being wet with secretion, becomes covered with dust and dirt. At first they are much swollen, but in a few days this diminishes, though they may remain distended for weeks. Soon after feeding, the tick moults, and then becomes active again, and is ready for another feed.

The Argasidæ pair at various times, one female being fertilized by several males. The female now becomes quiescent, and passes out its ova, a process requiring a week or more to be completed. During this process the head is forcibly flexed on the body, so that the palpi lie on each side of the body, while above the head is the prolapsed duct of the cephalic gland, forming a protuberant mass. The ova are not as numerous as those of the cattle ticks, and are generally laid in a loosely adherent mass.

The six-legged larva hatches in less than a week. In *Ornithodoros* it appears to be quiescent, making no attempt to obtain food, and in *O. moubata* does not leave the egg. In three or four days it moults, and becomes the eight-legged nymph, which is an active little creature, feeding readily. In *Argas* the larva is more vigorous, and feeds. It appears as though there were great differences in the life-history of the different species of the Argasidæ.

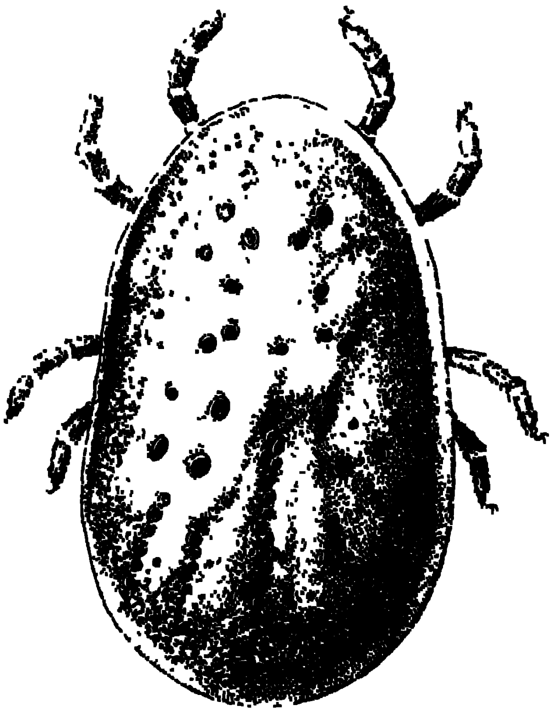


FIG. 320.—*Argas persicus* LATREILLE: FEMALE, DORSAL ASPECT.

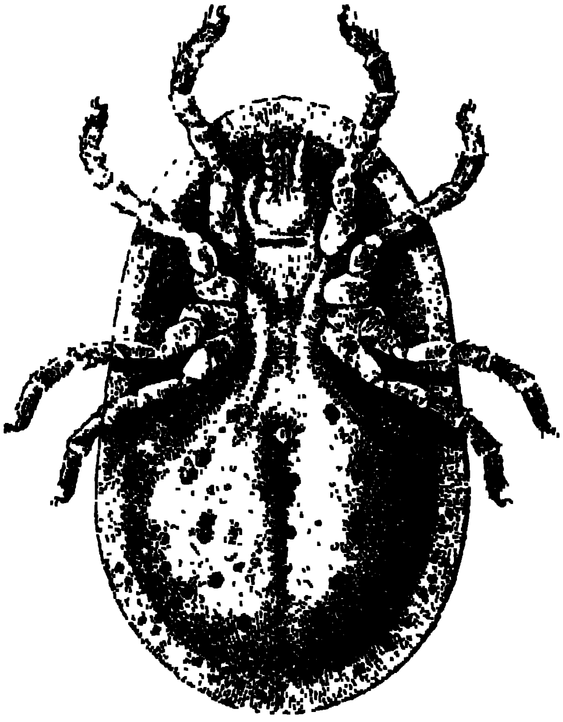


FIG. 321.—*Argas persicus* LATREILLE: FEMALE, VENTRAL ASPECT.

The adult Argasidæ appear to moult many times as they grow larger. They are preyed upon by insects.

Genera.—The Argasidæ are divided into four genera:—*Argas*, *Caris*, *Ornithodoros*, *Alectorobius*.

The diagnosis of these genera is as follows:—

1. Eyes absent, body usually flat, with thin borders, without deep ventral grooves: (*a*) No groove behind anus—*Argas*; (*b*) transverse groove behind anus—*Caris*.

2. Eyes present or absent; body more or less distended, with deep ventral grooves: (*a*) Without a fold of skin (sclerite) on each side of palpi—*Ornithodoros*; (*b*) with such a fold—*Alectorobius*.

There is, however, some doubt as to whether *Caris* is really entitled to be a separate genus.

Argas Latreille, 1796.

Synonyms.—*Nec Argas* Scoul, 1835; *Carois* Latreille, 1796; *Rhynchoporion* Hermann, 1804; *Caris* Latreille, 1806.

Definition.—Argasidæ with oval or flattened bodies, in which the rostrum is at least its own length from the anterior margin, which is less bluntly rounded than the posterior margin. No fold present around the base of the rostrum ventrally. Tegument roughened by wrinkles and folds, and marked by circular pits. Without eyes.

Type.—*Argas reflexus* Fabricius, 1794.

The number of species known is steadily increasing. The more important can be defined by the following table, modified from Neumann:—

- A. Posterior margin with rectangular festoons—*A. persicus*.
- B. Posterior margin with narrow festoons:—
  - I. Tegument with fine folds, body long, swollen—*A. hermanni*.
  - II. Tegument with large folds, body flat:
    - (α) Body narrower in front:—
      - (1) Anterior extremity flat and rounded—*A. reflexus*.
      - (2) Anterior extremity pointed:—
        - (*a*) With deep camerostome and dorsal hexagonal markings—*A. brumpti*.
        - (*b*) Without these—*A. æqualis*.
    - (β) Body almost as large in front as behind:
      - (1) Body short, a little longer than broad—*A. transgariepinus*.
      - (2) Body twice as long as broad—*A. cucumerinus*.

Argas reflexus Fabricius, 1794.

Synonyms.—*Acarus reflexus* Fabricius, 1794; *A. marginatus* Fabricius, 1794; *Rhynchoporion columbæ* Hermann, 1804.

Argas with yellowish body; male 4 by 3 millimetres, female 6 to 8 by 4 millimetres. Its distribution is mainly in Europe and America, where it lives in dovecots; but it can and does attack man, producing the symptoms already described.

Argas persicus Oken, 1818.

Synonyms.—*Rhynchoporion persicum* Oken, 1818; *Argas persicus* Fischer de Waldheim, 1820; *A. mauritianus* Guérin-Méneville; *A. miniatus* Koch, 1844; *A. americanus* Packard, 1872; *A. sanchezi* Dugès, 1891; *A. chinche* Goudot.

Argas with oval, brownish-red body. Male, 4 to 5 by 3 millimetres; female, 7 to 10 by 5 to 6 millimetres. Dorsal and ventral surfaces with pits in rows, and irregularly placed.

This *Argas* is widely distributed, being found in Asia, where, under the term 'garib-guez' (*punaise de Miana*), it has long had an evil reputation for causing sickness. It is also known in Quetta. In South Africa it occurs as a parasite of fowls and ducks, and is also known in the Sudan, Egypt, Turkestan, and Pekin. Under the name of *A. miniatus* it was described in the form of the chicken tick of the United States and the adobe tick of Mexico and Arizona. According to Balfour, it spreads the *Spirochæta marchouxi* in Sudanese fowls. Nuttall and Strickland have demonstrated the presence of an anticoagulin in the salivary glands and intestine of the tick.

Argas brumpti Neumann, 1907.

This tick was discovered by Brumpt in Somaliland. The dorsum is marked by symmetrical hexagonal depressed areas. Female, 20 by 13 millimetres. Nuttall says that, according to Brumpt, the bite is very painful, and causes pruritus lasting several days, and the site may remain indurated after seven years.

Argas cucumerinus Neumann, 1901.

Only the male of this tick is known. It has an oval elongated body, brownish-red in colour, 10 by 5 millimetres. It is found in Lima in Peru. Possibly this is merely a variety of *A. reflexus*.

Argas hermanni Audouin, 1827.

Argas with very fine skin folds and small rostrum. It is found in Abyssinia and Egypt. Possibly this also is only a variety of *A. reflexus*.

Argas æqualis Neumann, 1908.

Synonym. *Ornithodoros æqualis* Neumann, 1901.

Nuttall places this species with the Argasidæ. It was found in German East Africa by Fülleborn. In size it is 5 by 2·5 millimetres, with folded finely granulated integument.

Argas transgariepinus White, 1846.

Synonym. *Argas kochi* Neumann, 1901.

Argas with very compressed body, not much longer than broad—7·5 by 6 millimetres. Margin with irregular folds. Found in South Africa.

Caris Latreille, 1804.

Argasidæ with almost circular body, a little larger in front than behind, with a conspicuous transverse groove behind the anus.

Caris vespertilionis Latreille, 1796.

Synonyms.—*Carios vespertilionis* Latreille, 1796: *Argas pulchella* George, 1876.

Parasitic on bats.

Ornithodoros Koch, 1844.

Argasidæ with or without eyes. Rostrum surrounded ventrally by a camerostome. Tips of the palpi visible from above. Lateral borders of the body straight, sometimes concave. Integument mammillated, with hemispherical elevations. Two longitudinal coxal folds, a pair of supracoxal folds, one transverse pre-anal and one post-anal groove, and one longitudinal anal groove running from the anus to the post-anal groove.

Type.—*Ornithodoros savignyi* Audouin, 1827.

Eleven species are recorded: (1) *Ornithodoros savignyi* Audouin, 1827; (2) *O. moubata* Murray, 1877; (3) *O. turicatus* Dugès, 1876; (4) *O. megnini* Dugès, 1883; (5) *O. lahorensis* Neumann, 1908; (6) *O. tholozani* Laboulbène and Mégnin, 1882; (7) *O. pavimentosus* Neumann, 1901; (8) *O. furcosus* Neumann, 1908; (9) *O. erraticus* Lucas, 1849; (10) *O. coriaceus* Koch, 1844; (11) *O. canestrinii* Birula, 1895.

DIAGNOSTIC TABLE.

A. Eyes present:—

  Three knobs on the last segment of the fourth leg:—

    (*a*) Tegument with hemispherical protuberances:—

      (1) Eyes of equal size (Africa and India)— *O. savignyi*.

      (2) Anterior eyes larger (America)—*O. coriaceus*.

    (*b*) Tegument with flattened protuberances (Africa)— *O. pavimentosus*.

B. Eyes absent:—

  I. Subrectangular body nearly square (Mexico)— *O. turicatus*.

  II. Body more or less constricted behind the fourth pair of legs:—

    (*a*) With broad anterior end (Mexico)— *O. megnini*.

    (*b*) With narrow anterior end (Lahore)—*O. lahorensis*.

  III. Ovoid body, with broader posterior end:—

    (*a*) Anterior end broad and rounded (Central Africa)— *O. moubata*.

    (*b*) Anterior end tapering:—

      (1) Tarsi forked distally (Ecuador)— *O. furcosus*.

      (2) Tarsi slightly knobbed (Algeria)— *O. erraticus*.

      (3) Tarsi second to fourth markedly knobbed (Persia)—*O. tholozani*.

      (4) Tarsi first with three dorsal knobs, second to fourth with one knob (Persia)— *O. canestrinii*.

Ornithodoros savignyi Audouin, 1827.

Synonyms.—*Argas savignyi* Audouin, 1827; *Ornithodoros morbillosus* Gerstäcker, 1873; *Argas schinzii* Berlese, 1880.

This is the type species of the genus, and has been studied in detail by Neumann and Christophers.

It is common in Africa, India, and Aden, and perhaps elsewhere.

Morphology.—*Ornithodoros*, with two pairs of eyes appearing as circular, smooth, convex elevations, situated on the supracoxal fold above the bases of the first pair of legs, and between those of the second and third pairs. Body oval, constricted slightly between the third and fourth pairs of legs, yellow in colour when young, and blackish-brown when old. Integument covered with irregular hemispherical prominences pointed at their summits, between which are narrow depressions with hairs. Capitulum embedded in an infundibuliform camerostome, from which it is separated by a deep groove, in the dorsal portion of which can be seen the opening of the cephalic gland. Mandibles with a simple claw-like internal apophysis, and without middle apophysis. Teeth of the hypostome arranged in three longitudinal parallel rows. Two spines at the base of the hyposome, which is large.

Dorsum of the body marked by two transverse furrows, one just in front of the posterior border, and the other situate farther forward, marking off a median elevation with a central depression, and seven similar depressions, each of which becomes a deep sulcus posteriorly.

The ventral surface shows a well-marked pre-anal furrow, which laterally meets the supracoxal sulcus, which runs round the anterior aspect of the body as a well marked groove, defining the supracoxal fold, on which the eyes are situate. Behind the anus are three symmetrical longitudinal grooves, while a short V shaped depression abuts on the anus. The genital papilla is well marked, and surrounds the wide transverse opening.

The fourth pair of legs is one and a half times as long as the first The coxæ are contiguous, and diminish in size from the first to the fourth, and the first has the opening of the coxal gland. Christophers has observed that the fluid from this gland is alkaline and prevents coagulation of the blood. The stigmata are placed behind and above the supracoxal folds. The fifth joints of the first three pairs of legs with three teeth, the two proximal quadrangular, and the distal conical.

This tick is very hardy, and is said to be able to live for many months without food or moisture. It attacks human beings, and is found in Africa and India.

Pathogenicity. Not known.

Ornithodoros moubata Murray, 1877.

Synonyms.—*Argas moubata* Murray, 1877; *Ixodes moubata* Cobbold, 1882; *Ornithodoros savignyi* var. *cæca* Neumann, 1901.

O. moubata is of importance as the spreader of *Spiroschaudinnia duttoni*, the cause of Dutton's relapsing fever, or African tick-fever. The tick is distributed widely in Africa, where it is called bibo in Uganda, moubata in Angola, and tampan in Zambesi. Christy has described a similar tick in Brazil.

Morphology.—*Ornithodoros* without eyes, body oval, a little wider behind than in front, with a slight constriction between the third and fourth legs; colour varies with age from yellow-brown to dusky brown. Integument covered with irregular hemispherical prominences. Capitulum embedded in an infundibuliform camerostome. Mandible with external apophyses, with two widely separated teeth, and an internal apophysis, which is bidentate. Hypostome not much wider at the base than at the anterior third. Dorsum of the body marked by two short transverse grooves posteriorly and three pairs of pits, from each of which a sulcus runs backwards and inwards.

The ventral surface shows a well-marked pre-anal sulcus, which joins the supracoxal groove, as in *S. savignyi*; behind the anus are three pairs of longitudinal grooves. The stigmata are semilunar, situate above the supracoxal groove. The last segment of the fourth pair of legs is stout and compressed, with three knobs, the distance be n the first and second being equal to that between the second and third.

Tibiae and tarsi of the first three pairs of h three teeth -proximal, submedian and distal, the last being conica

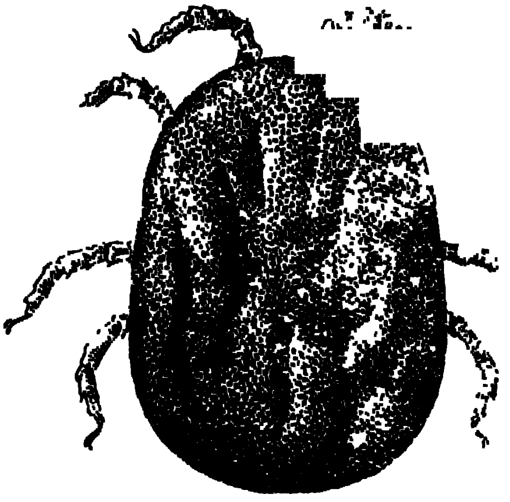


FIG 322 *Ornithodoros moubata* MURRAY: FEMALE DORSAL ASPECT. (× 1)

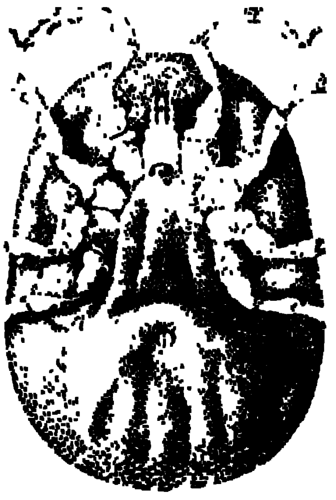


FIG. 323.- *Ornithodoros moubata* MURRAY: FEMALE, VENTRAL ASPECT. (1)

Life-History. -The female lays a variable number of eggs, from 70 to 130, which adhere together, and are golden-brown in colour; 881 by 776 μ. Inside these eggs the larva develop and moult, becoming nymphae, which hatch about the twentieth day at a temperature of 20° to 30° C. and a humidity of 71 to 77 per cent. After three or four days these nymphae suck blood. At first the position of the stigma is marked by only a small white spot and pit, but after the first moult this becomes clear. The genital pore is always absent until after the second moult.

The adult tick moults after each feed of blood, and may live about a year. They are night feeders, and rather resemble bugs in their habits. Leishman observed that the fluid secreted by the coxal glands prevents coagulation of the blood.

Pathogenicity. -It is the spreader of *Spiroschaudinnia duttoni*, and according to Wellman and Feldmann possibly of *Acanthocheilonema perstans*.

Ornithodoros turicatus Dugès, 1876.

Synonyms.—*Argas turicata* Dugès, 1876; *Ornithodoros americanus* Marx, 1895.

Ornithodoros without eyes; anteriorly the body is much narrowed. Tibiæ and tarsi with three small tubercles.

Habitat.—Mexico and Central America. Attacks men and fowls.

Ornithodoros megnini Dugès, 1883.

Synonyms.—*Argas megnini* Dugès, 1883; *A. americanum* Packard, 1893; *Rhynchoprion spinosum* Marx, 1895.

Ornithodoros with phial-shaped body; attenuated anteriorly. Females 5 to 6 millimetres by 3 to 4 millimetres. Males somewhat smaller.

This is the ear tick of American cattle, and has been found in the ear of man.

Ornithodoros lahorensis Neumann, 1908.

Ornithodoros without eyes. Male 8 by 4·5 millimetres. Female 10 by 5·6 millimetres Found at Lahore, India. Parasitic on sheep.

Ornithodoros tholozani Laboulbène and Mégnin, 1882.

Synonyms.—*A. tholozani* Laboulbène and Mégnin, 1882; *A. papillipes* Birula, 1895.

Ornithodoros without eyes. Males 4 to 6 millimetres in length and 2 to 4 millimetres in breadth Females 8 to 10 millimetres by 4 to 5 millimetres.

It is specially a parasite of sheep in Caucasia and Persia, but is very dangerous to man.

Ornithodoros pavimentosus Neumann, 1901.

Ornithodoros with eyes. Body covered with flat warts forming a pavement. South Africa. Only female known. 12 by 8 millimetres.

Ornithodoros furcosus Neumann, 1908.

Found in Ecuador. Female 10 by 5 millimetres.

Ornithodoros erraticus Lucas, 1849.

Synonyms.—*Argas erraticus* Lucas, 1849; *O. miliaris* Karsch, 1880.

Found in Algeria and Bengal. Length, 5 millimetres; breadth, 3 millimetres.

Ornithodoros coriaceus Koch, 1844.

Ornithodoros with eyes. Only one knob on the hind tarsus. America. Male 6·4 to 8·6 by 3·4 to 4·6 millimetres; female 9·5 to 13·8 by 5·3 to 8·2 millimetres.

Ornithodoros canestrinii Birula, 1895.

Synonym.—*Argas canestrinii* Birula, 1895.

Found in Persia. Male 10 by 5 millimetres; female 14 by 8 millimetres.

Alectorobius Pocock, 1907.

Argasidæ with folds of integument capable of being folded under the palpi. This genus is not recognized by Nuttall, as he considers it a synonym of *Ornithodoros*.

Type.—*A. talaje* Guérin-Méneville, 1849.

Alectorobius talaje Guérin Méneville, 1849.

Synonyms.—*O. talaje* Guérin and Méneville, 1849; *O. rudis* Karsch, 1880; *Alectorobius talaje* Pocock, 1907.

This is the chinch of South America and Mexico where it is a great pest. *A. coniceps* of South Europe and *A. capensis* of South Africa are varieties of this species.

FAMILY 2: IXODIDÆ Murray, 1877.

Synonyms.—*Ixodei* Duges 1834; *Ixodiden* Koch, 1844; *Ixodides* Gervais and van Beneden, 1859; *Ixodini* Canestrini and Fanzago, 1877; *Ixodinæ* Trouessart, 1892; *Anistomata* Marx, 1892.

Ixodoidea with a dorsal scutum and a terminal capitulum. The digit of the mandible has two apophyses, and the palpi are free.

Most of the ticks belong to this family, which has the following features:—

Morphology.—There is a dorsal scutum and a terminal capitulum. The mandible has a digit with two apophyses, of which the internal is short with one to four teeth, and the external long, with two to five teeth. The palpi are free. The second pair of legs is the shortest, and the fourth pair the longest. The tarsus has a pulvillum. The stigmata are situate posterior to the coxa of the fourth leg. The male is smaller and fatter than the female. The scutum covers the whole dorsum except a marginal region, the posterior portion of which, between the two stigmata, is generally divided into eleven festoons. The female has but a small scutum, situated anteriorly, and the capitulum has two symmetrical porose areas on its basal piece.

Type Genus.—*Ixodes* Latreille, 1796.

Life-History of the Ixodidæ.—When the pregnant female tick drops off the host, it at first appears to seek for a suitable place to lay its eggs. When this is found, it becomes quiescent, and the anterior part of the ventral surface between the first pair of legs becomes depressed, and forms a hollow, in which the head and genital orifice are situated. When an ovum passes out of the orifice, the tick moves slightly backwards. This oviposition takes about fifteen to twenty days. While it is proceeding the tick begins to shrivel and to show yellow areas, due to the distension of the Malpighian tubes with guanine. At the end of oviposition the tick dies.

From the egg comes a six legged larva, which generally climbs into some grass or bushes and waits to get on to a host. While so doing it may remain for months without food.

It now sucks blood, and drops off this first host and moults on the ground, becoming an eight-legged nymph, like an adult, but without generative apparatus, which again has to go in search of a second host and obtain a feed of blood, when it drops off and undergoes a second moult, turning this time into the sexually mature adult, which goes in search of a third host. Before feeding, the adult female is small, flat, and thin. When she arrives on the third host she drives her rostrum perpendicularly into the skin as far as its base, a hole being made by the mandibles.

The palpi do not enter the hole in the skin, but lie on each side.

The recurved hooks on the hypostome keep the tick in position, and can only with difficulty be detached. The tick now sucks the blood, and at the same time becomes fertilized and increases enormously in size by the addition of blood and the development of the eggs. She then drops off this third host and proceeds to lay her eggs.

The male does not gorge and does not increase so much in size, but sucks blood, which it requires for its fertilizing work.

The *Ixodidæ* are divided into two subfamilies.

SUBFAMILY 1. RHIPICEPHALINÆ Salmon and Stiles, 1901.

Synonyms. *Rhipistomidea* Koch, 1844; *Conipalpi* Canestrini, 1890; *Rhipicephalæ* Neumann, 1897; *Rhipistomidæ* Marx, 1896.

Ixodidæ in which the palpi are no longer than broad. Anterior portion of the body emarginate.

Type Genus. *Eurhipicephalus* Neumann, 1904.

Genera. *Eurhipicephalus, Margaropus, Hæmaphysalis, Dermacentor, Rhipicentor.*

SUBFAMILY 2. IXODINÆ Salmon and Stiles, 1901.

Synonyms. *Ixodidea* Koch, 1844; *Cultripalpi* Canestrini, 1890; *Ixodidæ* Marx, 1892; *Hæmalastoridæ* Marx, 1892; *Eschatocephalidæ* Marx, 1892; *Ixodæ* Neumann, 1899.

Ixodidæ with palpi longer than broad; rostrum long. Anterior portion of the body straight or emarginate.

Type Genus.—*Ixodes.*

Genera.—*Ixodes, Eschatocephalus, Ceratixodes, Aponomma, Amblyomma, Hyalomma.*

DIAGNOSTIC TABLE OF GENERA, FROM SALMON AND STILES.

RHIPICEPHALINÆ.

A. Eyes present:—
  I. Dorsal surface of capitulum hexagonal, sides drawn out laterally into sharp points.
    (*a*) Males with anal plates.
      1. Second and third palpal segments straight; stigmata comma-shaped- *Eurhipicephalus*.
      2. Second and third palpal segments drawn out laterally into sharp points: stigmata round *Margaropus*.
    (*b*) Males with rudimentary anal plates- *Rhipicentor*.
  II. Dorsal surface of capitulum rectangular, sides straight; male without anal plate *Dermacentor*.
B. Eyes absent- *Hæmaphysalis*.

Nuttall and Warburton's new classification of the Ixodidæ is as follows:—

Prostriata—Ixodidæ with anal grooves surrounding the anus in front—*Ixodes*.

Metastriata. Ixodidæ with anal groove contouring the anus behind, but this groove may be faint or obsolete.

Brevirostrata.—

Group I.: Inornate without eyes, but with festoons—*Hæmaphysalis*.
Group II.: Ornate or inornate with eyes, and with or without festoons
  Anal grooves marked.
    Ornate with festoons.
      Basis capituli rectangular dorsally—*Dermacentor*.
      Basis capituli hexagonal dorsally—*Rhipicentor*.
    Usually inornate with festoons
      Basis capituli usually hexagonal dorsally - *Rhipicephalus*.
  Anal grooves obsolete
    With short palpes *Margaropus*.
    With very short compressed palpes ridged dorsally and laterally—*Boophilus*.

Longirostrata.—

Group I.: Ornate or inornate, with eyes and with or without festoons basis capituli subtriangular dorsally. Male with a pair of adanal shields- *Hyalomma*.
Group II.: Generally ornate, with eyes and with festoons, basis capituli variable. Without adanal shields—*Amblyomma*.
  Subgenus *Aponomma* chiefly found on reptiles with poorly-developed or no eyes.

It will be observed that the genera Eschatocephalus and Ceratixodes are rejected and referred to the genus Ixodes. Another genus, *Neumanniella* Lahille, 1905, is also rejected, and it is referred to Aponomma.

SUBFAMILY RHIPICEPHALINÆ.

Eurhipicephalus Neumann, 1904.

Synonyms.—*Rhipicephalus* Koch, 1844; *Phauloixodes* Berlese, 1889.

Rhipicephalinæ with distinct eyes; base of the capitulum broader than long; hexagonal, or dorsal surface forming a projecting angle at each side. Palpi short and broad. First coxa with two large teeth. Male with one or two pairs of anal shield. (Fig. 324.)

Type Species.—*Eurhipicephalus sanguineus* Latreille, 1804.

Eurhipicephalus appendiculatus Neumann, 1901.

This is the brown tick of South Africa, where it spreads *Theileria parva* among cattle and buffaloes, causing 'coast fever.'

Morphology. Male, scutum does not quite cover the dorsum: festoons narrow; the median is prolonged into a caudal process. In front of the festoons, three wide longitudinal grooves. Size, 4 by 2·6 millimetres. Female, dorsal plate oval: porose area small.

Life-History. The eggs are laid in thousands on the grass, and hatch in about twenty-eight days into six-legged larvæ, which pass from the grass on to cattle, suck blood, and drop off replete in about three to four days.

They now remain dormant for about twenty-one days, and finally moult, giving rise to the eight-legged nymph.

The nymph proceeds to attack cattle and suck blood, taking the same length of time as the larva. It then drops off replete, and in about eighteen days moults and becomes an adult male or female tick, which again infests cattle. The female settles down quickly, and is joined by the male. In about four days the female, which has become fertilized and full of blood, drops off, and completes the life-cycle by laying the eggs, after which she dies.

What becomes of the male is not known.

Pathogenicity.—It spreads *Theileria parva*, the cause of coast fever in cattle, by the bites of the infected nymphs only—*i.e.*, infected larvæ and adults do not spread the disease, but the larva can hand the infection over to the nymph, which is the spreader.

Eurhipicephalus bursa Canestrini and Fanzago, 1878.

Synonym.—*Rhipicephalus bilenus* Pavesi, 1883.

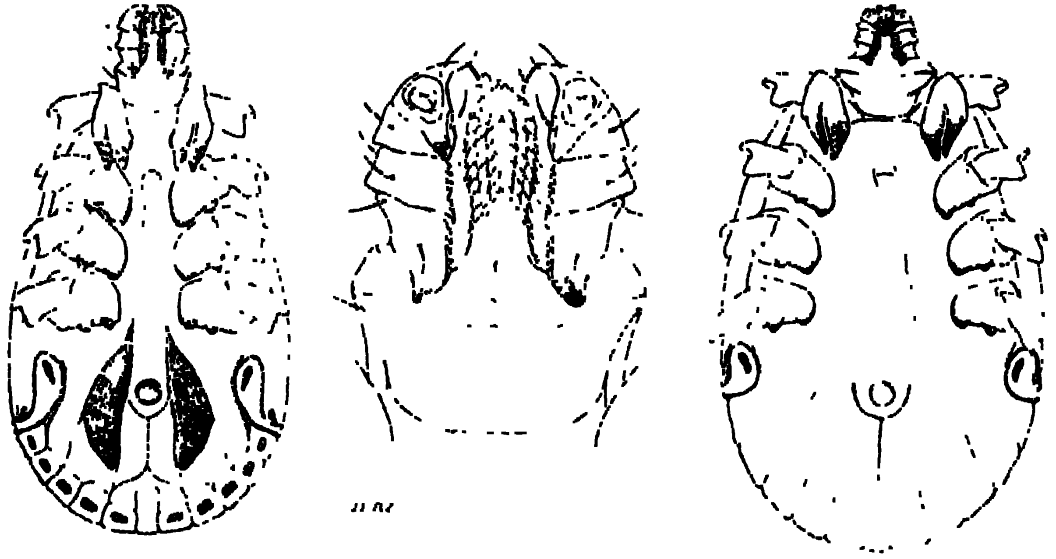
This species is widespread through Southern Europe, and is also known in Africa, West Indies, and Malaga, as a sheep, horse, cattle, and dog tick.

Morphology. Male, scutum half as long as wide; narrow anteriorly, with many punctations. Eleven festoons. Size 4·5 by 3 millimetres.

Female, when newly hatched, flat; when distended with blood, ovoid. Scutum oval, eyes about the middle of the length. Tegument with numerous punctations dorsally when young.

Life-History.—The female lays the eggs on grass, and these develop into larvæ, which attack a sheep, and moult on it in about eight days, forming nymphæ, which grow for twenty-one days, fall off on to the ground, moult, and become adults, which again infest sheep.

Pathogenicity.—It spreads *Piroplasma ovis*, which causes 'heart-water' in sheep, the infection being carried from an adult female through the eggs to the adult ticks of the next generation, which alone are capable of transmitting the disease.



FIGS. 324-326.—*Eurhipicephalus pulchellus* GERSTÄCKER, 1873: VENTRAL ASPECT.

a, Male (× 10); *b*, mouth parts (more highly magnified); *c*, female (× 10).

Eurhipicephalus simus Koch, 1844.

Synonyms.—*Rhipicephalus senegalensis* Koch, 1844: *Rh. prætentatus* Gerstäcker, 1893.

This tick is found in various parts of Africa—viz., Egypt, late German East Africa, and the Cape. It has several varieties—*e.g.*, *E. simus erlangeri*, *E. simus hilgerti*, *E. simus shipleyi*. In South Africa it is called the black pitted tick, because of its punctations, and causes 'coast fever' by spreading *Theileria parva*. Male oval, rounded posteriorly; 4 by 2·2 millimetres. Scutum brown-red. Female oval, 6 by 3 millimetres.

Eurhipicephalus sanguineus Latreille, 1804.

Synonyms.—*Ixodes sanguineus* Latreille, 1804: *I. rufus* Koch, 1844

Synonym of Nymph.—*Phauloixodes rufus* Berlese, 1889.

This is the common dog tick, by which *Piroplasma canis* is spread, which it acquires as an adult, and transmits in the succeeding nymphal and adult stages. It also spreads *Hæmogregarina canis*. It is practically cosmopolitan.

The female has an elliptical body, wider in front than behind: 11 by 7 millimetres, reddish-brown in colour. Scutum very small; integument nearly or completely without hairs: The mandibles have an internal apophysis with three teeth, arranged one internally and two externally; and an external apophysis with three teeth, arranged in series.

The male is 3·35 by 1·55 millimetres, with a scutum covering the dorsal surface, except at the sides and back. External apophysis with only two teeth.

Eurhipicephalus evertsi Neumann, 1897.

This is the red-leg tick, which spreads *Nuttallia equi*, and is found in Europe, Africa, and Asia. The life-history resembles *Eurhipicephalus appendiculatus* in the changes of host by larva and nymph. The infection is acquired in the nymphal stage, and transmitted by the adult. Size: male, 5 to 6 by 3 to 4 millimetres; female, 14 by 9 millimetres.

Margaropus Karsch, 1879.

Synonyms.—*Boophilus* Curtice, 1891, *Rhipicephalus* Neumann, 1897.

Rhipicephalinæ with eyes, though often indistinct: base and capitulum broader than long. Palpi short and broad; second and third segment thicker in the middle, and forming a sharp angle externally. Posterior margin of the first coxa slightly bidentate: stigmal plate round. Body without marginal festoons; anal groove absent. Male with two pairs of anal plates.

Type. *Margaropus annulatus* Say, 1821.

Only three or, according to Neumann, two species, of which two species (*M. annulatus*, *M. decoloratus*) may be one, the third being *M. lounsburyi* Neumann, 1907.

Margaropus annulatus Say, 1821.

Synonyms.—*Ixodes annulatus* Say, 1821; *Hæmaphysalis rosea* Koch, 1844; *Ixodes bovis* Riley, 1869; *Margaropus winthemi* Karsch, 1879; *Boophilus bovis* Curtice, 1880; and several others.

Female with elliptical body, as wide in front as behind. Scutum very small. Eyes small. Dorsal surface, with two antero-posterior grooves, interrupted towards their middle. Ventral surface with small sexual aperture and sexual furrows. Stigmata oval. Capitulum very short. Internal apophysis of mandible conical; the external with three teeth. Hypostome broad. Palpi very short. Legs short (*vide* Fig. 313).

Male with body oval, 2·15 by 2·35 millimetres, narrow anteriorly; widest opposite stigmata. Scutum brown-red, covering the whole dorsal surface with large punctata. Sexual orifice large, a little in front of the level of the second pair of legs. Festoons hardly marked. Two pairs of clypeal shields. Internal apophysis of the mandibles with bifid point: the external has two teeth. Coxa of first leg with a blunt anterior process and bifid posteriorly.

This tick has a very wide geographical distribution, being found in North and South America, the West Indies, Africa, Europe, Japan, and Australia: but the different countries show certain variations in the tick, and hence the species receive a little change in the name.

Life-History.—*Margaropus annulatus* begins its life with the egg on the ground, from which the larva emerges, and, gaining access to the host, undergoes its development into nymph and adult without the changes of host described in *Eurhipicephalus*.

When the adult female has gorged with blood, she drops off the host and lays her eggs.

Pathogenicity.—It is the spreader of *Piroplasma bigeminum*, the cause of Texas or red-water fever in cattle. The adult female acquires the *Piroplasma* and passes it on to the larva, which infects the host. It is also the carrier of *Spiroschaudinnia theileri*.

Varieties.—The names of the varieties are: (1) *M. dugesi* Mégnin, 1880, in North Africa; (2) *M. microphilus* Canestrini, 1887, in South America; (3) *M. australis* Fuller, 1899, in Australia, Asia, Africa; (4) *M. calcaratus* Birula, 1895, in the Caucasus; (5) *M. caudatus* Neumann, 1901, in Japan; (6) *M. argentinus* Neumann, 1901, in Buenos Ayres.

Margaropus decoloratus Koch, 1844.

This is looked upon as a variety of *Margaropus annulatus* Say by some authors. It is the blue tick of South Africa.

Morphology.—The clypeal plates in the male end in sharp points, and a caudal appendage is present. The hypostome has six rows of teeth.

Life-History.—It lives from the larval stage to the adult on the same host. The adult, when fully fed, drops off and lays the eggs on the ground.

Pathogenicity.—It is a spreader of *Piroplasma bigeminum*.

Rhipicentor Nuttall and Warburton, 1908.

Rhipicephalinæ with eyes, inornate, with festoons. Basis capituli hexagonal dorsally, and having very prominent lateral angles with short palps. Coxa I. bifid in both sexes. The male resembles *Eurhipicephalus* dorsally and *Dermacentor* ventrally. Coxa IV. is much the largest. There are no ventral shields or plates. Spiracles subtriangular or comma shaped.

Type.—*Rhipicentor bicornis* Nuttall and Warburton, 1908.

Rhipicentor bicornis Nuttall and Warburton, 1908.

Synonym.—*Rhipicephalus gladiger* Neumann, 1908.

This is an African species living on the horse in the Congo and Central Africa. It attacks and can live on man. Another species is *Rh. vicinus* Nuttall, 1908.

Dermacentor Koch, 1844.

Rhipicephalinæ with eyes; base of capitulum rectangular, broader than long. Dorso-submedian porose plate present; palpi short and thick; stigmata comma-shaped. Male without anal shields. The coxa of the fourth leg much larger than those of the others. Scutum ornamented.

Type.—*Dermacentor reticulatus* Fabricius, 1794.

In 1910 Stiles classified the species of Dermacentor into four groups, according to the microscopical structure of the stigmal plates in the adult.

A Adults with four longitudinal rows of large denticles on each half of hypostome, stigmal plate nearly circular without dorso-lateral prolongation, goblets very large - *D nitens*.

B Adults with three longitudinal rows of large denticles on each half of hypostome, goblets small medium, or large.
  Dorso-lateral prolongation of stigmal plate absent *Salmoni group*.
  Dorso lateral prolongation of stigmal plate distinct.
    Goblets of medium size - *Andersoni group*.
    Goblets small - *Reticulatus group*.

The *Salmoni group* includes *D. albipictus* Packard, 1869; ***D. salmoni*** Stiles, 1910; and *D. nigrolineatus* Packard, 1869.

The *Andersoni group* includes *D. occidentalis* Marx, 1892; ***D. parumapertus*** Neumann, 1901; *D venustus* Marx 1897; ***D. andersoni*** Stiles, 1905.

The *Reticulatus group* includes *D. reticulatus* Fabricius, 1794; ***D. variabilis*** Say, 1821.

Remarks.—There has been the greatest confusion as to the tick which causes Rocky Mountain fever. This was called ***Dermacentor occidentalis*** because Stiles considered that *D. andersoni* Stiles, 1905, was identical with *D. occidentalis* Marx, 1892, but the two forms have since been shown by him to be quite distinct. Therefore in any reference to a tick causing Rocky Mountain fever, no matter what name is used, it is important to understand that ***D. andersoni*** Stiles, 1905, is the species really referred to.

Dermacentor reticulatus Fabricius, 1794.

Synonyms.—*Acarus reticulatus* Fabricius, 1794; ***Ixodes reticulatus*** Fabricius, 1805; *I. marmoratus* Risso, 1826; ***Dermacentor albicollis*** Koch, 1844; *D. pordalinus* Koch, 1844; *D. ferrugineus* Koch, 1844; *Hæmaphysalis marmorata* Berlese, 1887.

Dermacentor with coarsely punctate stigmal plate.

This tick gains its importance from the fact that for some time it was considered to be the cause of the spread of Rocky Mountain fever, which was really due to the nearly related *D. andersoni*, with which it was long confused. It probably does not occur in America. It is widely distributed through Europe and Asia.

Dermacentor occidentalis Marx, 1892.

This tick was received by Marx from Occidental in California, and was first described by Neumann It is found in the north-western portion of the United States from California to Montana.

Morphology.—Male Oval, narrow in front, broad behind; scutum variegated brown and white Anteriorly there is an elliptical area, the pseudoscutum, closely representing the form and colour of the female scutum, and limited by a white border, and possessing two lateral brown stripes, with a median brown stripe or spots between them. Behind this there are four brown stripes arranged in a curve, open anteriorly. Posterior to these usually five brown stripes; one central and two lateral. Between these areas the whole dorsum is speckled with brown punctations. The eleven festoons are somewhat quadrangular, each composed of a white area with one brown spot, and speckled with brown punctations. Ventral surface with the first coxa bidentate, and the others with a single spine. Fourth coxa very large; about twice as large as the third. Generative aperture on a level with the second pair of legs. Stigma comma-shaped; hypostome with three rows of teeth on each side. Palpi longer than hypostome. Size, 5 by 2·5 millimetres.

Young female: Oval depressed body, broader posteriorly than anteriorly; reddish-brown in colour; about the same size as the male—5 by 2·5 millimetres. Scutum very large, and marked like the anterior part of the male, extending as far back as the third pair of legs, with eyes in the anterior part of the lateral border. Dorsal surface of abdomen with a marginal groove beginning behind the eyes, and three longitudinal grooves running backwards, the two lateral beginning just behind the scutum, and the median about the centre of the body. Posterior margin with eleven festoons. Ventral surface with fine hairs. Genital aperture at the level of the second coxa genital grooves close together at first, but diverging laterally behind the fourth coxa, and ending between the second and third external festoons. Anus with short anomarginal groove. Stigma comma-shaped.

Capitulum with the posterior lateral angle prolonged into a sharp point. Porose areas circular. Internal apophysis of the mandible with strong posterior tooth; external with three successive teeth. First coxa bidentate, other three with spines. Replete female: Swollen body laterally constricted at the stigmata, of deep brown or slate colour; size, 16 by 10 millimetres.

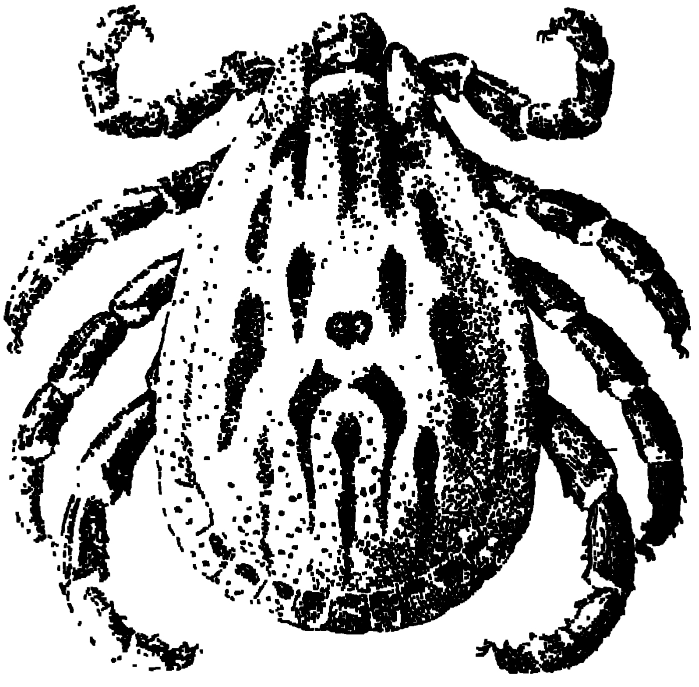


Fig. 347. *Dermacentor salmoni* Stiles, 1909: Male, Dorsal Aspect.

Life-History.—The egg hatches in seven to ten days, and produces a larva which feeds on some animal for several days, and then, becoming swollen and of a uniform slate-colour, drops off, and, becoming quiescent, moults and gives rise to the nymph. This nymph again attacks an animal, and when fed drops off, and in ten days moults and becomes the adult. The nymph however, can hibernate. If the adults do not obtain a host they die off quickly

Pathogenicity.—Nil.

Dermacentor andersoni Stiles, 1905.

Synonyms.—*Dermacentor occidentalis* of all writings on Rocky Mountain spotted fever until some time after 1910; *D. venustus* Marx (in part only); *D. andersoni* Kieffer, 1907.

Dermacentor with caudal margin nearly or quite semicircular. Colour, greyish to red or deep red-brown. Eyes not prominent. Scutum with whitish rust, and with large or small punctations.

Genital pore surrounded by hairs. Anal ring nearly circular. Stigmal plates with prominent dorso lateral prolongation, aperture and chamber large and elongate, goblets of medium size. Postero-lateral projections of plate small. Capitulum with short postero-lateral projections of base. External article with large recurved tooth, a smaller subapical, and a very small apical tooth. Hypostome with three rows of strong denticles. Palpi with lateral margin convex; first article with four or five bristles: third article rather triangular dorsally. Legs. outer spur of coxa I. longer than inner spur; trochanter I. with retrograde curved blade.

Male. Length, 4 by 2·5 millimetres broad. Body oval. Scutum covers dorsum except capitulum: deep reddish-brown, marked by four elongate spots arranged in semicircle; two elongated reniform spots behind these, one elongated median spot, and two shorter elongate submedian spots, and an indistinct forked spot.

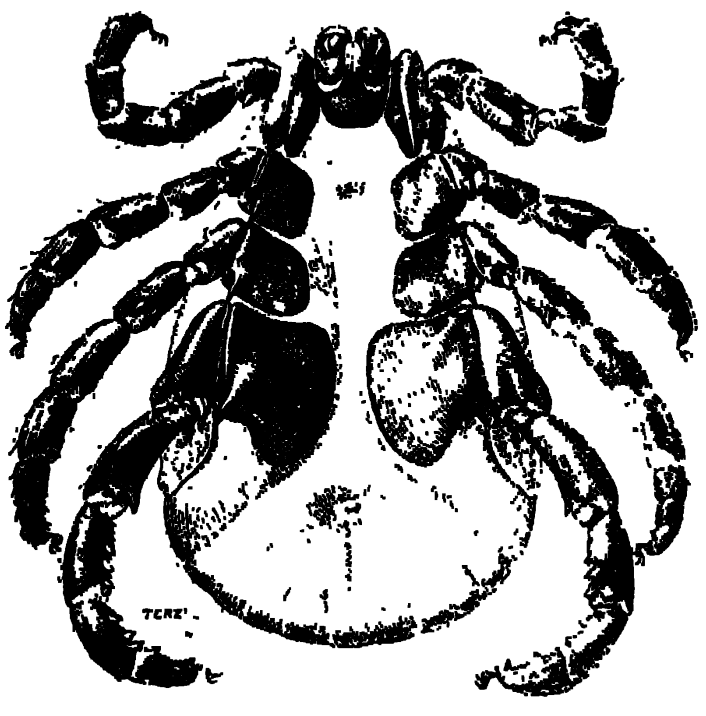


FIG. 328.—*Dermacentor salmoni* STILES, 1909: MALE, VENTRAL ASPECT

Female. Scutum, 1·56 to 1·62 millimetres in length by 1·9 millimetres broad; very conspicuous because of its whitish colour. Cervical grooves well developed. Venter with punctation and fine hairs. Genital grooves running parallel caudad.

Young Female. This is the form most commonly found. Length, 4·5 to 7 millimetres. Breadth, 2·3 to 2·6 millimetres. Body oval. Scutum covers about 0·43 of the length of the body. Eyes not very distinct. Vulva between coxæ II.

Replete Female. Length about 16 millimetres, and 6 millimetres to 9·5 millimetres thick. Eyes more distinct than in young female. Vulva may shift to level of first and second intercoxal space, and a radial groove may appear on each side between the anal and the genital grooves. Coxæ naturally farther apart than in young female owing to repletion.

Hexapode Larva.—0·656 millimetre in length by 0·316 millimetre in breadth, with the caudal end broader than anterior end.

Hosts.—Man, cattle, horses, dogs, rabbits, ground squirrels, and other squirrels.

Distribution.—Montana, Washington State, Colorado, and Idaho

Pathogenicity.—It is the carrier of the virus of Rocky Mountain fever, and also causes Tick Paralysis.

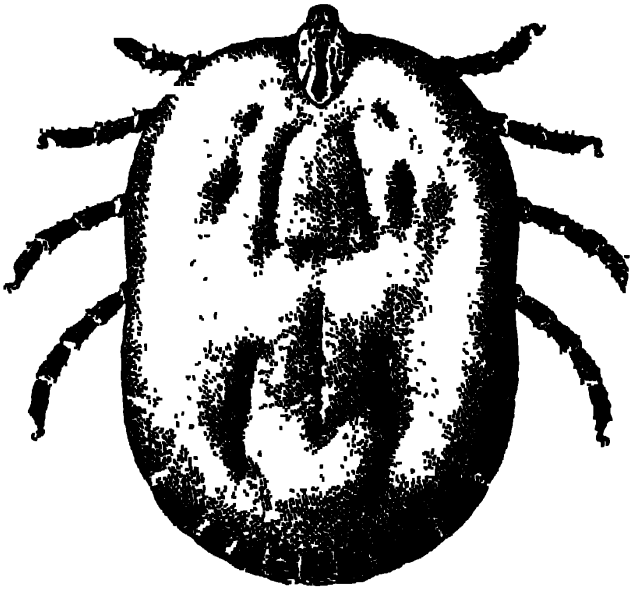


Fig. 329.—*Dermacentor salmoni* Stiles, 1900: Replete Female, Dorsal Aspect.

Hæmaphysalis Koch, 1844 (*vide* Figs. 316-319).

Rhipicephalinæ without eyes, with the base of the capitulum rectangular; twice as broad as long. Palpi triangular or crescentic. Stigmata circular or comma shaped. Anal shields absent. Tegument brownish.

Type. *Hæmaphysalis concinna* Koch, 1844.

Species.—The most important species are: *H. concinna*, *H. leachi*, *H. flavii*, *H. punctata*, the life history of the last named having been studied in detail by Nuttall, Cooper, and Robinson, while according to Stockmann it transmits *Piroplasma ovis*.

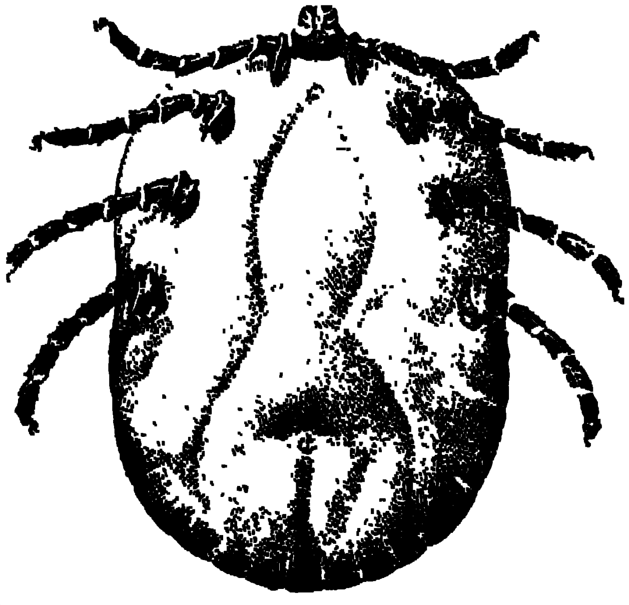


Fig. 330.—*Dermacentor salmoni* Stiles, 1909: Replete Female, Ventral Aspect.

Hæmaphysalis leachi
Audouin, 1827.

Synonyms.—*Ixodes leachi* Audouin, 1827; *Rhipistoma leachi* C. L. Koch, 1844; *Rhipicephalus ellipticum* C. L. Koch, 1844; *Rhipidostoma leachi* Karsch, 1878; *Hæmaphysalis leachi* Neumann, 1897.

This species is found in Africa, Sumatra, and New South Wales. It is the South African dog tick.

The male is 3 by 1·5 millimetres, with yellowish-red scutum, finely punctated dorsum, with eleven marginal festoons. Palpi longer than hypostome. Coxæ of all legs, with a short spine.

The replete female is 9 by 5 millimetres; scutum oval, larger than wide. Second segment of palpi long and spiny.

Life-History.—The larva, after feeding, drops off the dog, and moults. The nymph attacks another dog, feeds, drops off, and moults. The adult attacks a third dog, feeds, drops off, and lays eggs which develop larvæ.

Pathogenicity.—It is the spreader of *Piroplasma canis* among dogs, causing their biliary fever. Nuttall and Hadwen have shown that this canine piroplasmosis can be successfully treated by hypodermic injections of 6 c.c. of a 1 per cent. solution of trypanrot, or 4·5 to 5·5 c.c. of a saturated solution of trypanblau.

SUBFAMILY IXODINÆ.

The following diagnostic table, modified slightly from Salmon and Stiles, will indicate the genera:-

A. Eyes absent:—
  I. Pre-anal crescentic groove opens posteriorly:—
    (*a*) Palpi valvate—*Ixodes* (Fig. 331).
    (*b*) Palpi clavate—*Eschatocephalus*.
  II. Post-anal crescentic groove open anteriorly—*Aponomma*. (Fig. 333).
  III. Without anal groove in the female: one anal shield in the male—*Ceratixodes*.
B. Eyes present:—
  I. Anal plates absent—*Amblyomma* (Fig. 336).
  II. Anal plates present on males—*Hyalomma* (Fig. 339).

Ixodes Latreille, 1796.

Synonyms.—*Cynorhaestes* Hermann, 1804; *Crotonus* Duméril, 1822.

Ixodinæ without eyes, and with long palpi hollowed on the internal surface. Tarsi without terminal spurs. Pre-anal groove open posteriorly.

Male with scutum not covering the lateral and posterior margins: no festoons: stigmata oval. Ventral shields seven in number; one pregenital, one median, two epimeral, one anal, and two adanal.

Female with three dorsal longitudinal grooves and two longitudinal genital grooves ventral, and the anal crescentic groove already mentioned.

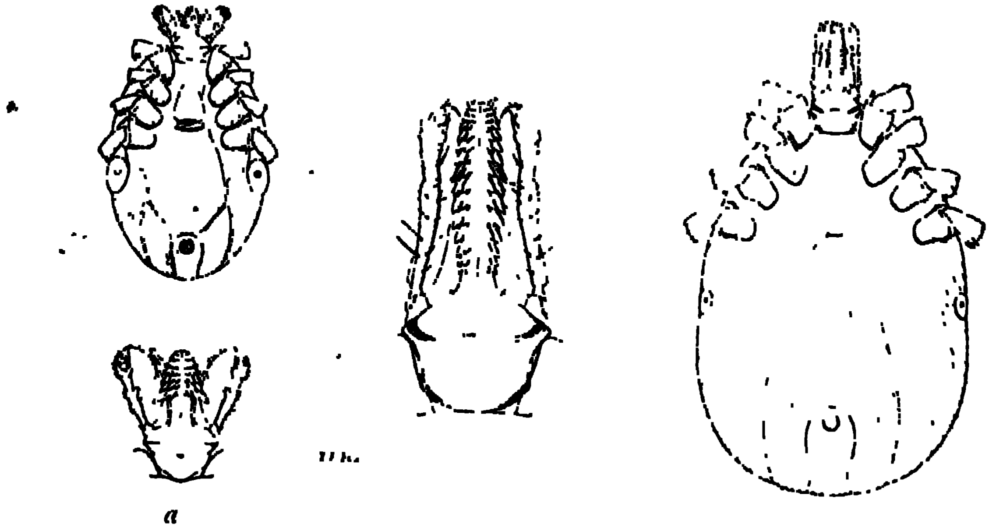
Type Species. *Ixodes ricinus* Linnæus, 1758.

Ixodes ricinus Linnæus, 1758.

Synonyms.—*Acarus reduvius* Linnæus, 1758; *A. ricinus* Linnæus, 1758.

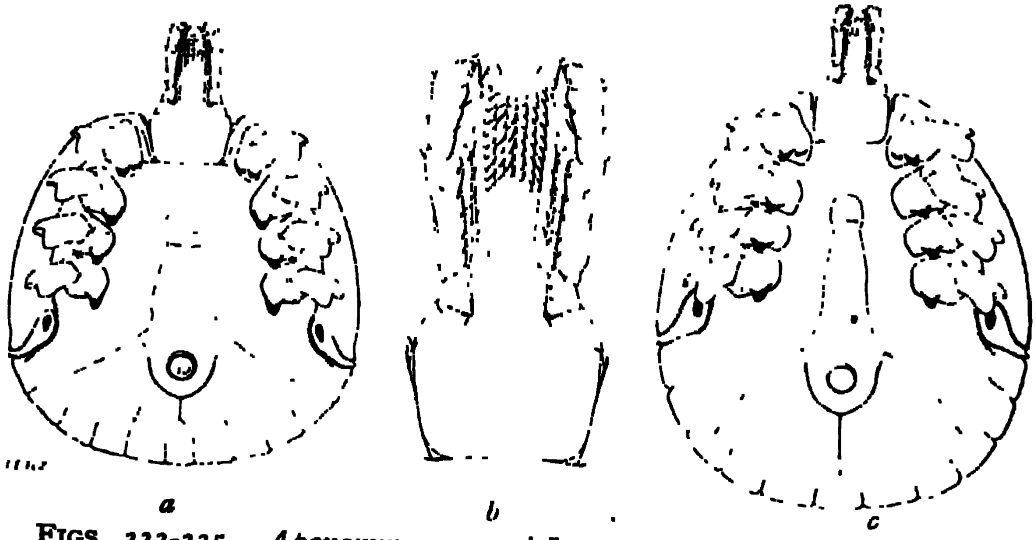
This is the castor-oil tick, and is found in Europe, North Africa, and North America on man, sheep, goats, cattle, horses, dogs, cats, rabbits, bats, birds, etc.

The male has an oval body, broader posteriorly, 2·5 by 1·5 millimetres. Scutum convex, deep red-brown. Genital pore on a plane with the third coxa. Pregenital and anal shields well marked. Capitulum long.



FIGS. 331-332.—*Ixodes pilosus* KOCH, 1844: VENTRAL ASPECT. *a*, Male (× 10) and mouth parts; *b*, mouth parts and female (× 10).

The female, when young, has a flat, oval body. Replete female is like a castor-oil bean, 10 to 11 by 6 to 7 millimetres, of ashy colour. Tegument covered with fine, short hairs. Dorsal surface with three well-marked posterior grooves and two anterior.



FIGS. 333-335.—*Aponomma gervaisi* LUCAS, 1847: VENTRAL ASPECT. *a*, Male (× 15); *b*, mouth parts (more highly magnified); *c*, female (× 15).

Genital pore at the level of the fourth coxæ. Genital grooves unite in front of the vulva. Well-marked pre-anal crescentic groove, open posteriorly. Stigmata whitish. Porose areas elongated transversely. Mandibles with two teeth on the internal apophysis, and external with five teeth.

Life-History.—The female lays about 1,000 eggs in about one to two weeks; the eggs take six weeks to hatch into a larva, which remain one week on the first host and then four weeks on the earth before it becomes a nymph. This stage requires one week on the second host and eight weeks on the earth before it becomes the adult, which seeks the third host, copulates, sucks blood, and drops off to lay eggs.

Pathogenicity.—It acquires *Piroplasma bigeminum* from infected cattle in the adult stage, and spreads it to fresh cattle in the larval and nymphal stages.

Ixodes hexagonus Leach, 1815.

Synonyms.—*Ixodes autumnalis* Leach, 1815; *I. erinacei* Audouin, 1832; *I. reduvius* Audouin, 1832; *I. sexpunctatus* Koch, 1847.

This is the European dog tick.

Pathogenicity.—According to Blanchard, the tick can transmit *Piroplasma canis* Piana and Galli Valerio, 1895.

Eschatocephalus Frauenfeld, 1853.

Synonyms.—*Sarconissus* Kolenati, 1857; *Hæmalastor* Neumann, 1889.

Ixodinæ without eyes, and with a long rostrum. Palpi pyriform in the male and claviform in the female. Pre-anal groove opening posteriorly. Stigmata circular. Legs long.

Male with dorsal and ventral irregular chitinous thickenings.

Female with very fine parallel grooves.

Type Species.—*E. vespertilionis* C. L. Koch, 1844.

There are over seven species found on bats and in caves.

Aponomma Neumann, 1899.

Synonym.—*Ophiodes* Murray, 1877.

Ixodinæ without eyes, and with the base of capitulum usually pentagonal, with dorso-lateral border very short; palpi long. Post-anal groove. Ventral sexual grooves.

Male nearly as broad as long, with a scutum marked with green spots covering the whole dorsal surface.

Female scutum shorter than broad.

Type Species.—*Aponomma gervaisi* Lucas, 1847.

These ticks are found chiefly on reptiles, but are also found on other animals.

Ceratixodes Neumann, 1904.

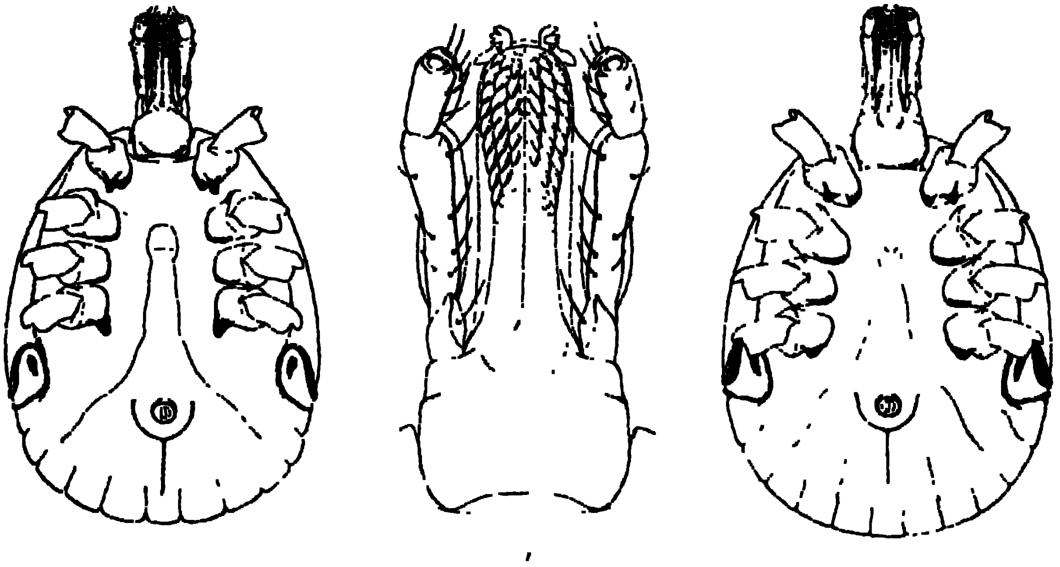
Ixodinæ with long palpi, without eyes, and without anal groove in female. Stigmata circular. One anal and two adanal shields in the male.

Type Species.—*Ceratixodes putus* Cambridge, 1879. It lives on sea-birds, and is found on cliffs, while *C. signatus* Banks, 1908, is known in North America.

Amblyomma Koch, 1844.

Ixodinæ with flat eyes; rostrum long, with valvate palpi. Anal groove semicircular, opening anteriorly. No median ano-marginal groove; no anal plates in the male. Stigmata triangular. Nearly always eleven festoons.

Type Species.—*Amblyomma cajennense* Koch, 1844.



FIGS. 336-338.—*Amblyomma hebræum* C. L. Koch, 1844: VENTRAL ASPECT. *a*, Male (× 7); *b*, mouth parts (more highly magnified); *c*, female (× 7).

Amblyomma hebræum C. L. Koch, 1844.

Synonyms.—*A. annulipes* C. L. Koch, 1844; *Ixodes poortmani* Lucas, 1850; *A. hassalli* Marx and Neumann, 1899.

This tick is found in Africa, especially in Cape Colony, where it is called the 'bont' or variegated tick, and is the spreader of 'heart water' in sheep and goats.

Morphology.—Male (*vide* Fig. 336) with sulphur-yellow-coloured scutum, variegated with brown, and finely punctated and marked with longitudinal grooves. Marginal festoons light-coloured except the two extreme festoons. Female with brown and white scutum, as broad as long; body of a fully replete female, 24 by 15 millimetres.

Life-History.—The usual life-history for Ixodidæ.

Pathogenicity.—Transmits 'heart-water' in sheep

Hyalomma Koch, 1844.

Ixodinæ with eyes, rostrum long, palpi valvate, anal groove semicircular, opening forwards, uniting sexual grooves, and followed by a median ano-marginal groove. Male with two pairs of ventral shields, two adanal and two lateral. Female with triangular stigmata.

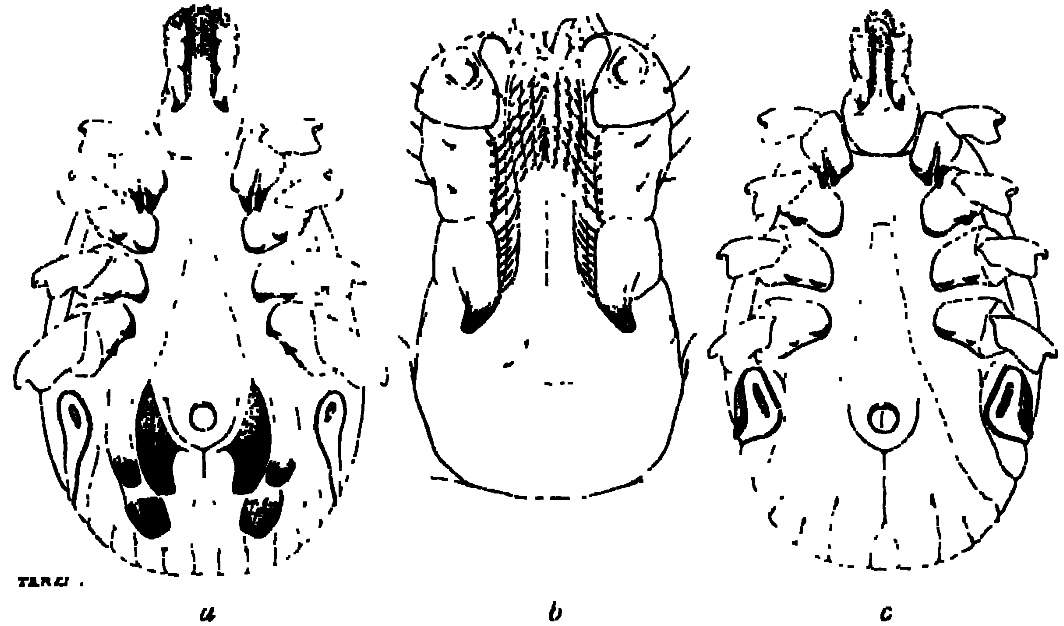
Type Species.—*Hyalomma ægyptium* Linnæus, 1758.

Only a few species:—*H. ægyptium*, *H. crassitarsus*, *H. affine*, *H. syriacum*, *H. rhipicephaloides*, *H. hippopotamense*, *H. monstrosum*.

Hyalomma ægyptium Linnæus, 1758.

Synonyms.—*Acarus ægyptus* L., 1758; *Ixodes camelinus* Fischer, 1823.

This tick is found in Africa, particularly in Egypt and South Africa; in Asia, particularly in Southern India; in Europe, especially in France and Italy. The adults attack cattle, especially sheep and goats, and also at times man. The larvæ and nymphæ are supposed to attack birds, not cattle.



Figs. 339-341.—*Hyalomma ægyptium* Linnæus, 1758 (× 8): Ventral Aspect *a*, Male (× 8); *b*, mouth parts (more highly magnified); *c*, female (× 8).

The male is almost black, with a pale marginal stripe, with a small, triangular, often white, median festoon.

The female is brown, with light blue stripes. Scutum, which as a rule is as broad as long, possesses numerous punctations, and is indentated behind the eyes.

Life-History.—This appears to require further investigation.

Pathogenicity.—Can transmit *Piroplasma bovis* to oxen.

SUBORDER IV. PROSTIGMATA.

The suborder Prostigmata contains two superfamilies, which are of importance in medicine.

Superfamily A: Trombidoidea.—Prostigmata in which the last joint of the palpi is bent down towards the penultimate joint, which usually ends in a claw. Body often with many hairs.

Superfamily B: Eupodoidea.—Prostigmata with simple palpi, in which the last joint of the palpi is not bent down towards the penultimate joint. Body with few hairs.

SUPERFAMILY A: TROMBIDOIDEA.

The Trombidoidea include the following families, which are of importance in medicine:—(1) Trombididæ; (2) Tetranychidæ; (3) Cheyletidæ.

FAMILY TROMBIDIDÆ.

Trombidoidea with soft skins, and chelate mandibles adapted for biting.

There are two important genera which may be differentiated as follows:—

A. Distal segment of palp with single claw—*Trombidium*.
B. Distal segment of palp with two claws—*Microtrombidium*.

Trombidium Latreille, 1795.

The larvæ of this genus are the harvest-mites, and are widely distributed. *Leptus americanus* Riley and *L. irritans* Riley are American species, being found in the United States and Mexico. *Trombidium tlalsahuate* Lemaire, 1867, is the *Tlalsahuate* of Mexico. The zoological names of the 'pou d'agouti' of Guiana, the 'niaibi' of New Granada, the 'colorado' of Cuba, the 'mouqui' of Para, the 'bête rouge' of Martinique and Honduras, are not known. It must be confessed that there is a great deal of uncertainty about the genus and species of these larvæ, and the subject evidently requires revision.

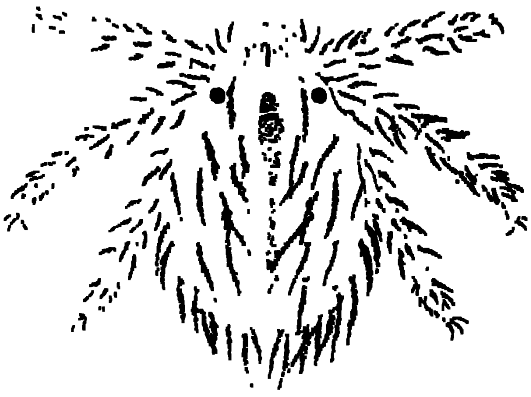


FIG. 312. *Microtrombidium akamushi* BRUMPT, 1910
(After Tanaka from *Centralb. fur Bakteriologie Par und Inf.*)

Morphology.—They are six-legged larvæ with prominent claws on the tips of their legs, provided with a powerful hypostome, which they drive through the skin. Around this hypostome the tissues of the host are supposed to form a tube.

Life-History.—Only the larvæ appear to be parasitic; the adults apparently are not.

Pathogenicity.—They cause itching, redness, and swelling of the affected part, which, if scratched, may become eczematous, and even at times suppurate.

Treatment.—Sulphur ointment kills them.

Genus **Microtrombidium** Haller, 1882.

Definition.—Trombididæ in which the distal segment of the palpus terminates with two stout claws.

Remarks.—These mites are quite common. Thus *Microtrombidium autumnalis* Shaw, 1790, is the harvest bug of England, and is commonly found in the South of England during August and September. It is also common in France during the hot and dry months. Bruyant raised a nymph in 1910 which was thought at first to be *M. pusillum* Hermann, but this is now thought to be doubtful. It is also found in Germany. It generally attacks small mammals such as dogs and cats. *Acarus batatus* Linnæus of Surinam perhaps belongs here. *M. wichmanni* Oudemans is found in New Guinea and Celebes.

Microtrombidium akamushi Brumpt, 1910.

Synonyms.—*Akamushi* (red mite); *Kedani* (hairy mite); *Shashitsu* (sand mite); *Shimamushi* (island mite); *Tsutsugamushi* (dangerous mite); *Yōchūbyō*.

Definition.—*Microtrombidium* of various characters, probably covering several distinct species, with and without all dorsal hairs of the palp feathered. Hair on galea of maxilla always strongly feathered. Hairs on dorsum of palp not feathered, except that on the tibia. Tarsal claw trifurcate. Last tarsus without long fine tactile hair.

Remarks.—The form shown in Fig. 342 may be a distinct species from *M. akamushi*, because all the dorsal hairs on the palp are feathered. This may be called *Microtrombidium brumpti* Hirst, 1915.

These are the mites which cause Japanese river fever, called *tsutsugamushi fever*.

Morphology.—The larva is orange red in colour, 0·16-0·24 millimetre in length, by 0·10-0·21 millimetre in breadth. The palpi are leg-like, and the body and legs are very hirsute.

The *scutum* is oblong, not wide, with straight posterior margin and usually seven hairs. The pseudostigmata are nearer the posterior than the anterior margin.

Eyes are well developed.

Dorsal hairs are 2, 8, 6, 8-10, 8, with a few posterior hairs.

The first coxa has two hairs. The hair on the galea of the maxilla is strongly feathered, while those on the dorsal surface of the palp are plain, except the one on the tibia, which is feathered. Tarsus with seven feathered hairs and a blunt rod-like hair. Legs slender and moderately long, with strongly feathered hairs.

Life-History.—*The akamushi* does not attack insects nor spiders, but will attach itself to man and to small mammals—monkey, dog, cat, rat, mouse, rabbit, and guinea-pig.

The mite remains on its host for three to four days, during which it swells up and turns pale. It then drops off and finds shelter under the ground, where a metamorphosis takes place in some five to six days, during which a nymph forms under the larval skin, and from which it escapes.

The newly hatched nymph, 0·4-0·57 × 0·25-0·285 mm., is a minute eight-legged creature, which, though it crawls about, is neither parasitic nor predaceous, but it feeds upon the juice of potatoes, melons, and other vegetables. After some growth the nymphs seek shelter under the earth and become pupæ.

The pupa is formed from the elongated body of the nymph, inside which the adult form develops, and which in a few days emerges.

The imago is at first without sexual organs, which begin to develop. Meanwhile the adult grows and undergoes more than one ecdysis, and in about ten weeks arrives at sexual maturity.

The eggs are laid singly in earth, but oviposition has not been observed, and the earliest egg known is the deutovum, 0·21-0·24 × 0·17-0·22 mm., inside which the chorion, having split the pale vitelline membrane, could be seen containing the red akamushi, which hatched out after three weeks' incubation.

Microtrombidium wichmanni Oudemans, 1905

Its larva attacks man and animals in Celebes.

Microtrombidium vandersandei Oudemans, 1905.

Synonym.—*Microtrombidium* Van der Sander.

The larva of this Trombidium occurs in New Guinea, and attacks man and animals. Its local name is 'Gonone.'

Metatrombidium Oudemans, 1909.

Metatrombidium poriceps Heim and Oudemans, 1904, has been found on fowls, dogs, and men.

FAMILY TETRANYCHIDÆ.

Trombidoidea with first and second pairs of legs without spines; skin with few shields; palpi not much thickened on base, moving vertically; eyes usually present. First pair of legs do not end in long hairs. Coxæ more or less in two groups. Body with fewer longer hairs. No dorsal groove; often spinning threads; tarsi never swollen. Mandibles styliform.

Genus Tetranychus Dufour.

Definition.—Tetranychidæ without cephalothoracic tubercles. Few legs, slightly longer than body, which is not twice as long as broad. Legs slender. Integument not tessellated dorsally. Palpi ending in a distinct thumb.

Tetranychus molestissimus Weyenbergh, 1886.

This mite is found in the Argentine and Uruguay. It is small and of red colour, living in a web on the interior surface of the leaves of *Xanthium macrocarpum*. From December to February it attacks mammals and man, thrusting its hypostome into the skin and causing severe itching. Another species—*T. telarius* (var. *russeolus*) L., 1758—may attack human beings.

FAMILY CHEYLETIDÆ.

Trombidoidea without spinous processes on the legs; skin with few if any shields; palpi much thickened at the base, moving laterally; last joint often with two pectinate bristles without eyes. First leg ending in several long hairs.

Cheyletus Latreille, 1796.

These are very small mites, distinguished by having enormous palpi, with pectinate bristles. *Cheyletus eruditus* has been described in the external auditory meatus of a man.

Acaropsis Moquin-Tandon, 1863.

Acaropsis mericourti Laboulbène has been found in the human external auditory meatus.

SUPERFAMILY B. EUPOPOIDEA.

FAMILY BDELLIDÆ.

No specialized seta on cephalothorax; integument not chitinized or leathery; palpi composed of four or five segments; cephalothorax large and clearly separated from abdomen; palpi large, geniculate, and bearing distally long tactile bristles; mandibles chelate

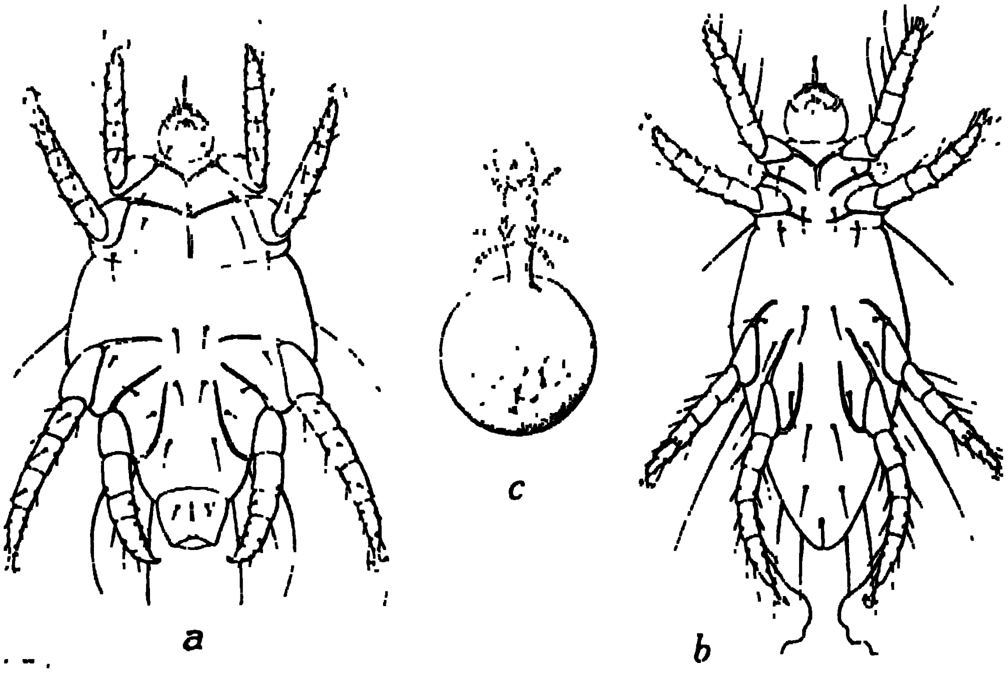
Tydeus molestus Moniez, 1889.

This mite was imported into Belgium in Peruvian guano, and caused much trouble to man and beast.

FAMILY TARSONEMIDÆ.

With marked sexual dimorphism and tracheæ. No ventral suckers.

Tarsonemus hominis Dahl found in cancerous tissues in man, is probably an accidental contamination of the preserving fluids.



FIGS. 343-345. *Pediculoides ventricosus* NEWPORT.
a, Male (× 350); *b*, female (× 220); *c*, distended female (× 60).

Genus Pediculoides Targioni-Tozzetti.

Pediculoides ventricosus Newport, 1850.

Synonyms.—*Heteropus ventricosus* Newport, 1850; *Acarus tritici* Lagrèze-Fossot and Montané, 1851; *Physogaster larvarum* Lichtenstein, 1868; *Pediculoides tritici* Targioni-Tozzetti, 1878; *Sphærogyna ventricosa* Laboulbène and Mégnin, 1885; *Tarsonemus monounguiculosus*.

This mite causes severe itching and urticarial eruptions on the breast, arms, face, neck, and shoulders of persons handling corn and barley, which contains it, in India, Algeria, and Europe.

Morphology.—Males are oval, 0·12 by 0·08 millimetre, with six pairs of dorsal hairs and a lyre-shaped lamella.

Female cylindrical, 0·2 by 0·07 millimetre; becomes much distended posteriorly when gravid.

Life-History.—They live on the stalks of cereals, and feed on animal and vegetal juices. The adult hatches directly from the egg.

Pathogenicity.—They cause diffuse erythema, urticaria, and itching.

Nephrophages Miyake and Scriba, 1893.

Nephrophages sanguinarius Miyake and Scriba, 1893. It is a very doubtful parasite of man; it was found in bloody urine passed by a man in Japan.

SUBORDER V. ASTIGMATA.

This suborder includes the superfamily Sarcoptoidea.

SUPERFAMILY SARCOPTOIDEA.

Astigmata with small three-pointed palpi adhering for some distance to the hypostome, with usually ventral suckers. Two families concern us (1) Tyroglyphidæ, (2) Sarcoptidæ

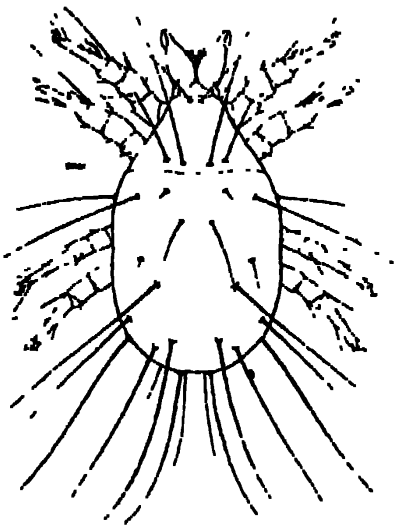


Fig. 346.—*Tyroglyphus longior* var. *castellanii* Hirst 1912: Dorsal Aspect.

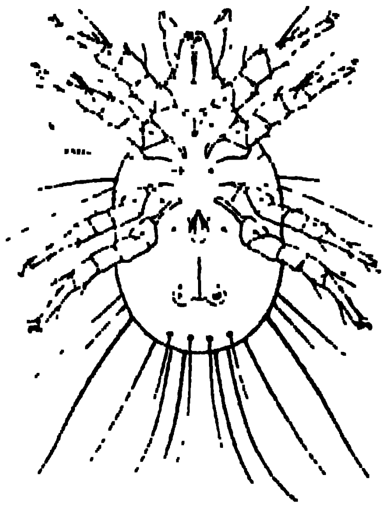


Fig. 347. *Tyroglyphus longior* var. *castellanii* Hirst 1912: Ventral Aspect.

Family 1: Tyroglyphidæ.

Very small mites without eyes; only accidental parasites being found in flour, sugar, cheese, etc.

Tyroglyphus Latreille, 1796.—With smooth dorsum; cephalothorax with four long bristles and no stout spines on tarsi; with claws and suckers. *Aleurobius farinæ* (De Geer) in corn may get into the skin They are the cause of so-called vanillismus. According to Theobald, Linnæus reported a case of dysentery as being due to this species (*Acarus dysenteriæ*).

Tyroglyphus siro Linnæus, 1758, is supposed to be the cause of vanillismus, and *T. longior* Gervais, 1844, is found accidentally in fæces, urine, or pus

T. longior var. *castellanii* Hirst, 1912, was found by Castellani in copra and on people affected by copra itch in Ceylon. In this variety, in contrast to *T. longior*, there is no pair of short hairs on the ventral surface, behind the anal suckers.

Glyciphagus Hering, 1838.—With dorsum covered with hairs

G. prunorum Hermann (synonym, *G. domesticus* de Geer, 1808) is the cause of grocer's itch.

Rhizoglyphus Claparède, 1869—*R. parasiticus* Dalgetty, 1901.—With short legs, armed with spines. Tarsi end in a claw. Live on plants.

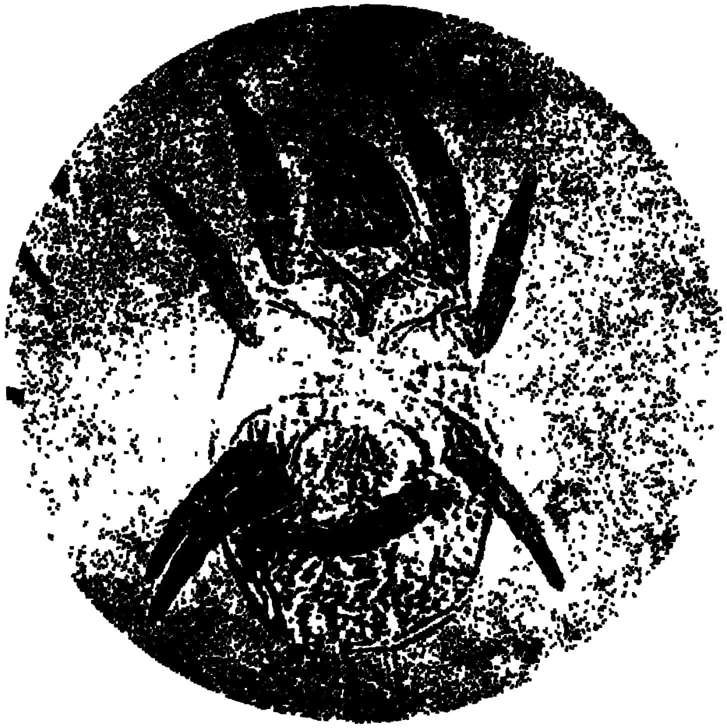


FIG. 348.—*Rhizoglyphus parasiticus* DALGETTY, 1901.
(From a photograph by J. J. Bell.)

This is the species which causes trouble in the feet of Indian coolies. Bell described a large circular, superficial sore on the sole of the foot, caused by many of these parasites invading the skin (see Chapter XCVI.).

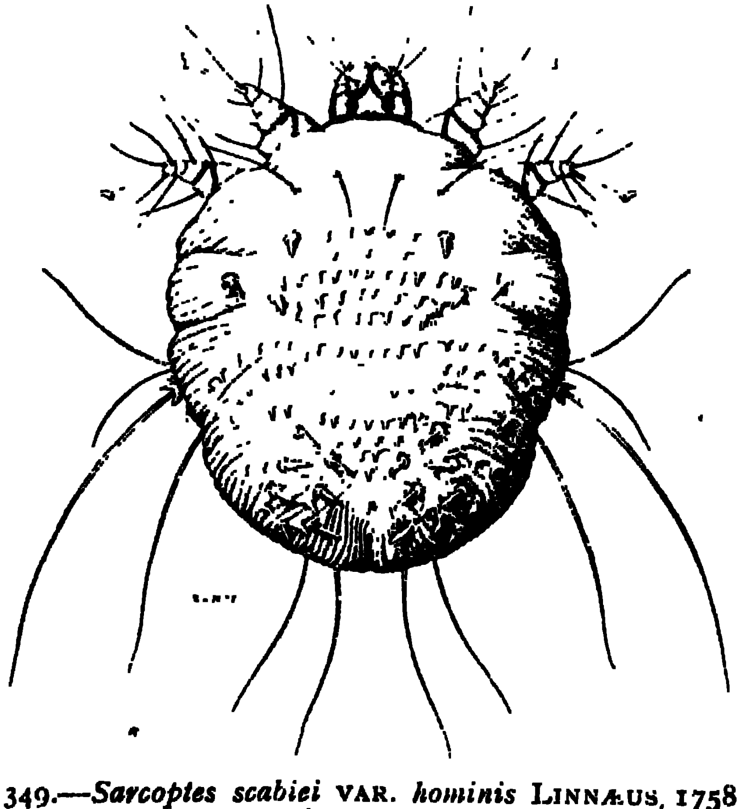


FIG. 349.—***Sarcoptes scabiei*** VAR. ***hominis*** LINNÆUS, 1758: FEMALE
(× 125.)

Histiogaster Berlese, 1883—*H. spermaticus* Trouessart, 1900.—This mite, which feeds on vegetables, appears to have been introduced into a patient by means of a catheter, and to have formed a cyst in the testis in a man in India.

Carpoglyphus Robin, 1869.—*C. alienus* Banks has been found in purulent urine passed by a man. Probably it was a contamination.

FAMILY 2: SARCOPTIDÆ.

Sarcoptoidea without genital suckers, without clinging apparatus, with transverse vulva. Lines in skin.

Sarcoptes Latreille, 1806.—Sarcoptidæ with round or slightly oval bodies; posterior two pairs of legs concealed beneath the body; tarsi end in simple long pedicles with ambulatory suckers.

Sarcoptes scabiei var. hominis Linnæus, 1758.—Female lives in furrows in the epidermis, in which it lays its eggs. Posterior legs end in spines. Males occur on the surface and die after copulation. Posterior legs end in suckers. Six-legged larva hatches in four to eight days.

Sarcoptes minor Furstenberg, 1861.—Usually a parasite of cats; has been found on man.

Sarcoptidæ as Internal Parasites. Sarcoptidæ have been described by Newstead and Todd as internal parasites in monkeys. An Acarid-like parasite was found by Castellani in the omentum of a negro in Uganda. This parasite somewhat resembled *Cytoleichus sarcoptoides* Heguin, which lives in the air sacs, and at times the liver and kidneys, of fowls.

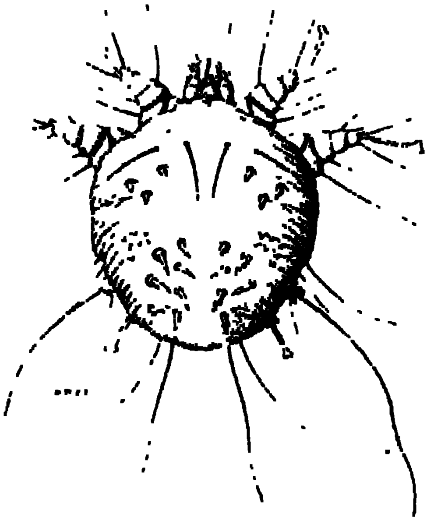


FIG. 350.—*Sarcoptes scabiei* VAR. *hominis* LINNÆUS, 1758: MALE. (× 125.)

Notœdres Railliet, 1893—*N. cati* Railliet, 1893.—Cause of the itch in the cat, and transmissible to man.

Cytoleichus sarcoptoides Mégnin.—Synonym *Cytodites nudus* (Vizioli, 1868), in fowls in the Sudan.

Cytoleichus hominis Hirst, 1917. Found by Castellani, in 1902, embedded in the fat of the omentum of a negro in Uganda.

Chorioptes bovis Gerlach and **Psoroptes equi** Gervais are stated by Zürn and Hirst to attack man.

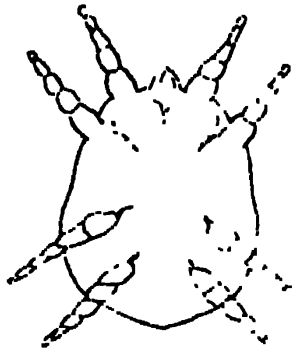


FIG. 351.—*Cytoleichus hominis* HIRST, 1917.

SUBORDER VI. VERMIFORMIA.

Very minute Acarina, with abdomen elongated and annulated without tracheæ and with epimeres on the legs.

This suborder contains only one family.

FAMILY DEMODICIDÆ.

Vermiformia with eight legs, living on animals. This family includes only one genus—*Demodex* Owen, 1843.

Demodex Owen, 1843.

With the family characters. This genus has been recently revised by Hirst. The species of *Demodex* live in the sebaceous glands and hair-follicles of mammals and man. The mouth consists of a rostrum, which is arranged for sucking. The palpi are three-jointed, and pressed to the under surface of the rostrum. The legs are eight in number, short, and consist of three segments with small terminal ungues. The abdomen is tapering, striated dorsally and ventrally, and rounded at the tip. The anus is situated at the anterior end of the abdomen

Demodex folliculorum Simon, 1842.

Synonyms.—*Acarus folliculorum* Simon, 1842; *D. folliculorum* Owen, 1843; *Macrogaster platypus* Miescher, 1843; *Simonea folliculorum* P. Gervais, 1844; *Steatozoon folliculorum* Wilson, 1847.

This parasite was first discovered by G. Simon, of Berlin, in 1842, in the contents of pustules of *Acne sebacea*.

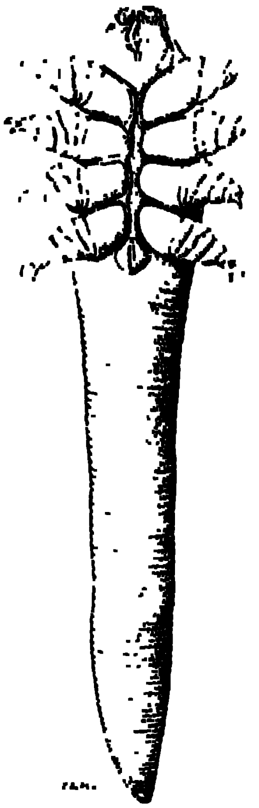


FIG. 352.—*Demodex folliculorum* Simon 1842. (× 150) (Partly after Berlese.)

About the same time Henle had found them in hair-follicles in the external auditory meatus, and Topping a variety in the dog. Two other species are known: *D. phylloides* Cook in pigs and *D. bovis* Stiles in cattle. *D. folliculorum hominis* is cosmopolitan, living in the sebaceous follicles of the face.

Male measures 300 μ by 40 μ, and the female 380 μ by 45 μ.

Life-History.—The eggs are 60 to 90 μ in length by 20 to 50 μ in breadth, and heart-shaped or fusiform. The egg hatches out a six-legged larva, which develops into an eight-legged nymph, from which the adult appears.

Pathogenicity.—Usually said to be nil, but a few authorities suspect the parasites to produce acne-like eruptions, and Borrel considers they play a part in the spread of cancer and leprosy.

ARACHNIDÆ INCERTÆ SEDIS.

LINGUATULIDA.

Parasitic Arachnoidea with ringed, elongated, vermiform bodies, possessing two pairs of hooks in the neighbourhood of the jawless mouth.

Remarks.—The *Linguatulida* have been found parasitic in man both in the adult and larval conditions, but the adult is much rarer than the larva. They have been found in Europe and Africa, and reported from the West Indies, but this was in a negro from West Africa. It is not impossible that they will be found to be far from uncommon parasites when the medical history of the West Coast of Africa is better known. When dealing with cases showing obscure abdominal or pulmonary symptoms in that part of the world, the medical man should remember these parasites.

Morphology.—The body is white in colour and vermiform in appearance, and, indeed, they were long mistaken for worms.

It is elongated, flattened, or cylindrical, and marked by a variable number of rings, and is usually divisible into two regions—an anterior broader portion called the cephalothorax, and a posterior, more attenuated, called the abdomen. It is covered with a chitinous cuticle pierced by pores, called stigmata, which have nothing to do with respiration, being merely the orifices of epidermal glands.

The mouth is situated anteriorly, and is either terminal or subterminal, with a chitinous ring. Two pairs of chitinous hooks, retractile into grooves, are situate on either side of the mouth, and are looked upon by Stiles as antennæ and palpi. There are no legs. The anus is terminal at the posterior end of the abdomen, with the female aperture situate just in front. The male generative pore is on the ventral surface, near the anterior end of the abdomen. The sexes are distinct. The mouth leads into a simple straight alimentary canal, which ends in the anus. There are no circulatory or respiratory organs. The nervous system consists of a ventral mass and a circumœsophageal commissure.

Life-History.—The female produces eggs, which, escaping from the definitive host, pass into the intermediary host, and there hatch out a four-legged larva, not unlike an embyro *Acarus*. This embryo undergoes complete metamorphosis, and forms a nymph resembling the adult, which does not, as a rule, mature, until it reaches its definitive host again.

Genera. —*Linguatula* Frölich, 1789; *Porocephalus* Humboldt, 1811; *Reighardia* Ward, 1899; and *Raillietiella* Sambon, 1909; but only the first two contain species parasitic in man.

Linguatula Frolich, 1789.

Linguatulida with depressed body, rounded dorsum, and crenate margins. Body cavity forming diverticuli into the lateral parts of the rings.

Species.—*Linguatula serrata* Frölich, 1879.

Linguatula serrata Frölich, 1789.

Synonyms. —*Tænia rhinaria* Pilger, 1802; *Polystoma tænioides* Rudolphi, 1810; *Linguatula tænioides* Lambinet, 1816; *Pentastoma tænioides* Rudolphi, 1819. **Nymph.**—*Pentastoma denticulatum*.

The adult lives in the nasal cavity and frontal sinus of the dog, wolf, fox, and rarely in the horse, mule, sheep, goat, and man in Europe; while the larva exists in sheep, oxen, horses, rarely in cats and dogs. Its real host appears to be the dog, especially sheep-dogs.

Habitat.—Europe, especially Central France.

Morphology.—The male is white in colour, 18 to 20 millimetres in length, and 3 millimetres broad. The female is greyish-white or brownish, owing to the contained ova.

Life-History.—The eggs, which are ovoid, 90 by 70 μ, are laid in the nasal cavities of the dog, and expelled by sneezing. If they fall on grass, they may enter the alimentary canal of a herbivorous animal, in whose intestine the embryo hatches. This embryo measures 130 by 60 μ, and possesses two pairs of legs and an anterior perforating apparatus composed of a stylet and two hooks.

It now bores its way into the liver, lungs, or some other organ, and in about eight weeks becomes encysted, losing all its appendages and measuring 275 by 180 μ.

A succession of ecdyses results in the formation of the nymph, which resembles the adult, except that it possesses numerous chitinous spicules on its skin, and by the sixth to the seventh month is about 6 to 8 millimetres in length.

These nymphæ now wander about the host, and are supposed to reach the bronchi, and thus to leave the herbivorous host and reach the dog either by the nose or mouth, in the nasal cavities of which they moult and become sexually mature, copulating about the sixth to seventh week after infection.

Pathogenicity.—Both the larva and the adult may be found in man, the former in the lung, rarely in the liver, spleen, or intestinal wall. The latter has but rarely been met with, and then appears to be due to embryos wandering into the nose and developing directly. Hitherto it has only been found in man in Europe and Central America.

Porocephalus Humboldt, 1811.

Linguatulida with cylindrical body and continuous cœlom.

Type Species.—*Porocephalus armillatus* Wyman, 1847.

Species.—There are about twenty known species, of which *P. armillatus* and *P. moniliformis* are known to occur in man, and will be described below, but Sambon suspects that *P. crotali*, *P. clavatus*, *P. stilesi*, and *P. najæ* will probably also be found in man as scientific work in parasitology extends.

Pathogenicity.—They cause porocephalosis in man and animals.

Porocephalus armillatus Wyman, 1847.

Synonyms—Adult.—*Linguatulida armillata* Wyman, 1847; *Pentastomum polyzonum* Harley, 1856; *Porocephalus moniliformis* Neumann, 1899, *pro parte*. **Nymph.** *Pentastomum diesingi* Beneden, 1849; *P. euryzonum* Diesing, 1850; *P. leonis* Weddell, 1863; *P. constrictum* von Siebold, 1852; *P. protelis* Hoyle, 1883; *Linguatulida constricta* Küchenmeister, 1855.

Porocephalus with cylindrical body, slightly flattened on its anterior face, and surrounded by about sixteen to twenty-two distinct rings, separated from one another by a wide interval. The body tapers from the middle backwards.

Remarks.—The larva of this parasite was discovered by Pruner in the liver of two negroes in Cairo in 1847, and subsequently by Bilharz, Fenger, Kearney, Crawford, Marchoux, Chalmers, and others; while the adult was discovered by Wyman in 1848 in the lungs of the African python. The adult was discovered by Savage in *Python sebæ* and described by Wyman in 1845. Sambon has recently studied both adult and larva.

The adult lives in African pythons and snakes (*Python sebæ*, *P. regius*, *Bitis nasicornis*, and *B. arietans*). The larval forms usually occur in *Proteles cristatus*, *Cynocephalus maimon*, and other monkeys; in *Erinaceus æthiopicus*, the African hedgehog; and in *Felis leo*, the lion.

Morphology.—Female 9 to 12 centimétres in length and 5 to 9 millimetres in breadth, with eighteen to twenty-two rings, each 1 to 2 millimetres in width. The cephalothorax extends from the anterior end of the body to the first body-ring, which is often very indistinct. Dorsally this region is convex, while ventrally it is concave, and carries the mouth, in front of which there are two papillæ, and on either side of which there are two hooks. Genital opening about 1 millimetre in front of the anus, which is terminal. Male 3 to 4·5 centimetres in length and 3 to 4 millimetres in breadth, with sixteen to seventeen rings. Genital opening in the middle of the ventral surface at the anterior end of the abdomen.

FIG. 353.—*Porocephalus armillatus* WYMAN: MALE, NATURAL SIZE.

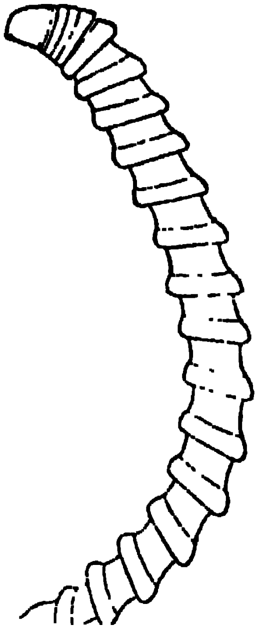


FIG. 354.—*Porocephalus armillatus* WYMAN: FEMALE, NATURAL SIZE.

(After Sambon.)

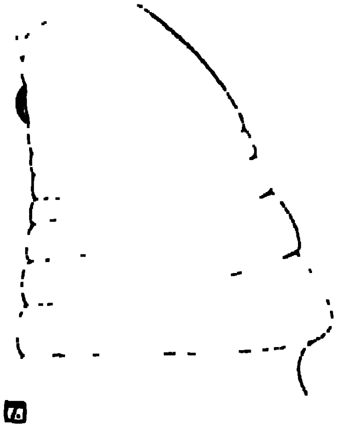


FIG. 355.—LATERAL ASPECT OF THE CEPHALOTHORAX OF *Porocephalus armillatus* WYMAN. (× 5.)

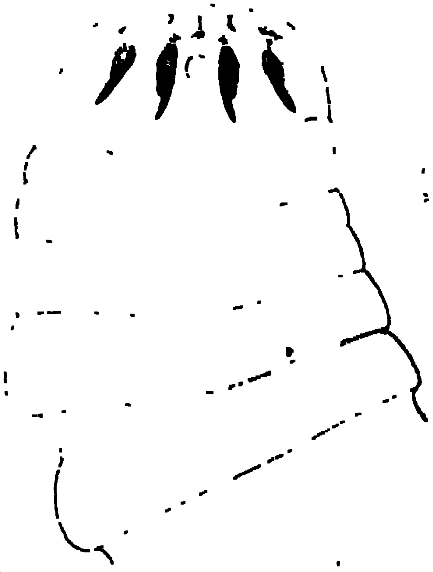


FIG. 356.—VENTRAL ASPECT OF THE CEPHALOTHORAX OF *Porocephalus armillatus* WYMAN. (× 5.)

(After Sambon.)

Life-History.—Probably this resembles that of *Linguatula serrata*, with the difference of hosts. In man the nymphæ are found not merely encysted in the lungs and liver, but moving freely through the peritoneal cavity and in the small intestine. Sambon considers that the eggs pass from the snake into water, and thence into animals and man while drinking, and become larvæ and nymphæ, which later gain access to the snake when the host is killed and eaten.

FIG. 357.—POSTERIOR END OF *Porocephalus armillatus* WYMAN. (× 5.) (After Sambon.)

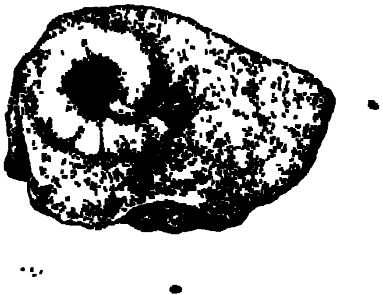


FIG. 358.—NYMPH OF *Porocephalus armillatus* WYMAN, ENCYSTED IN THE LIVER. (After Sambon, from our West African case.)

Pathogenicity.—This will be described later (Chapter LXXXIII.).

Porocephalus moniliformis Diesing, 1836.

Synonyms.—Adult.—*Pentastoma moniliforme* Diesing, 1835; *P. moniliforme* Leuckart, 1860; *Linguatula moniliforme* Mégnin, 1880; *Porocephalus moniliformis* Stiles, 1893. **Nymph.**—*Pentastomum tornatum* Creplin, 1849, *pro parte*; *P. aonycis* Macalister, 1874; *Porocephalus armillatus* Stiles, *pro parte*.

Porocephalus with twenty-six to thirty-one rings.

Remarks.—This parasite, which was discovered by Czermak in the lung of *Python molurus* Linnæus in 1828, and was first described by Diesing in 1835, has been carefully studied by Sambon, who remarks that it so strikingly resembles *P. armillatus* in general appearance and structure that at first sight it may be easily mistaken for it.

Morphology.—It is more slender, tapers more caudad; with twenty-six rings in the male and twenty-eight to thirty-one rings in the female. In fresh specimens it is bright lemon yellow in colour, with genital opening on the mid-ventral surface of the first body-ring in the male, and on the mid-ventral surface of the terminal body-cone 1 millimetre in front of the anus in the female. The anus is terminal.

Life-History.—The life-history is unknown.

Hosts.—The hosts of the adult are *Python molurus* Linnæus (the Indian python), *Python reticulatus* Schneider (the reticulated python), in which it lives in the lungs; while the hosts of the nymph are man, monkeys, tigers, leopards (?), civets, otters, and dogs (?).

Distribution.—India, Indo China, Southern China, the Philippines, Sumatra, Java.

Pathogenicity.—So far only two cases have been recorded in man—one at Djambi in Sumatra in 1906, when a nymph was found encysted beneath the serous coat of the small intestine of a Djambi native who died of dysentery, and the other was found in the liver of a native Filippino who died of tuberculosis. The liver in this latter case showed signs of atrophic cirrhosis.

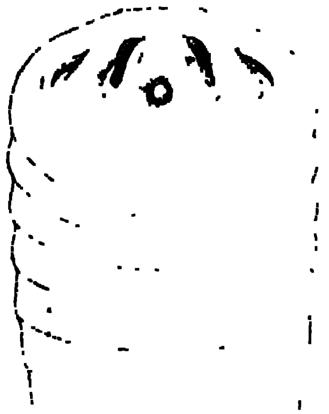


FIG. 359.—VENTRAL ASPECT OF THE CEPHALOTHORAX OF *Porocephalus moniliformis* DIESING, 1836. (× 5.)

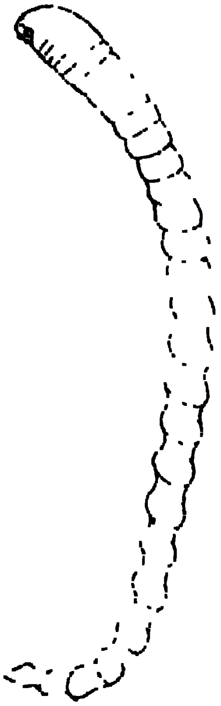


FIG. 360.—*Porocephalus moniliformis* DIESING, 1836: FEMALE, NATURAL SIZE.

(After Sambon.)

Species imperfectly described in Man.

In addition to the well-known cases of porocephalosis due to *Porocephalus armillatus* and *P. moniliformis*, there are the following cases to be discussed—viz., Welch's parasite, Osler's parasite, and Flint's parasite. Osler's parasite is considered to be doubtful, as it was passed *per urethram*, and might, according to Sambon, have been a sparganum.

Welch's Parasite.

In the *Lancet* of November 16, 1872, F. H. Welch had an article on 'The Presence of an Encysted Echinorhynchus in Man.' This parasite was damaged in extraction, and his drawing was not very instructive, but was sufficient to convince Cobbold, R. Blanchard, and Sambon that it represented a Linguatulid, and it shows two sets of hooks. The last-named observer comes to the conclusion that it may be either a very early nymph of *Porocephalus moniliformis* (provided with caducous accessory hooks), or it may be *P. najæ* Leuckart, 1860 (which is found in the abdominal muscles and peritoneum of the cobra), or *P. crociduræ* Parona, 1890 (found in *Crocidura fuliginosa*, a musk-shrew), or it may be a new species.

Porocephalus najæ Leuckart, 1860.

Synonym.—*P. najæ sputatricis* Leuckart, 1860.

Morphology.—Body imperfectly cylindrical, with about fifty rings. Length, 4·5 millimetres long by 0·6 millimetre broad.

Distribution.—Found in cysts in the abdominal muscles and peritoneum of the cobra.

Flint's Parasite.

Flint described the parasite at a meeting of the New York Pathological Society on December 12, 1876, as occurring in a man from Albany, Gentry County, Montana. This man had cavities in his lungs, and coughed up 75 to 100 parasites, which could crawl about the floor and could live for ten days in a bottle: moreover, they could resist freezing.

With regard to these parasites, which at the time were considered to be *Porocephalus armillatus* (*i.e.*, *Pentastomum constrictum*), Sambon points out that, if genuine Linguatulida, they can hardly belong to an African species, as the case occurred in America, and therefore he is inclined to believe that they must belong to *P. crotali* Humboldt, 1808, which are found as adults in *Crotalus adamanteus* Beauvois, *C. horridus* Linnæus, and *C. terrificus* Laurent, while the nymphæ have been found in *Marmosa murina* Linnæus, the murine opossum.

Porocephalus crotali Humboldt, 1808.

Synonyms.—*Echinorhynchus crotali* Humboldt, 1808: *Distoma crotali* Humboldt, 1808: *Distoma crotali durissi* Rudolphi, 1809: *Porocephalus crotali* Humboldt, 1811: *Polystoma proboscideum* Rudolphi, 1814: *Pentastoma proboscideum* Rudolphi, 1819; *Linguatula proboscidea* van Beneden, 1849, *pro parte*: *Porocephalus humboldti* Mayer, 1852: *Linguatula quadriuncinata* Mayer, 1852; *Porocephalus moniliformis* Mégnin, 1880, *pro parte*. **Nymph.**—*Pentastoma subcylindricum* Diesing, 1836.

Remarks.—This porocephalus was discovered by Humboldt in the lungs of the tropical rattlesnake.

Morphology.—When fresh, it is of a bright yellowish colour, with elongate, incurved, cylindrical body, somewhat flattened ventrally and club-shaped anteriorly, and is transversely encircled by over eighty flat bands. It is said to have an ovoid-shaped mouth on a line with the hooks, and two prominent papillæ.

Distribution.—It is thought to be coextensive in its distribution with the genus *Crotalus*—*i.e.*, the United States, Mexico, and Brazil.

Pathogenicity.—Possibly it is the cause of one form of porocephalosis in man.

CLASS IV. CRUSTACEA LAMARCK, 1815.

Aquatic Arthropoda which breathe by means of gills.

Crustaceans can hardly be considered as human parasites, for they have very rarely occurred as such—*e.g.*, *Caligus curtus* in the cornea, and *Gammarus pulex* in the stomach.

ORDER COPEPODA Latreille, 1831.

It must, however, be remembered that the Copepoda are of importance, because a species of *Cyclops* has been found to be the intermediary host of *Dracunculus medinensis* the guinea-worm. An excellent paper on the species found on the Gold Coast is contributed by Graham to vol. i. of the 'Annals of Tropical Medicine and Parasitology.' The Cyclops live in fresh water in any ditch, pond, or well

Prophylaxis.—It is recommended to treat a well with sufficient quicklime to render the water suddenly hot in order to kill these crustaceans. The well must, of course, be closed for some time after this proceeding, until the percentage of lime has diminished to reasonable proportions. A simpler remedy is to boil all water before drinking It has been also suggested to add 1 pound of caustic soda to 180 gallons of water 0·07 per cent. for the same purpose. Leiper's recommendation is, however, the best, and this is to raise the temperature of the well water to 65° C by blowing in steam, as he finds that all Cyclops die if the water is raised to 65° C. He calculates that it requires 87 gallons of water as steam to raise 1,000 gallons of water from 15° to 65° C., and that this requires 1 pound of coal or its equivalent in oil per gallon of water, and that for every square foot of grate 15 pounds of coal can be burnt per hour, so that if the grate is 1 square foot it will require 5·8 hours to raise 87 gallons of water as steam *i.e.*, 12 square feet of grate give 90 gallons of water as steam in half an hour.

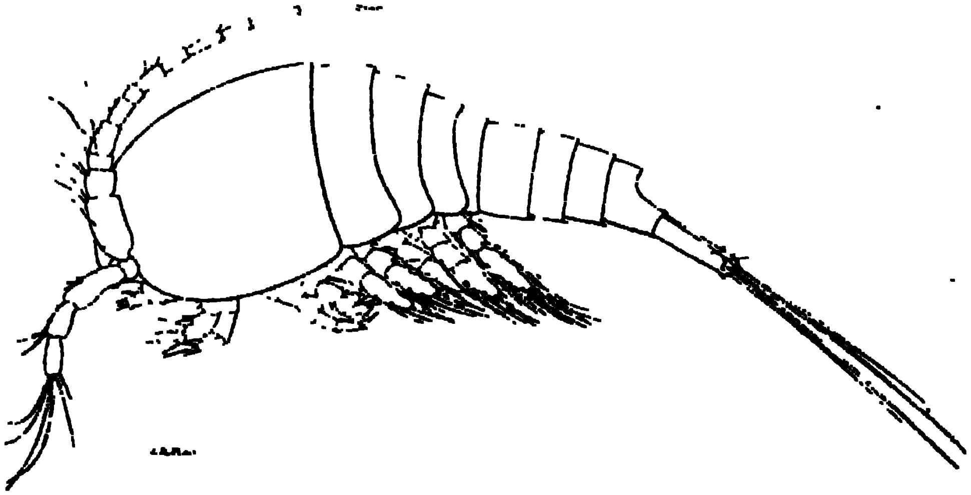


FIG. 301. CYCLOPS SP. (?).

CLASS V. CHILOPODA LATREILLE, 1837.

Arthropoda with three prosthomeres. The first post-oral somite is the mandibular; the second and third post-oral somites carry the maxillæ, while the fourth has its appendages converted into very large powerful jaws, which are provided with poison-glands. The remaining somites carry single-clawed

walking-legs, one pair to each somite. Body anomomeristic, showing from 17 to 175 somites behind that which carries the poison glands. They breathe by tracheæ, and the genital ducts open on the penultimate somites.

Family 1: Scolopendridæ.
Family 2: Lithobiidæ.
Family 3: Scutigeridæ.

Family 1: Scolopendridæ Leach, 1812.

Chilopoda with antennæ, possessing few joints, and with few ocelli.

Geophilus carpophagus Leach, *G. electricus* Linnæus, *G. cephalicus* Wood, *G. similis* Leach, have been found as accidental parasites about nineteen times in the nasal cavities and their neighbouring sinuses in man in Europe. *G. electricus* Linnæus has been found in the alimentary canal about four times.

Family 2. Lithobiidæ Newport 1844.

Chilopoda with many-jointed antennæ, numerous ocelli.

Lithobius forficatus L. and *L. melanops* have been found in the nasal cavities in three cases in man.

Family 3. Scutigeridæ Gervais, 1837.

Chilopoda with antennæ at least as long as the body and faceted eyes instead of ocelli.

Scutigera coleoptrata has been found in the alimentary canal.

Other species found in the alimentary canal are: *Chætechelyne vesuviana* Newport (found also in the nasal cavities), *Himantarium gervaisi*, *Stigmatogaster subterraneus*.

Pathogenicity.— In the nose these parasites cause inflammation with, at times, no flow of mucus, and at others a large discharge of it, associated with headache, which is generally more or less continuous, but may show remissions. In addition to these local symptoms general symptoms such as convulsions, anginiform attacks, dyspnœa, etc., may be induced through irritation of the fifth nerve. There is no evidence that these parasites cause any of the symptoms by their venom. They are generally expelled in attacks of sneezing, or spontaneously. The best methods of making them leave the nostrils are applications of snuff, eau de Cologne, or turpentine; but in some instances it will be necessary to open a sinus—*e.g.*, the frontal sinus—by surgical means in order to remove the parasite.

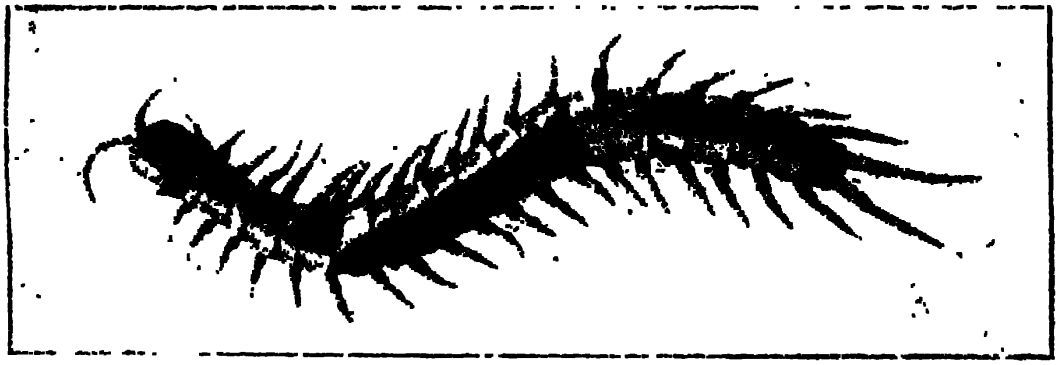


Fig. 302.—Scolopendra Species (?)
(This is a very common species in Ceylon.)

In the alimentary canal the symptoms will give rise to the suspicion of helminthiasis. They are—pain in the abdomen, cramp, nausea, vomiting, and reflex nervous symptoms.

Treatment does not appear very satisfactory.

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CHAPTER XXIX

THE HEXAPODA

Synonym—Remarks—Morphology—Internal anatomy—Life-history—Habits—Enemies—Pathogenicity—Collection—Classification—References.

Synonym.—*Insecta.*—Arthropoda breathing by means of tracheæ, with antennæ on the head, three pairs of legs, and usually two pairs of wings on the thorax, which is composed of three segments. Abdomen with generally nine apparent segments.

Remarks.—The Hexapoda, or insects, are known to be of the utmost importance in the spread of disease, for the researches of Manson, Ross, Grassi, and others have shown that they are agents in the propagation of the parasites of filariasis, malaria, and other diseases.

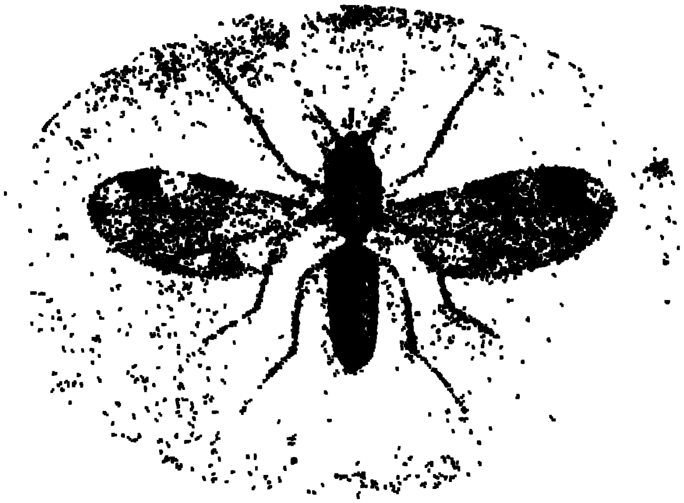

FIG. 363.—*Culicoides brucei*, A TYPICAL DIPTEROUS INSECT. (From a photograph by J. J. Bell.)

Morphology.—The body is distinctly divided into head, thorax, and abdomen. The head is composed of the fusion of about six segments, which are the ocular, antennal, intercalary (probably homologous with the second antennal segment of the Crustacea), mandibular, maxillary, and labial; but whether the hypopharynx represents a seventh segment or not is doubtful. The head carries, in addition to the eyes, four pairs of appendages, one for each somite or segment, except the intercalary segment, which is pre-mandibular. These appendages are the antennæ, the mandibles, the maxillæ, to which are attached palpi called the maxillary palps, and a second pair of maxillæ usually fused to form the lower lip or labium, which generally carries a pair of labial palps.

The exoskeleton of the head is composed of sclerites—that is to say, more densely chitinized regions of the integument—which are: (1) The clypeus; (2) the epicranium; (3) the gula.

The clypeus is the sclerite situate on the anterior portion of the dorsal surface, and carrying the labrum; in flies it is often called the face.

The epicranium is the larger part of the head, and may be subdivided into an anterior frons and a posterior occiput. The genæ form the sides of the head, meeting the epicranium and the gula at the occipital foramen.

The gula is the sclerite in the median ventral line which carries the basal part of the labium called the submentum. There is no exoskeleton at the posterior part of the head ventral to the occipital region, which thus forms a foramen in the hard tissues called the occipital foramen, through which the soft structures of the head communicate with those of the thorax.

The antennæ appear to be sensory organs, and the mandibles to vary in structure according as to whether the mouth is to be used for biting or sucking. In the former case they are broad and strong, while in the latter they are styliform. The first pair of maxillæ, similarly, may be broad, strong organs or styliform organs.

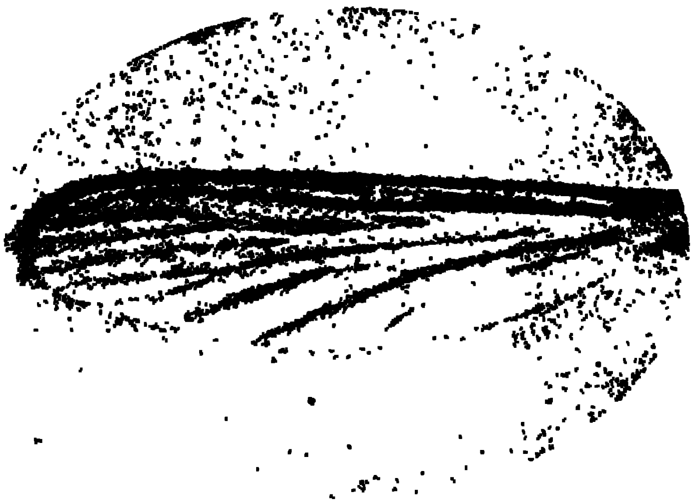

FIG. 304. WING OF A MOSQUITO TO ILLUSTRATE THE VENATION. (From a photograph by [illegible] Bell.)

In addition to these appendages the mouth shows an upper lip or labrum, which is simply a sclerite attached to the cephalic shield, and may have a median projection from its internal surface called the epipharynx, while the labium has a similar one called the hypopharynx. Thus the mouth parts of an insect may be very complicated, with labrum and epipharynx, mandibles, maxillæ, and maxillary palps, labium, and hypopharynx.

The thorax is joined to the head by a neck, and is subdivided into three segments—prothorax, mesothorax, and metathorax. These somites are by no means simple horny rings, but have their chitinous exoskeleton split up into hard pieces joined together by soft material. The hard pieces are a dorsal plate called 'the notum' a ventral plate called 'the sternum,' and lateral plates called 'pleura.' Further the terms, 'pro,' 'meso,' and 'meta,' are applied to these, indicating the region to which they belong—'pronotum,' 'mesonotum,' and 'metanotum'; 'pro-,' 'meso-,' and 'metasternum'—while each pleuron is divided into an anterior episternum and a posterior epimeron. According to Audouin, a typical thoracic segment should have a notum composed of præscutum, scutum, scutellum, and post-scutellum, but all these parts are seldom seen.

Each somite of the thorax carries a pair of jointed walking-legs, in which the segments or articles are named coxa, trochanter, femur, tibia, and tarsus (consisting of several joints, the first joint of which is sometimes called the metatarsus); some authorities have caused much confusion by calling the first tarsal joint the metatarsus, and the real second tarsal joint the first tarsal joint, and so on. The last tarsal joint is terminated by claws or ungues, between which other appendages called empodia and pulvilli are to be found, as will be explained later.

Typically, the mesothorax and the metathorax should each carry a pair of wings. These are transparent and strengthened by nervures, ribs, or veins, which are chitinous canals containing blood-spaces, nerves, and tracheæ. The areas between the nervures are called cells. The wings, however, become much modified in the different orders, and may be entirely absent. The arrangement of the nervures in the wing is called the 'venation,' and has been restudied by Comstock and Needham, who find that the primitive type is composed of two main tracheal branches, an anterior and a posterior. The anterior breaks up at the base of the wing into four longitudinal branches—the costa, subcosta, radius, and media—while the posterior has also four branches, of which the first is called the cubitus, and may be subdivided into two; and the other three are simple and are called the anal veins—first, second, and third. The costal vein is unbranched, and runs along the anterior margin of the wing. The subcostal vein typically divides into two branches, the radial vein into five branches, and the median into four

This primitive type is altered by atrophy or coalescence, leading to the reduction of the veins. The latter may take place from the base towards the tip, or from the tip towards the base of the wing, called outward and inward coalescence respectively. The wing cells may be named as follows.—

1. Costal Cell between the Costa and the Subcosta
2. Mediastinal, between the Subcosta and the Radius
3. Marginal, between Radius 1 and Radius 2.
4. First Submarginal, between Radius 2 and Radius 3.
5. Second Submarginal between Radius 3 and Radius 4
6. Third Submarginal, between Radius 4 and Radius 5
7. First Posterior, between Radius 5 and Media 1
8. Second Posterior between Media 1 and Media 2.
9. Third Posterior, between Media 2 and Media 3.
10. Fourth Posterior, between Media 3 and Media 4.
11. Fifth Posterior, between Media 4 and Media 5.
12. Sixth Posterior between Media 5 and Cubitus 1.
13. Seventh Posterior, between Cubitus 1 and Cubitus 2
14. First Anal, between Cubitus 2 and Anal 1
15. Second Anal between Anal 1 and Anal 2
16. Axillary between Anal 2 and Anal 3.
17. Spurious Cell, behind Anal 3

But all these cells are not present in any one given type of wing, owing to coalescence of the nervures, and hence the arrangement of the cells is different. Besides this, the venation is complicated by the presence of transverse veins, as will be explained later; moreover, wings may be absent, as in the lice.

The abdomen usually consists of ten somites, without appendages, composed of dorsal and ventral plates connected together and to preceding and succeeding segments by soft membranes. The posterior segments are often modified with reference to reproduction, possessing claspers in the male, and ovipositors in the female. The anal opening is on the last abdominal segment, and the reproductive aperture on the penultimate segment.

Internal Anatomy.—The mouth lies between the labrum above and the labium below, and leads into an oral cavity.

The salivary glands in most of the genera which we have to consider are well developed, and are, as a rule, not connected with the mouth, but open into a common duct which communicates with a groove or canal on the hypopharynx, and so opens near the tip of the proboscis

From the mouth a pharynx leads through an œsophagus, with a dilatation called the crop, into a proventriculus or masticatory stomach, which latter communicates with the mesenteron or chylific ventricle, whose juncture with the intestine is defined by the openings of the cæcal Malpighian tubules. This is an important landmark, defining where the stomach ends and the intestine begins. The intestine is subdivided into small intestine, colon or large intestine, and rectum. The last-mentioned may possess rectal glands, while anal glands may open into the rectum just in front of the anus, and are useful to the insect by forming the secretion which gives rise to repulsive odours.

With regard to the proventriculus, it should really be a powerful muscular organ lined with chitin, and possessing teeth, bristles, etc., but in the Diptera it will be found to be much degenerated. The Malpighian tubules, which number from four to six, are excretory in function. The alimentary canal possesses longitudinal and transverse muscular coats and a lining of epithelial cells.

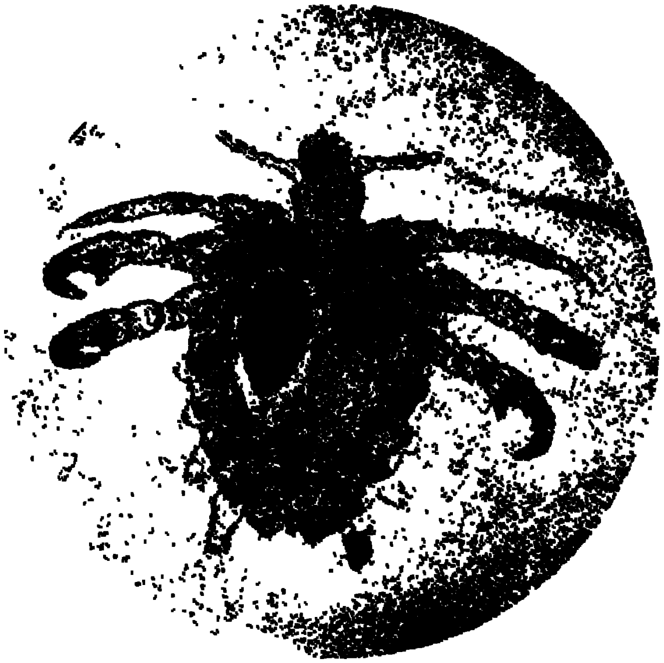

FIG. 305.—*Phthirius pubis* LINNÆUS, 1758, TO ILLUSTRATE AN INSECT WITHOUT WINGS.
(From a photograph by J. J. Bell.)

The stigmata or openings of the respiratory system are situate on the membranes, on the side of the body in the thorax and abdomen, and are very varied in number. They are never to be found on the head or on the last abdominal segment. From the stigmata the tracheæ, or air-tubes, ramify all over the body. These tracheæ are kept open by spiral thickenings of the chitinous lining membrane.

The fat-bodies are lobulated masses packed beneath the skin and between the organs, and are supposed not merely to represent reserve material, but to be of great importance in metabolism.

The circulatory system consists of a dorsal longitudinal vessel divided into chambers, which pulsate, and an anterior aorta, from which blood flows freely into the cœlom or body cavity. From this it returns to the heart by two lateral vessels and one dorsal and one ventral vessel. The blood is colourless, and contains amœboid cells.

As already mentioned, some insects possess poison glands.

The nervous system and sense organs will not be described here, as they are not of importance in tropical medicine.

The male reproductive organs consist of testes, vasa deferentia, ductus ejaculatorius, and an external copulatory organ. The female reproductive organs are two ovaries, which consist of a series of egg-tubes, and oviducts, which are united together to form the single oviduct, the lower portion of which is a vagina. This receives the cement glands and the sebaceous glands, which provide the secretion for gluing the eggs together, and the receptaculum seminis, beneath which is the bursa copulatrix, which is sometimes separated from the vagina.

Life-History.—This is very varied. In general terms the spermatozoa, bound into bundles of spermatophores, are introduced by the external copulatory organ, which, when protruded, is surrounded by the claspers in the form of a sheath, into the bursa copulatrix. The ovum, starting from the terminal portion of the ovarian tube, obtains, as it passes downwards, its food-yolk and its shell or membrane, the chorion, which has a small gap, the micropyle. On arrival at the junction of the oviduct and the spermatheca, or receptaculum seminis, the spermatozoa enter via the micropyle, and fertilize the egg. These eggs may be strung together, as they are laid, into masses by means of the sebaceous secretion mentioned above. The egg may develop directly into the adult, but this is only in the lowest forms. Usually the egg develops into a larva, which becomes a nymph or pupa, and thus into an adult, often called the 'imago.' This series of changes is called a metamorphosis. The pupa may present three forms:

1. *The free pupa*, with appendages free.
2. *The obtect pupa*, with appendages and body bound together.
3. *The coarctate pupa*, in which the pupa is contained in a puparium formed from the larval skin.

The larva is a most vigorous feeder, but the pupa does not take nourishment as a rule, though there are marked exceptions, especially among the Rhynchota and Siphunculata.

Habits.—We are mainly concerned with the predatory or blood-sucking insects. As a rule, only the female sucks blood, which, apparently, it does with a view of obtaining rich nourishment for its eggs. It is this habit which makes these insects of importance in tropical medicine, because not merely does it cause irritation by the introduction of secretions from the insects' salivary glands and mouth (alimentary canal), but also leads to the introduction into the victim of the germs of disease. Again, as we shall see later, larvæ are apt to become parasitic in man and animals, and in this way cause disease.

Enemies.—Insects and their larvæ have many enemies in birds, reptiles, fish, and other insects. Cannibalism is also met with, especially among mosquito larvæ.

Pathogenicity.—The principal disease-spreading insects are the Diptera—for example, the *Anophelinæ* disseminate malaria, the genus *Stegomyia* yellow fever, and the genus *Culex* filariasis, and perhaps dengue fever. Some species of *Glossina* are responsible for the African trypanosomiases, while they and other flies spread the animal trypanosomiases.

In addition, the common house-fly is an important factor in the dissemination of typhoid and perhaps dysentery in tropical countries. Fleas are now known to be the spreaders of plague, and bugs perhaps of some of the relapsing fevers. This is a sufficient list of ills to commend insects and their habits to the serious notice of the medical practitioner of the tropics.

How to Collect Blood-Sucking Flies.—Mr. Austen, of the British Museum (Natural History), has informed us that he will be pleased to send anyone, on application, a pamphlet giving full directions as to the collection and preservation of blood-sucking flies.

Classification.—The Hexapoda are classified into the following orders:—

1. Aptera.
2. Neuroptera.
3. Orthoptera.
4. Mallophaga.
5. Thysanoptera.
6. Hemiptera.
7. Anoplura.
8. Diptera.
9. Lepidoptera.
10. Hymenoptera.
11. Siphonaptera.
12. Coleoptera.

But the only orders which contain species important as spreaders of disease or as human parasites are—

1. Anoplura.
2. Mallophaga.
3. Hemiptera.
4. Diptera.
5. Siphonaptera.
6. Coleoptera.

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The *Annals and Magazine of Natural History*, *Parasitology*, and the *Journal of Parasitology*, *Deutsche Entomologische Zeitschrift*, Transactions of the Entomological Society of London, *Entomologische Zeitung*, *Entomologisch Nachrichten*, *Entomologists' Annual*, *Entomologists' Monthly Magazine*, *Bulletin della Società Entomologica Italiana*, *Annales de la Société Entomologique d. France*. Wystsman's 'Genera Insectorum' is perhaps the most useful; i started in 1902, and is still being reproduced. See also the *Tijdschrift voo Entomologie* and the *Revue Entomologique*.

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CHAPTER XXX

MALLOPHAGA AND ANOPLURA (LICE)

General remarks—Mallophaga—Anoplura—Pediculidæ—Pediculinæ—Hæmatopinidæ—References.

GENERAL REMARKS

THE *wingless* insects which occur as ectoparasites on mammals belong as a rule to the *Mallophaga* and the *Anoplura*, when they are generally called 'lice,' or to the *Siphonaptera*, when they are called fleas, while some few belong to the *Pupipara*.

The Mallophaga (biting lice) and Anoplura (sucking lice), however, differ from the Siphonaptera (fleas), in that in the former the whole of the life-history is spent upon the vertebrate host, while in the latter the larvæ live in soil or in protected areas in houses. Moreover, the fleas can change from one host species to another, while the lice have an extraordinary limitation, as they may spend generations on individual hosts, and generally only change from one host to another of the same species by actual contact, and as a rule die in a few days if separated from a host or if a host dies.

This limitation to one given species of host has been ably demonstrated by Kellogg, who has pointed out that it explains many of the curious features of their evolution.

Kellogg and Mjoberg believe that the Mallophaga and the Anoplura are fairly closely related to one another. They think that it is possible that the Mallophaga are the more primitive, especially as no Anoplura are known on marsupials, while Mallophaga are present, which they think points to the possibility of these mammals being older than the sucking lice, especially as the known genera of two-clawed Mallophaga found on mammals are limited to marsupials, while the two-clawed condition is common to the Hexapoda generally, while all the Anoplura found on mammals are one-clawed.

It is possible that the ancestors of the Mallophaga may have been related to the ancestors of the book louse (*Atropos divinatoria*), which belongs to the Psocidæ, a family of the Neuroptera, there being perhaps a common psocid-mallophagan ancestor, from which, by process of evolution, the Psocidæ and the Mallophaga, and later the Anoplura, were evolved. The difference in the mouth parts of the Mallophaga and Anoplura is looked upon as being adoptive rather than palegenetic in character.

The relationship of the Psocidæ to the Mallophaga lies in the common external and internal characters, as well as in their habits, and more especially in a very curious pharyngeal sclerite, which is thought to be a modified hypopharynx, which is found in both these groups and nowhere else in the Hexapoda.

Once started on their evolution, the Mallophaga have been influenced mainly by the fact that they live in a sort of 'island isolation' on given species. This condition of life, which is exactly similar for many different species, is suitable for the production of many varieties of one and the same species, and hence the description of a given species has to be of a very flexible character, but it is opposed to the production of those more distinctive differences which are utilized to make genera and families.

Hence, although in these orders the varieties and species may be many, the genera and families are but few in number. Thus, for example, in the *Mallophaga* there are about 1,500 known species grouped into 27 genera, 4 families, and 2 suborders.

The important difference between the Mallophaga and the Anoplura is that the former have a masticatory mouth, while the latter have a sucking mouth.

ORDER MALLOPHAGA Nitzsch, 1818.

Synonyms. *Mandibulata* De Geer, 1778, *Ricinidæ*.

Nomenclature. The name Mallophaga is derived from μαλλός, wool, and φαγειν, to eat.

Definition. Hexapoda usually of small size, wingless, provided with biting mouth parts and with simple incomplete metamorphosis. Habitat, epizoic parasites on birds and mammals.

Historical.—The first descriptions and illustrations of these animals are to be found in Redi's 'Esperienze intorno alla Generazione degl' Insetti,' published in Florence in 1668, where the illustration on Plate 2, called 'Pollino de Piccion Grosso,' is the same as Linnæus' *Pediculus columbæ*, or pigeon louse, and Nitzsch's *Lipeurus baculus*, a name by which it is still known, while the figure termed 'Pollino dell' Arzevola o Lonquetola' on Plate 12 is the same as Nitzsch's *Trinoton luridum*, the duck louse. Linnæus classified all these bird lice under the generic term of 'Pediculus,' from which they were separated by De Geer, in 1778, under the term 'Ricinus,' because their masticatory mouth, enabling them to eat pieces of skin, hairs, and feathers, distinguished them from the blood-sucking species, for which the name 'Pediculus' was retained.

The name 'Ricinus' was changed into 'Nirmus' by Hermann in 1804, while the whole of the species known at the time were classified and named by Nitzsch in 1818, since which date our knowledge of these parasites has been increased by Denny in 1842, Giebel in 1874, Piaget in 1880 and 1885, Taschenberg in 1882, Kellogg in 1908, 1913, and 1914, as well as by many other observers whose papers may be found in the *Bulletin of Entomological Research* and in the *Annals and Magazine of Natural History*. To all these works the reader is referred for a fuller knowledge of these interesting parasites than that which can be given in the present work.

Morphology. The Mallophaga vary in size from 1·5 to 10 mm., and from 1-2 mm. in breadth, but the majority are small, about 2·5 millimetres in length. The body is strongly chitinized, smooth, wingless, and flattened dorso-ventrally. The mouth parts are of the biting type, with well-developed mandibles, and in some species the labial palps are easily seen. The eyes are represented by a single pair of ocelli placed at the lateral margins of the head. The antennæ are 3-5 segmented, and may be concealed in a groove, or the ventral aspect of the cheeks, or may be exposed.

The prothorax is distinct, but the meso- and meta-thoraces are sometimes united, and may also be with difficulty differentiated from the abdominal segments. The legs are flattened, long, and strong, and end in one or two claws.

The body varies in colour, being whitish, pale brownish, or dark brown in colour, and marked by darker spots and bands, which are caused by chitinization.

The pharyngeal sclerite may be present or absent, as may be the accompanying glands; the crop may be simple or have a sac-like diverticulum. Ingluvial glands may be present or absent, and the testes may number four to six and the egg tubes three to five.

Life-History.—Owing to the fact that these parasites die in a few hours to seven days if removed from the body of the host, and also in a few days if the host which they do not leave is killed or dies, the life-story of not a single species has so far been completely worked out. It is, however, known that the eggs are fastened to the hairs or feathers of the host, and that the young when hatched are like the parents, but smaller, paler, and without characteristic skin markings; they attain their adult characters without metamorphosis.

They run freely about the host, feed upon hairs and feathers, and very rarely upon dried blood, and usually pass from bird to bird or animal to animal by contact, being rarely found away from the host, which they probably slightly irritate, because birds are seen to be constantly cleaning their feathers. They have been found to be parasitic on about 100 species of mammals, representing 48 genera, 24 families, and 5 orders, and 1,100 bird species, or 33 orders of birds out of a total of 35 orders.

Classification. The principal factor which has influenced the evolution of this curious group of animals is isolation, each host being, according to Kellogg, like a small island, so that each species is made up of many dislocated small groups, and this is why each species has to be given a very flexible description, and why many varieties might be made from one species. This condition of life is opposed to producing larger variations which might be used to make genera and families, and the life conditions of many of the species are very similar. Hence varietal specific distinctions are many, and generic and family few.

Hence some 1,500 species are known which can be divided into two suborders, each 4 families and 27 genera. The mammalia-infesting families are only two in number, the Gyropidæ and Trichodechitidæ, characterized by having two-clawed members, and each of those families by only one genus. The bird-infesting families are also two in number, and have respectively 15 and 10 genera.

The following table gives the differentiation of the suborders' families:—

SUBORDER 1: ISCHNOCERA Kellogg, 1896.

Antennæ exposed, filiform, three- or five-segmented; no maxillary palpi, mandibles vertical, crop with sac-like diverticula; ingluvial glands present, testes four, egg tubes five.

A. Antennæ three-jointed, tarsi one claw. Habitat, mammals—*Trichodectidæ.*

B. Antennæ five-jointed, tarsi two claws. Habitat, birds—*Philopteridæ.*

SUBORDER 2. AMBYCERA Kellogg, 1896

Antennæ concealed, clavate or capitate, four-segmented, maxillary palpi present, mandibles horizontal, crop single; ingluvial glands absent, testes six, egg tubes three to five.

A. Tarsi with one claw. Habitat, mammals—*Gyropidæ.*

B. Tarsi with two claws. Habitat, birds—*Liotheidæ.*

The genera parasitic on mammals may be recognized as follows:—

SUBORDER ISCHNOCERA Kellogg, 1896

Family Trichodectidæ Burmeister 1835

This family contains only one genus, *Trichodectes* Nitzsch, 1818, which is parasitic on mammals and has tarsi with only one claw.

SUBORDER AMBYCERA Kellogg 1896.

Family Gyropidæ Burmeister, 1835.

This family contains only one genus, *Gyropus* Nitzsch, 1818, parasitic on mammals and with tarsi armed with only one claw.

ORDER ANOPLURA Leach, 1815.

Synonyms.—*Pediculina* Burmeister, 1835; *Siphunculata* Meinert, 1891; *Pseudorhynchota* Cholodkowsky, 1903; *Lipognatha* Börner, 1904; *Ellipoptera* Shipley, 1904.

Definition.—Hexapoda with labrum and labium joined together to form a rostrum or proboscis, which is armed with recurved hooklets, and contains a hollow extensile sucker formed by the mandibles and maxillæ. Eyes without facets. Antennæ five-jointed. Thorax with little traces of segmentation. Wings absent. Legs with hook-like terminal joints, suitable for clinging. Last abdominal segment rounded in male, notched in female. Metamorphosis incomplete. Habitat, epizoic on mammals.

Historical. The sucking lice were known to the ancients, for Aristotle was acquainted with the pubic louse, while references can be found in the works of Theophrastus, Dioscurides, Galen, and Pliny.

The more modern writers are Moffat, 1634, Camerarius, 1652, Redi, 1668, Leeuwenhoek, 1697, and Swammerdamm in 1737, several of whom give excellent figures of these parasites.

In 1758 Linnæus, in his 'Systema Naturæ,' gathered a heterogeneous collection of species, including some of Mallophaga and Anoplura, in his genus Pediculus; and in 1815 Leach gave the more commonly used name to the order, which included the Mallophaga as well as the sucking lice.

We have already seen how the species of Mallophaga were separated from this composite genus Pediculus, and it now remains to point out that Leach in 1815 created the genera *Phthirius* for *Pediculus pubis* and *Hæmatopinus* for *Pediculus vituli*, *P. asini*, and *P. suis*.

Later important investigations were made by Nitzsch, 1818, Burmeister, 1835, Denny, 1842, Giebel 1874, Piaget, 1880, and especially by Enderlein in his 'Lause Studien,' published in 1904, and by Della Torre in 1908.

We have seen that Mjoberg and Kellogg consider that the Anoplura are derived from ancestors common to them and the Mallophaga, being separated by the alterations induced by sucking blood.

Morphology.—The anatomy will be dealt with under the heading Pediculidæ, and need not detain us here, except to invite attention to the characters of the mouth parts, which are so modified as to form a sucking mouth, while the pharynx performs the rôle of a sucking pump.

Classification. The order is divided into four families, some of which are capable of being subdivided into subfamilies. The number of genera is 15, and the known species are about 100, which are all parasitic on mammals.

The following table, taken from Della Torre, enables the families to be differentiated:—

A. Head not prolonged into a nozzle-like projection. Antennæ three to five segments. Tibia with a thumb-like process. Tibia and tarsus very short and thick. Legs clinging in character.

  I. Body flattened. Mesothorax and three to eight abdominal segments, with stigmata. Antenna three to five segments. Tibia with thumb-like process.

(*a*) Head broader than thorax. Eyes large pigmented. Pharynx short and broad. Proboscis short and pressed against thorax—*Pediculidæ* Leach, 1815.

(*b*) Eyes very small or absent. Pharynx long and narrow. Proboscis very long—*Hæmatopinidæ* Enderlein, 1904.

II. Body thick and heavy. Mesothorax, metathorax, and two to eight abdominal segments, with stigmata. Eyes absent. Back part of the head widened backwards. Antennæ four to five segments. Tibia with short strong thumb-like process. Thick short spines on the body. Female gonopodia elongated and narrow—*Echinophthiridæ* Enderlein, 1904.

B. Head prolonged into a nozzle-like projection, at the anterior end of which lies the mouth opening. Antennæ five segments. Tibia without thumb-like process. Tibia and tarsus very long and thin. Legs not clinging in character—*Hæmatomyzidæ* Enderlein, 1904.

FAMILY I: PEDICULIDÆ Leach, 1815.

Definition.—Anoplura with flattened body, and head not prolonged anteriorly into a nozzle-like projection, with large prominent, pigmented eyes, three to five jointed antennæ, and short proboscis. Pharynx short and broad. Paroglossæ (fulturæ) very strong and broad, with broad arms. Stigmata on mesothorax and third to eighth abdominal segments. Legs suitable for clinging. Tibia and tarsus thick. Tibia with a thumb-like process.

Remarks.—The Pediculidæ are found all over the world, on man as well as on animals. They cause much irritation by their bites, which may become infected, causing impetigo. Apart from this, however, they have recently been suspected of spreading blood-parasites—*e.g.*, *Trypanosoma lewisi* and *Hæmogregarina gerbilli*—which are believed to undergo development in them; and, in addition, they contain parasites peculiar to themselves—*e.g.*, *Herpetomonas pediculi*.

Morphology.—The head is usually clearly defined, but the thorax may or may not be so well defined from the abdomen. Eyes may be present or absent—a fact which appears to depend upon whether the host is nocturnal or not in its habits. The antennæ are usually five jointed. The mouth consists of a proboscis, composed of labrum and labium, which is armed with recurved booklets, and contains the maxillæ and mandibles, which take the form of a suctorial tube. The thoracic segments are fused together. The thorax may be as broad as the abdomen, or narrower. There are no wings. The legs have four segments, of which the terminal one carries a strongly curved claw. The abdomen has, if statements can be trusted, a various number of segments, differing in the different genera.

The last segment in the female has a slit-like opening guarded by two chitinous plates, while in the male there is in the same situation a horny papilla surrounded by spines.

Internal Anatomy.—Christophers and Newstead have studied the anatomy of *Hæmatopinus stephensi* Christophers and Newstead, 1906, parasitic on *Gerbillus indicus* (the Indian field-rat).[1]

The alimentary canal consists of a mouth followed by a chitinous pharyngeal pump into which the ducts of the salivary glands open, and an œsophagus which leads into the mid-gut. This second part of the canal consists of two portions of which the first appears to be a crop and the second a chylific ventricle. There are four Malpighian tubules. The intestine shows no differentiation into small and large. The rectum is globular, with a distended posterior portion containing the rectal papillæ. The fat-body is well developed. The female generative organs consist of two ovaries with oviducts. Each ovary consists of five to six follicular tubes. The two oviducts unite into a common duct, and there is a spermatheca. The male organs are testes, vasa deferentia, vesiculæ seminales, and penis.

Life-History.—The ova, which are attached to the hairs of the host, give rise larvæ, which closely resemble the adults

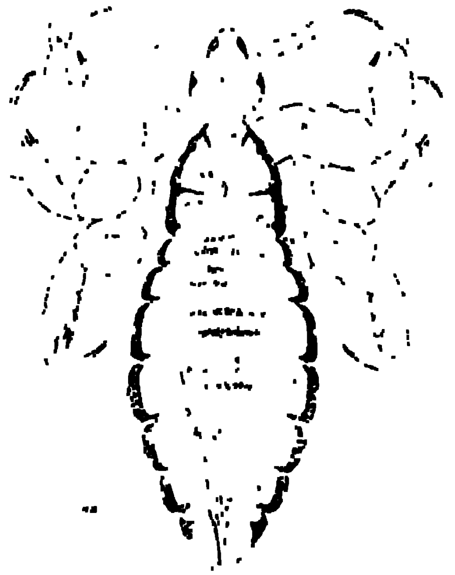

FIG. 306.—*Pediculus humanus* L.: MALE. (× 25.)

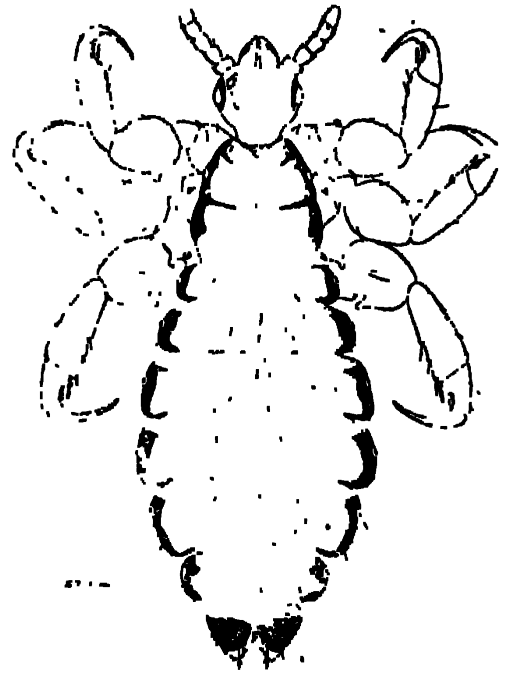

FIG. 307.—*Pediculus humanus* L.: FEMALE (× 25.)

Pathogenicity.—Lice are important carriers of disease, being vectors in certain forms of relapsing fever, in typhus, and in trench fever, etc.

Classification.—The Pediculidæ are subdivided into two subfamilies, which may be recognized as follows:—

A. *Pediculidæ* with five-jointed antennæ—*Pediculinæ*.
B. *Pediculidæ* with three-jointed antennæ—*Pedicinæ*.

SUBFAMILY A: PEDICULINÆ Enderlein, 1904.

Definition.—Pediculidæ with five-jointed antennæ.

Classification.—The Pediculinæ contain two genera, both of which are parasitic on man, and which may be differentiated as follows:—

(*a*) All legs strong, distinct neck, thorax narrower than abdomen—*Pediculus*.
(*b*) Forelegs long, slender, with three claws; no neck; thorax broader than abdomen—*Phthirius*.

Genus Pediculus Linnæus, 1758.

Definition.—Pediculinæ with distinct neck and thorax narrower than abdomen. Legs all strong with strong claws. Thumb-like projection of the tibia long, thin, and covered with bristles. Abdomen long and narrow, with segments not compressed together, and without lateral hook-like processes on the fifth to eighth segments. Two-jointed telson carries ventrally a pair of cone-like processes. Female gonopodia clamp-like and bent inwards.

Classification.—Only four species are at present assigned to the genus Pediculus:—

P. humanus Linnæus, 1758, found on man
P. corporis de Geer, 1778, found on man.
P. punctatus Rudow, 1869, found on *Bos grunniens*.
P. consobrinus Piaget, 1880, found on *Ateles pentadactylus*.

There is a doubt as to whether *P. punctatus* is really a pediculus, and *P. consobrinus* is said by Neumann to be indistinguishable from *P. humanus*, therefore the species are reduced to two:—

P. humanus Linnæus, 1758.
P. corporis de Geer, 1778

These are very alike, and have been thought to be only varieties of one another. Interbreeding seems to be possible. The following points may help to differentiate them

1. Found on the human head, with well-defined abdominal segments marked by a festooned lateral border—*P. humanus*.
2. Found in the clothing, larger than *P. humanus*, with broader thorax and lateral borders of abdomen less festooned, and segments not quite so distinctly indicated—*P. corporis*.

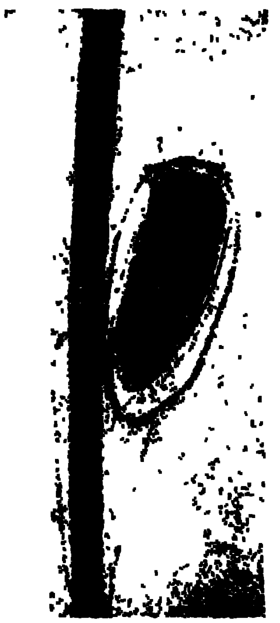

FIG. 308.—EGG OF *Pediculus humanus* LINNÆUS, 1758. ATTACHED TO A HAIR. (× 35 DIAMETERS.)

(From a photograph by J. J. Bell.)

Pediculus humanus Linnæus, 1758.

Synonyms.—*Pediculus humanus* var. 1 Linnæus, 1766: *P. humanus* var. *capitis* de Geer, 1778; *P. cervicalis* Leach, 1817; *P. capitis* Nitzsch, 1818; *P. humanus* Csiki, 1904; *P. nigritarum* Latreille.

Definition.—Pediculus often varying in colour somewhat according to the human race, on which it is parasitic, with thorax often narrowing distinctly anteriorly, well-defined abdominal segments marked by lateral festoons. Thumb-like projection on the tibia armed with a spine. Habitat, homo.

Remarks. This is the head louse, which is cosmopolitan in distribution, but varies in colour on the different races, as was pointed out by Murray, being very dark on African negroes and Tamils, and said to be yellow on Chinese and Japanese, and orange on Hottentots.

On Europeans it is light grey in colour. Daniels says that the pediculi of Chinese do not pass readily to Tamils, though in our experience the pediculi of native servants, Sinhalese and Tamils, will pass to Europeans.

These pediculi are extremely common in the tropics, and it is an every-day scene to witness natives busy at work killing them on their friends' heads.

Morphology.—The head louse is about 2 millimetres in length by 1 millimetre in breadth. The female is larger than the male, and exists in greater numbers. The head is triangular, the thorax broad with short legs, and the margins of the abdomen are dark.

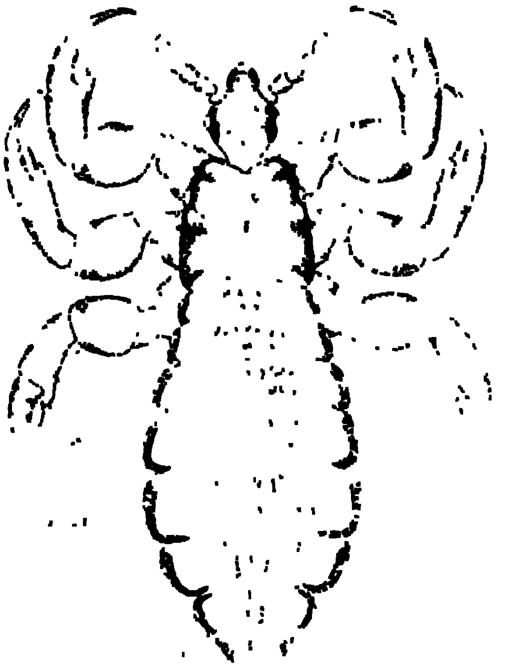

FIG. 369.—*Pediculus corporis* DE GEER: MALE (×25.)

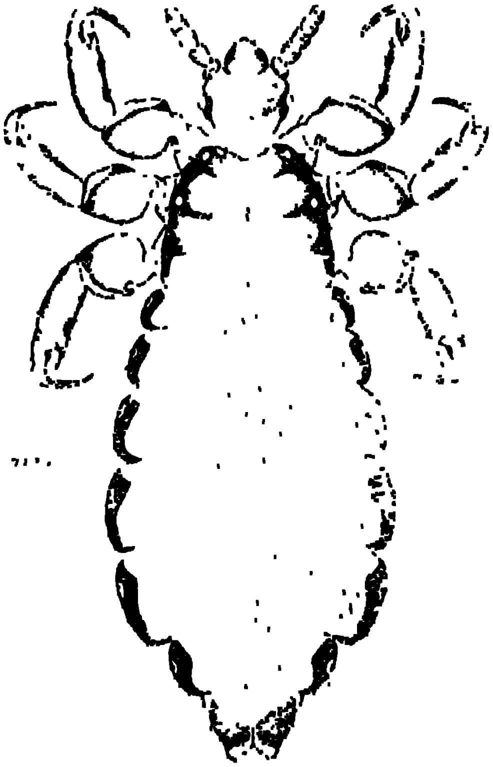

FIG. 370.—*Pediculus corporis* DE GEER: FEMALE (×25.)

Male.—The posterior somite is rounded off and prominent, with a circular opening dorsally which is the common aperture of the genital and alimentary canal. The penis is simple, wedge-shaped, and is usually seen protruding dorsally.

Female.—The last abdominal segment is deeply notched at the apex, where the anus is situated. The vagina opens on the ventral surface.

Life-History.—The female lays fifty to sixty eggs, which are attached firmly to the hairs by the secretion of the cement gland. In about six days these eggs hatch. The young pediculi become fully developed in fourteen to twenty days.

Pathogenicity.—It can carry typhus and produce a form of impetigo.

Treatment.—White precipitate ointment or common paraffin oil may be used.

Pediculus corporis de Geer, 1778.

Synonyms.—*P. humanus* Linnæus, 1758; *P. humanus* var. 2 Linnæus, 1766: *P. humanus* var. *corporis* de Geer, 1778; *P. vestimenti* Nitzsch, 1818; *P. corporis* Csiki, 1904.

Definition.—Pediculus usually dirty-white in colour, thorax only slightly narrowed anteriorly, abdominal segments not very distinctly defined and not well festooned laterally. Thumb-like projection on the tibia without a spine. Habitat, homo.

Remarks.—This louse lives in the folds and seams of the clothes.

Morphology.—It is larger than *P. humanus*, and has an oval, elongated head, with large antennæ. The thorax is more segmented than in *P. humanus*, and the legs more developed, with larger claws.

Life-History.—It lays seventy to eighty eggs, measuring 0·7 to 0·9 millimetre, in the seams of the clothing, which hatch in three to four days, and become mature in fifteen to eighteen days.

Pathogenicity. It is a carrier of typhus fever, trench fever, and certain forms of relapsing fever.

Treatment. Boil or steam the clothes in a sterilizer at 212° F.

Genus Phthirius Leach, 1815.

Pediculidæ with the anterior legs weak, armed with large short claws; abdomen broad and short, with first to fifth segment so strongly compressed that the stigmata appear to be in one segment. Fifth to eighth segments with lateral tooth-like process, of which the two last are long. Habitat, homo.

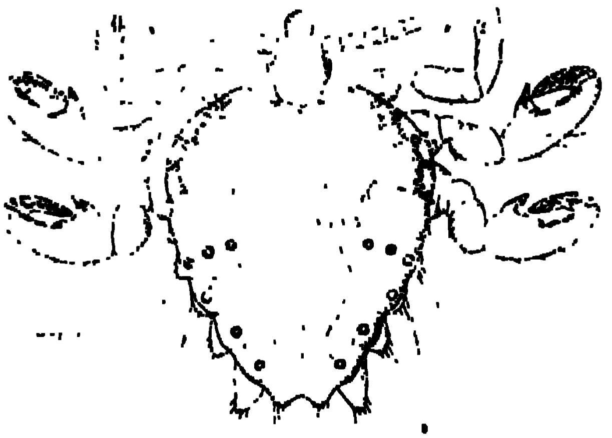

Fig. 371.—*Phthirius pubis* Linnæus: Female. (× 25.)

Phthirius pubis Linnæus, 1758.

Synonyms.—*Pediculus pubis* Linnæus, 1758; *P. inguinalis* Reichard, 1759; *Phthirius inguinalis* Leach, 1815; *P. tabescentium* Alt, 1818; *P. pubis* Küchenmeister, 1855.

Remarks.—*P. pubis* is the pubic or crab-louse, and is more common on men than on women. It usually infests the pubic hairs, but may also be found on the eyelashes and on the eyebrows.

Morphology.—The body in general is flat and broad, with a rounded head bearing antennæ with five segments, and two small eyes. There is a neck. The broad, flat thorax is merged into the abdomen, and carries three pairs of legs, of which the anterior pair is slender, and possesses a straight claw suitable for walking, and the two posterior pairs have claws suitable for clinging.

The female measures 1·2 to 2 millimetres in length by 1·5 millimetres in breadth. The male is half the size of the female.

Life-History.—The female lays ten to fifteen eggs, which it attaches to hairs. These hatch in seven days, and the resulting pediculi become mature in about two weeks.

Pathogenicity.- It produces often a dermatitis, with itching and a greyish discoloration of the skin, said by Dugnet to be caused by a pigment produced by the parasite. Erasmus Wilson says that reddish deposits may be seen on the hairs, due to the fæcal matter of the parasite.

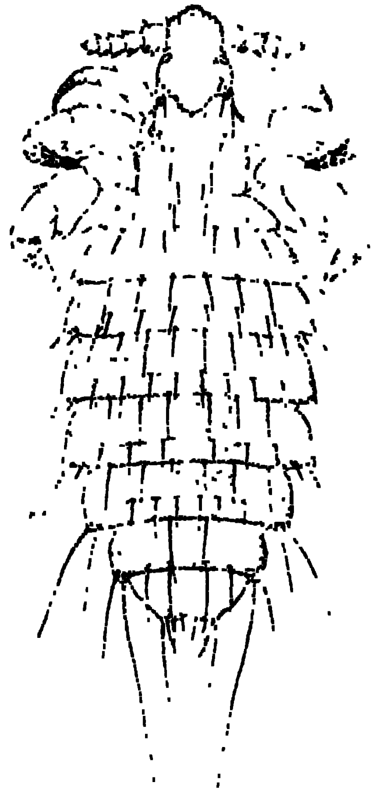

FIG. 372.—*Polyplax spinulosa* BURMEISTER: FEMALE.

Treatment.--White precipitate ointment or some other mercurial preparation.

SUBFAMILY B: PEDICININÆ
Enderlein, 1904.

Definition. Pediculidæ with three-jointed antennæ.

Remarks. Only one genus, *Pedicinus* Gervais, 1844, is known, and there are three known species found on monkeys—viz., *P. eurygaster* Burmeister, 1835 (synonym, *P. microps* Nitzsch and Giebel, 1864), found on *Pithecus sinicus* (Linnæus, 1771); *P. longiceps* Piaget, 1880, found on *Lasiopyga mona* (Schreber, 1775); and *P. piageti* Strobelt, 1881 on *Pithecus brevicaudus* (Elliot, 1909).

FAMILY 2: HÆMATOPINIDÆ
Enderlein, 1904.

Definition. Anoplura with head broadest behind, and not prolonged anteriorly into a nozzle-like projection. Eyes rudimentary or absent. Antennæ three to five segments. Proboscis very long. Pharynx long and narrow. Paraglossæ very small. Mesothorax and third to eighth abdominal segments with stigmata. Row of hairs on each abdominal tergite and sternite. Legs suitable for clinging. Tibia and tarsus very short and thick. Tibia with a thumb-like projection. Pretarsal sclerite sometimes present.

Classification.- Enderlein has divided the family into three subfamilies, which may be recognized as follows:--

A. Antennæ with five segments:-
  I. Eyes rudimentary, situate on the extremity of a forwardly directed fork-like lateral process from the posterior aspect of the head. Mandibles well developed. Forelegs larger and stronger than other legs. Pretarsal sclerite present—*Hæmatopininæ*.
  II. Eyes and eye process absent, mandibles rudimentary. Forelegs smaller than other legs. Pretarsal sclerite absent—*Linognathinæ*.
B. Antennæ with three segments—*Euhæmatopininæ*.

SUBFAMILY HÆMATOPININÆ Enderlein, 1904.

This subfamily contains only the genus *Hæmatopinus* Leach, 1817, with some twenty known species, of which the type *H. suis* (Linnæus, 1758) Leach, 1817, is found on *Sus scrofa* Linnæus; other species are found on equines, bovines, camels, antelopes, deer, conies, and monkeys.

SUBFAMILY LINOGNATHINÆ Enderlein, 1904.

This subfamily contains five genera, which may be recognized as follows:—

- A. Abdomen with strongly chitinized tergites, sternites, and pleurites. Tergites and sternites partly subdivided. Pleurites extended backwards and outwards, making sides of abdomen segmented. Hind legs stronger than middle legs. Claw of hind leg short and much compressed, and fittable into tarsus.
  - I. Abdomen elongated; 1-7 sternites and 2-7 tergites, divided into two plates lying one behind the other. Each plate with a transverse row of strong long hairs. Pleura without serrated process on the inner side. Stigmata small—*Polyplax* Enderlein, 1904.
  - II. Abdomen more or less elongated. Pleura two to six, provided with a dorsal and ventral long knife like pointed process. Four to seven tergites and sternites, composed of three secondary segments, each with a transverse row of long broad scale like hairs, third tergite and sternite composed of two rings each. Anterior ring is broader than posterior—*Hoplopleura* Enderlein, 1904.
- B. Abdomen without sclerites, with smooth border. Hind legs same size as middle leg:—
  - I. Each sternite and tergite of the abdomen with two or three transverse rows of very long closely set hairs—*Linognathus* Enderlein, 1904.
  - II. Each sternite and tergite of the abdomen with one transverse row of hairs:—
    - (*a*) Stigmata large, and those on the abdomen raised like tubercles and standing out above the hinder border of that segment—*Solenopotes* Enderlein, 1904.
    - (*b*) Stigmata very small, and not raised as tubercles—*Hæmodipsus* Enderlein, 1904.

The genus Polyplax contains a rapidly increasing number of species. The one illustrated in Fig. 372 is *P. spinulosa* (Burmeister, 1839), which is found on *Epimys norvegicus* Erxleben, 1777, in Europe.

SUBFAMILY C: EUHÆMATOPININÆ Enderlein, 1904.

This subfamily has two genera with one species, and this can be recognized as follows:—

- A. Hind legs with femur and tibia armed with projecting rectangular, stalked, sheath like appendages—*Euhæmatopinus* Osborn, 1896.
  Species: *E. abnormis* Osborn, 1896, on *Scalops aquaticus* in North America.
- B. Hind legs normal—*Hæmatopinoides* Osborn, 1891.
  Species: *H. squamosus* Osborn, 1891, on *Geomys bursarius* in North America.

REMAINING FAMILIES.

The family *Echinopthiriidæ* Enderlein, 1904, contains three genera—viz., *Antarctophthirius* Enderlein, 1904—with two species, *Echinophthirius* Giebel, 1871, with three species, and *Lepidothirius* Enderlein, 1904 with only *L. macrorhini* Enderlein, 1904.

The family *Hæmatomyzidæ* Enderlein, 1904, contains one genus, *Hæmatomyzus* Piaget, 1869, and one species, *H. elephantis*, on the Ceylon elephant

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CHAPTER XXXI

HEMIPTERA

Hemiptera — Gymnocerata — Clinocoridæ — Reduviidæ — Hydrometridæ — Aradidæ — Reference.

ORDER HEMIPTERA Linnæus, 1742.

Synonyms. —*Rhyngota* Fabricius: *Rhynchota* Burmeister.

Definition. Hexapoda with four wings, the front pair being either membranous or half horny and half membranous, but both pairs may be wanting in the parasitic species. Mouth suctorial. Metamorphosis complete.

Remarks. —The Hemiptera include the cochineal insect, *Coccus cacti*; the Aphidæ, plant-lice; and, in particular, the cicadas, whose shrill notes wake the quiet of an African forest. The anterior wings are called hemelytra, and usually consist of three portions:

1. The clavus—the hard, coriaceous portion next to the scutellum.
2. The corium—hard, coriaceous portion occupying the whole of the area between the clavus and the membrane.
3. The membrane—apical portion.

The posterior pair are the true wings.

In the Clinocoridæ the corium is divided into three portions:—

1. Internal—corium proper.
2. External and basal—embolium.
3. External and apical—cuneus.

Classification. —The order is divided into two suborders:—

SUBORDER I.: HOMOPTERA.—With both pairs of wings membranaceous.

SUBORDER II.: HETEROPTERA.—With the front pair of wings half horny.

The first will not be considered here.

HETEROPTERA.

This suborder has two series:—

Series 1, *Gymnocerata* Fieber.—Antennæ conspicuous.

Series 2, *Cryptocerata* Fieber.—Antennæ hidden.

GYMNOCERATA Fieber.

The families of importance to us are:—

Clinocoridæ.
Reduviidæ Stephens.
Aradidæ.
Hydrometridæ.

These families can be diagnosed, according to Distant, in the following manner:—

- A. Species not aquatic; abdomen not clothed beneath with a silvery, velvety pubescence; scutellum not reaching to the base of the membrane nor to the middle of the abdomen.
  - (1) Mesopleuræ and metapleuræ composed of one piece; hemelytra without cuneus.
    - (*a*) Tarsi three jointed. Rostrum short, stout, bent at the base, so that in repose it does not lie against under-surface of the head; ocelli behind eyes; hemelytra complete with distinct membrane—*Reduviidæ.*
    - (*b*) Tarsi two-jointed, anterior legs normal and inserted on the disc of the prosternum. Hemelytra neither reticulate nor cellular—*Aradidæ.*
  - (2) Mesopleuræ and metapleuræ composed of seven pieces; hemelytra with a cuneus and an embolium; ocelli absent—*Clinocoridæ.*
- B. Species aquatic or semi-aquatic; abdomen clothed beneath with a silvery velvety pubescence; antennæ four-jointed—*Hydrometridæ.*

Family Clinocoridæ.

Synonym.—*Acanthiadæ.*

Definition.—Gymnocerata without ocelli, with elytra so short that the abdomen is left uncovered. Tarsi three-jointed.

Remarks.—This family contains the bugs as so called in medical literature. There are eight genera—*Clinocoris* Petersonn, 1829; *Œciacus* Stal, 1873; *Loxaspis* Rothschild, 1912; *Cacodmus* Stal, 1873; *Aphrania* Champion, 1900; *Hæmatosiphon* Champion, 1900; *Bertilia* and *Leptocimex* Roubaud, 1913—and by some authorities these are gathered into two subfamilies, *Clinocorinæ* and *Hæmatosiphoninæ*, with about twenty species in all, of which twelve are parasitic on bats.

CLINOCORINÆ.

Clinocoris Petersonn, 1829.

Synonyms.—*Cimex* Linnæus, 1758; *Acanthias* Fabricius, 1803; *Klinophilos* Kirk, 1899.

Nomenclature.—*Koris* Aristotle; *Cimex* Pliny.

Definition.—Clinocoridæ with the anterior margin of the thorax strongly excavated and with prominent lateral angles.

Remarks.—There can be no doubt that originally bugs fed upon vegetable juices, and that it is only within geologically recent periods that they have taken to blood. Thus the field bug, *Lyctocoris campestris*, which is found under stacks of corn in Europe, may find its way into barns and stables, and will then attack horses and cattle, though under normal circumstances it would merely suck vegetal juices. The relationship to bats is interesting, as apparently the family is essentially a family of bat parasites.

Type Species.—*Clinocoris lectularius* (Linnæus, 1758).

Other Species.—*C. rotundatus* Signoret, 1852; *C. ciliatius* Eversmann, 1841; *C. pipistrelli* Jenyns, 1839 (spreads *Trypanosoma vespertilionis*); *C. columbarius* Jenyns, 1839; *C. fœdus* (vary rare): *C. dissimilis*; *C. improviso* (very rare); *C. pelosellus* (America); *C. peristeræ*.

C. boncti Brumpt, 1910, of our previous editions becomes *Leptocimex boncti* (Brumpt, 1910), and *C. inodorus* of previous editions becomes *Hæmatosiphon inodorum*, which is found on fowls and may enter dwellings.

Clinocoris lectularius Linnæus, 1758.

Synonyms.- *C. lectularius* Meriett, 1667; *Cimex lectularius* Linnæus, 1758; *Acanthia lectularius* Fabricius, 1794.

Definition.--Clinocoris with short, broad head, with two prominent eyes, but no ocelli; antennæ four-jointed, apical joints slender; elytra rudimentary and lie over the metathorax; prothorax semilunar, with extended anterior angles; abdomen uncovered, with seven segments and an eighth anal appendage: legs slender, anterior tibia twice as long, and posterior three times as long as the tarsi, which are three-jointed: proboscis flexed into a groove beneath the head and prothorax.

Historical.---The bed bug was well-known to the ancient peoples of Asia and also to the Romans, who called it *Cimex*. It seems to have come to Europe from the East, and to have reached Germany in the twelfth century, England about 1500, while Thomas Moffat says it was recognized in London in 1503--but then he was writing one hundred years after the event. Originally it was known as the wall-louse or chinch, and the term 'bed-bug' is apparently of recent origin. Both males and females suck blood, and are suspected of spreading Obermeyer's relapsing fever.

Morphology.—It is reddish-brown in colour, with short, broad head carrying two eyes, two antennæ composed of four segments, of which the first and second are stout, and the third and fourth slender. The mouth consists of a proboscis, which is composed of an upper part—the labrum—which is small, and a lower curved portion. This is large and jointed—the labium—inside which are four stylets, the two outer being the mandibles, and the two inner the maxillæ. There are no palpi. The prothorax is semilunar, with two rounded horns. The dorsum is raised in the median line. The mesothorax is triangular, with the apex posteriorly. The metathorax is covered dorsally by the elytra, which are two small chitinous plates belonging to the mesothorax, but consist of clavus, corium, empodium, cuneus, and membrane. The abdomen, which is rounded in shape, with seven segments and an eighth anal appendage, is broadest opposite the third segment. Posteriorly it is covered with round hairs. Length, 5 to 6 millimetres. Male smaller than female with penis flexed into a notch between seventh and eighth segments.

Internal Anatomy.—The mouth leads into the pharynx, beneath which is a syringe organ or salivary pump, into which the salivary glands open. The pharynx leads via the œsophagus into a large crop. There is the usual mid-gut, intestine, and rectum.

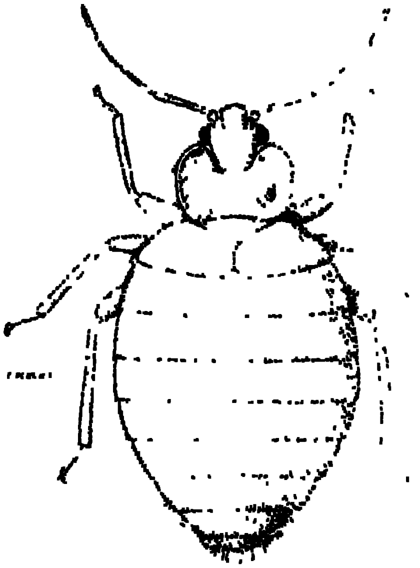

FIG. 373.—*Clinocoris lectularius* L.: MALE. (× 10)

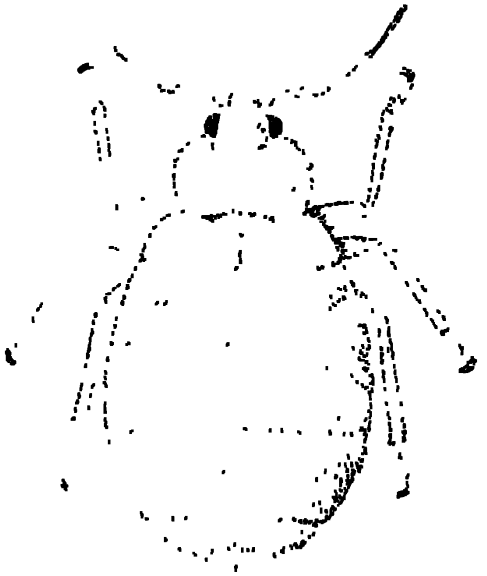

FIG. 374.—*Clinocoris lectularius* L.: FEMALE. (× 10)

Life-History.—They live in cracks in floors, walls, and furniture during the day, and issue forth at night to suck blood from human beings. They are capable of emigration from house to house. The female lays some fifty eggs three or four times a year. Complete development is said to require eleven weeks, but may be completed in as short a time as seven weeks.

The eggs, which are oval, 1·12 millimetres in length, and white in colour, take about seven to ten days to hatch. The larva grows slowly, moulting about five times, at intervals of about eight days, after which the wing-pad appears, showing that the adult stage is reached. They feed only upon blood.

Bionomics.—*Bite.*—In biting, they extend the proboscis, and feel about, testing the skin with the delicate hairs, then pierce it by the stylets, and inject saliva by the syringe, causing congestion of the area, when the blood runs up the grooves in the stylets by capillary attraction into the pharynx.

Smell.—The peculiar odour is due to the secretion of sac-like glands situated at the base of the abdomen, and opening on each side of the metasternum. The secretion is a clear, oily, volatile liquid, which is supposed to be protective in function.

Pathogenicity.—It is quite possible that they spread *Spiroschaudinnia recurrentis*, the cause of Obermeyer's relapsing fever. The effects of their venom have already been described.

Prophylaxis.—Bugs are by no means without their enemies, of which the most marked is the common red house-ant (*Monomorium pharaonis*), while another enemy is the common cockroach; but, despite these foes, bugs are extremely common in tropical hospitals.

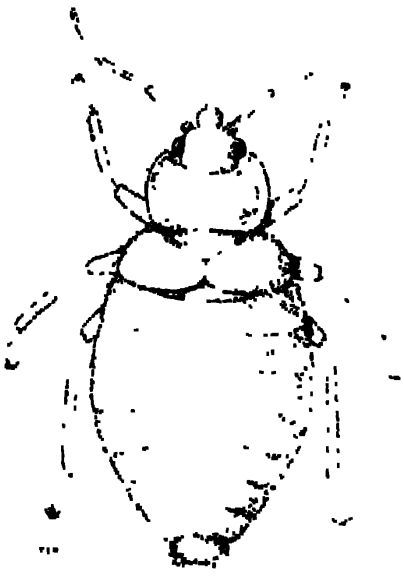

FIG. 375.—*Clinocoris rotundatus* Signoret: Male. (×10.)

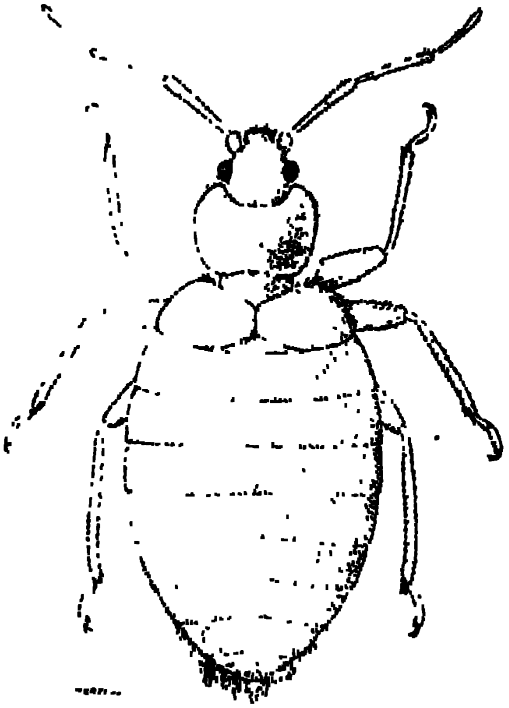

FIG. 376.—*Clinocoris rotundatus* Signoret: Female. (×10.)

The first step in prophylaxis is, of course, strict cleanliness, and the use of painted iron bedsteads which can be easily taken to pieces and washed. Another good means is to make use of mattresses and pillows covered with Willesden canvas, which can easily be washed. The mattress should be in sections, and not all in one piece, as otherwise it is difficult to manipulate. The most useful substances for killing bugs are acetic acid, camphor, and carbolic acid. Acetic acid poured into the joints of a bedstead is said to kill the bugs rapidly. Kerosene is often used, but does not appear to be very effective. Pyrethrum is also used. Apart from bedsteads, the whole room may be infected, in which case fumigation with sulphur is quite the best remedy, 4 ounces being burnt for each 1,000 cubic feet of space, and the room left closed for four or five hours, in order that the gas may act thoroughly.

Clinocoris rotundatus Signoret, 1852.

Synonyms. *Cimex rotundatus* Signoret, 1852: *Cimex macrocephalus* Fieber, 1861. This is the Indian bed-bug, which is found in India, Ceylon, Burma, Assam, and Malaya in Asia, and also in Sierra Leone, Mauritius, Réunion, St. Vincent, and Porto Rico.

Morphology.- *C. rotundatus* differs from *C. lectularius* by being darker in colour, with a shorter, narrower head, with a prothorax with rounded borders, and with a longer, narrower abdomen.

Pathogenicity.- According to Patton it spreads *Leishmania donovani*, the parasite of kala azar or tropical febrile splenomegaly

Clinocoris ciliatus Eversmann, 1841.

Synonym. *Cimex ciliatus* Eversmann, 1841.

This bug is found in Kasan, in Russia. It requires reinvestigation.

Morphology.- It is smaller than *C. lectularius*, yellowish-red in colour, and thickly covered with hairs. Length, 5·3 millimetres.

Pathogenicity.—Not known

Genus Œciacus Stal, 1873.

Clinocorida with the anterior margin of the thorax slightly excavated, and with only slightly projecting lateral angles.

Type Species.—*Œciacus hirundinis* Jenyns, 1839, also *Œciacus vicarius* in martin and swallow nests in North America.

Loxaspis Rothschild, 1912.

Clinocorida with anterior margin of thorax very narrow, scutellum transversely oblong, with posterior margin produced centrally into a point.

Type Species.- *L. mirandus* Rothschild, found on a bat in Uganda, and found in 1913 by Marshall on bats in Sennar, Anglo-Egyptian Sudan; also *L. seminitens* on bats in Java. *L. [illegible]* Roubaud 1913; on bats and bites man

Genus Cacodmus Stal, 1873.

C. villosus on Natal, Transvaal, and Nyassaland bats, *C. ignotus* on African bats; *C. indicus* on Indian bats

Genus Aphramia Champion 1900

Aphramia barys.

Genus Hæmatosiphon Champion, 1900.

H. inodorum, usually found on fowls, but may enter dwellings.

Genus Bertilia.

B. valdiviana under the bark of trees in Chili

Genus Leptocimex Roubaud, 1913.

L. boneti, synonym *Cimex boneti* Brumpt, 1901, found on man in the higher regions of the Ivory Coast and in Haute Guinée.

FAMILY ANTHOCORIDÆ.

Gymnocerata with embolium, membrane with one to four nerves, which arise at the tip and along the side of a triangular basal cell. Antennæ cylindrical.

Genera.- *Anthocoris* Fallén, 1829, and *Lyctocoris* Hahn, 1835.

Anthocoris Fallén, 1829.

Two species of importance—*A. kingi* Brumpt, 1910, in the Egyptian Sudan, and *A. congolensis* Brumpt, 1910, in the Belgian Congo

Lyctocoris Hahn, 1835.

Lyctocoris campestris Fabricius is said to attack man.

FAMILY REDUVIIDÆ.

Gymnocerata with long, narrow heads and distinct neck. Eyes large and prominent; proboscis short, thick, and curved; antennæ long, slender at the tip; legs long; elytra with three divisions when present; tarsus three-jointed.

The genera which will be noted here are: *Reduvius*, *Conorhinus*, *Lamus*, *Reduviolus*, *Rasahus*, *Melanolestes*, but *Harpactor*, *Eulyes*, *Arilus*, *Prionotus* also bite man and animals.

In addition, it may be mentioned that Wellman found *Phonergates bicoloripes* Stal, which is locally known as 'ochindundu,' in the act of sucking the juices of *Ornithodoros moubata*. It is well known that the Reduviidæ attack other insects and ticks. He also mentions that the same insect produces a more painful effect upon man than the bite of the tick *O. moubata*.

Reduvius Fabricius, 1803.

Body moderately elongate, head oblong, ante-ocular portion of head larger than post-ocular portion, eyes large, completely extending across the lateral parts of the head; rostrum with second joint much larger than first; pronotum transversely constricted before the middle anterior lobe with a strong central sulcus or fissure, which is broadly extended to the disc of the posterior lobe. Anterior much shorter than posterior lobe Scutellum with apical spines, legs moderately long and slender, anterior femora normal, interior tibiæ furrowed

Reduvius personatus Linnæus, 1758.

This is the wheel or masked bug found in Europe and the United States, and known for the severity of its bite; for it causes pain, swelling and irritation in the affected area which may last as long as a week.

Conorhinus Laporte, 1832.

Synonym.—*Triatoma* Wolf, 1802.

Reduviidæ with head long, porrect, and more or less distinctly impressed behind eyes; rostrum with first joint very much shorter than second; antennæ inserted on the sides of the head about midway between eyes and apex; ocelli placed very far apart; prosternum broadly sulcated; abdomen frequently with the disc flattened; posterior tibiæ longer than the femora.

The species of *Conorhinus* are mostly found in South America, and live on the blood of mammals and of insects, including bed-bugs. Some of the more important are: —*C. sanguisugus*, *C. rubrofasciatus* de Geer, *C. renggeri* Herrich-Schaeffer, *C. nigrovarius*, *C. protractus*, and *C. variegatus*.

Conorhinus sanguisugus Leconte, 1855.

This is the blood-sucking cone nose of America, which feeds upon the blood of insects, including bed-bugs, and of mammals, including man. The bite is

very severe, and causes much swelling and irritation. It is a night-flier, and has an odour like that produced by bugs.

Morphology.—It is a large dark brown insect, with pink markings and a flattened body and very narrow pointed head, with a strong, thick, long proboscis. The thorax is provided with wings

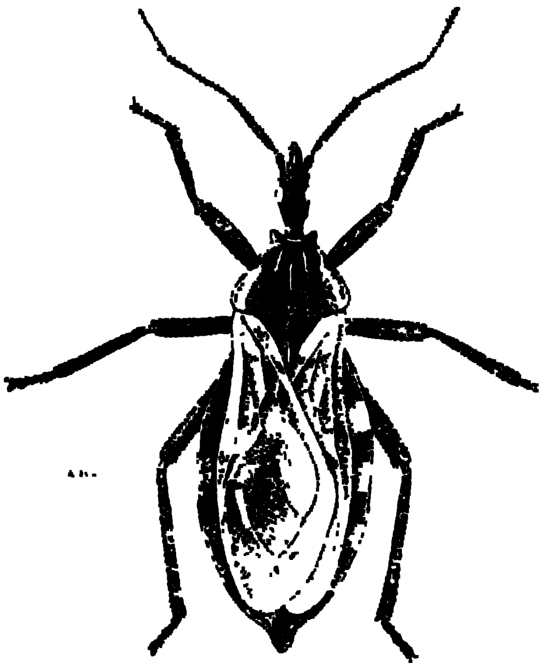

FIG. 377.—*Conorhinus sanguisuga* LECONTE, 1855: FEMALE. (× 2)

Life-History.—The eggs when first laid are white, but later change to yellow, and finally to pink. The larva hatches in about twenty days, and is very active. It moults twice and becomes the pupa, which also moults twice, the last stage showing wing pads. The pupa is also active.

Habits.—In addition to feeding upon blood, these insects may suck the juices of decomposing flesh.

Pathogenicity.—Its bite at times is followed by severe general symptoms, such as swelling in different parts of the body, nausea, etc., as well as local pain.

Remedy.—Sweet oil is advised as a remedy for the local pain.

Conorhinus rubrofasciatus de Geer. This is the Malay bug found in Africa (Sierra Leone and Madagascar), in Asia (Ceylon, India, Malaya, China, and the Philippine Islands). It is said to produce a very severe bite. *Conorhinus renggeri* Herrich-Schaeffer is the black bug of the Pampas. *Conorhinus nigrovarius* is the 'bichugue' of South America and bites severely. *Conorhinus protractus* is the big bed bug of Utah.

Lamus Stål, 1859.

Reduviidæ with the head much shorter than the thorax, with a conical preocular portion, with the basal segment of the rostrum longer than the apical. Antennæ, which are inserted a little in front of the eyes, are more than twice as long as the head, ocelli present. Scutellum unarmed; legs rather slender; anterior femora slightly thinner than the posterior and armed with spines.

Lamus megistus Burmeister.

Synonym.—*Conorhinus megistus* Burmeister; *Triatoma megista.*

Chagas has demonstrated that *Lamus megistus* is the carrier of *Trypanosoma cruzi*. This *Reduviid* attacks men and animals, and, owing to its habit of biting the face, is called 'Barbeiro' by the indigenous population.

Morphology.—*L. megistus* Burm. is a large black insect with numerous regularly arranged red markings, and differs from *C. rubrofasciatus* de Geer, which is closely allied to it, by the fact that

C. rubrofasciatus is of a dull dark brown colour with markings on the pronotum, and with dusky yellow or brick-red elytra and connexivum.

Pathogenicity.—It is the cause of South American trypanosomiasis.

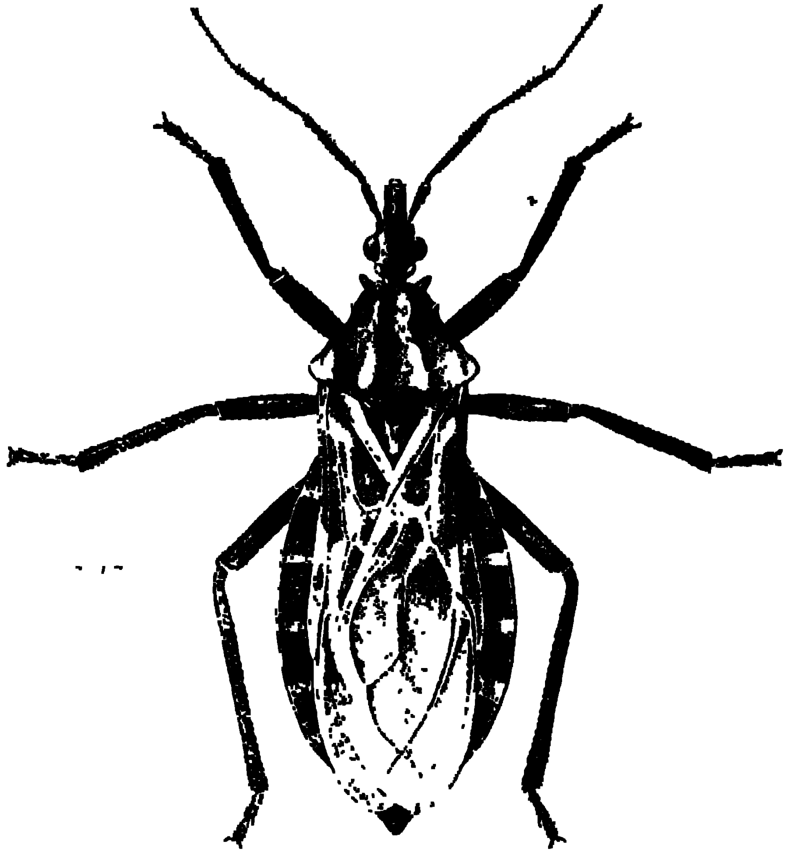

FIG. [illegible].—*Lamus megistus*, Burmeister, 1835.

Reduviolus Kirby, 1837.

Reduviolus subcoleoptratus Kirby, 1837, has once been recorded as a human blood-sucker in the United States.

Rasahus Amyot and Serville, 1843.

Rasahus biguttatus Say, 1831, is found in the houses in Cuba, Panama, and Para, where it really seeks the bed bug, but bites man also.

Melanolestes Stål, 1866.

Melanolestes morio Erichson, 1848. Found under stones during the day in Guiana, Mexico, and the United States of America. Bites man.

M. abdominalis Herrich-Schaeffer, 1848, in the same regions as *M. morio.*

FAMILY HYDROMETRIDÆ.

The Hydrometridæ, or water bugs, are interesting to the student of tropical medicine, because Patton has traced out the development of a Crithidia resembling *Leishmania donovani* in one of them, as has been described in the chapter on Protozoa, p. 567.

FAMILY ARADIDÆ.

Broad, very flat bugs, with four segments in the antenna and three in the proboscis. No cuneus. Tarsus two segments.

Dysodius lunatus Fabricius is the 'Pito' bug of South American houses, which bites severely.

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CHAPTER XXXII

THE DIPTERA

CULICIDÆ AND THEIR ALLIED FAMILIES

Diptera: Morphology—Classification—Culicidæ—Corethridæ—Chironomidæ—Psychodidæ—Simulidæ—References.

DIPTERA.

Definition.—Hexapoda with two well-developed transparent wings and two rudimentary wings in the form of halteres. Mouth parts well developed, adapted for piercing and sucking or for suction. Mesonotum forms by far the larger portion of the thorax. Metamorphosis is complete.

Remarks.—The Diptera are by far the most important order of the Hexapoda as regards tropical medicine, for they include the blood-sucking flies, which are capable of carrying disease; also certain flies which cause disease by depositing their eggs in cavities or on the surface of the body, with the result that the larvæ enter the nose, and cause disease by gnawing away mucous membrane, cartilage, and even bone, or the alimentary canal, in which they may cause serious symptoms. Apart from these, it must be remembered that flies, particularly the common house fly, may mechanically, either externally or by its alimentary canal, carry and deposit germs on food, by which means human beings become infected with disease.

Morphology.—The most important points in the morphology of the Diptera in general may be briefly mentioned

Head.—The head in certain families shows an anterior depressed area, the lunula, bounded by an arched suture, which passes over the base of the antennæ This is the invaginated 'ptilinum,' or vesicle, by which the imago breaks its way out of the pupa. With regard to the antenna, it is of great importance whether it is many- or few-jointed. In the latter case it often carries an arista on the third joint, which may be looked upon as representing the remainder of the larger antennæ of other species

The mouth parts, though composed of the typical labrum, epipharynx maxillæ, mandibles, hypopharynx, and labium, will be found to be very different in the various species of biting flies. More especially are the labial palps altered in *Glossina* and *Stomoxys*, becoming armed with teeth and capable of making the hole in the skin which is necessary for the sucking of the blood.

Thorax. In many cases the thorax is largely composed of mesothorax, the pro- and meta-thoraces being much reduced The wings are of importance. Some genera possess a prolongation backwards, called the squama, which conceals the halter. The venation of the wing has a peculiar nomenclature, which will be more fully explained under the heading Culicidae, but which may here be compared with the typical arrangement of Comstock and Needham, from which it differs mainly by the form of coalescence called 'inward' which means that two veins have coalesced from the tip towards the base of the wing.

Typical Names		Dipterous Names
Costa		Costa.
Subcosta		Subcosta
Radius 1		First Longitudinal
Radius 2 Radius 3	Coalesced	Second Longitudinal.
Radius 4 Radius 5	Coalesced	Third Longitudinal
Media 1 Media 2 Media 3 Media 4	Coalesced more or less	Fourth Longitudinal.
Cubitus 1 Cubitus 2		Fifth Longitudinal.
Anal 1 Anal 2		Sixth Longitudinal
Anal 3		Seventh Longitudinal.

The above table shows the two ordinary systems of nomenclature for the chief veins of the Diptera at present in use. The terms in the right hand column are older than the other ones and are generally employed by English writers. In addition to the longitudinal veins there are several transverse veins, viz.:

1 The Humeral from the Costa to Subcosta.
2 The Radio-medial or anterior from the Radius to the Media.
The distal Medio-cubital or posterior from the Media to the Cubitus.
4 The proximal Medio-cubital or anterior Basal.
The Cubito-anal or posterior Basal.

The wing shows a costal cell, generally subdivided by the humeral vein, a subcostal, a marginal, a variable number of submarginal, a posterior, and an anal cell. The second anal vein is often wanting and represented by merely an infuscation. In addition there are generally an anterior or radial, a posterior medial and an anal or cubital basal cell. In the Culicidae the first submarginal and the second posterior cells are often called the fork cells. In the first posterior it is important to note whether it is closed, and does not reach the margin of the wing owing to the junction of the media with the radius, or open, or partially open and does reach the margin of the wing. A discal cell in the middle of the wing is present in some genera. It is bounded either by the media or by that vein and the cubitus.

The legs possess the usual number of segments, but with regard to the nomenclature of these segments there is a certain amount of confusion. The fifth tarsal segment carries two claws and usually two pulvilli or pads, while between them lies the empodium in the form of a bristle or third pad, which may be looked upon as a sixth tarsal or claw segment.

Abdomen. This has usually nine segments, which may be reduced by the fusion of segments, especially in connection with the male and female generative organs. The genitalia, especially the male, are of importance in classification, and will be mentioned in detail under the heading Culicidae.

The body is adorned by scales and hairs. The former have been made use of by Theobald to classify the Culicidae, while the latter may be strongly developed in places, and have been used in flies as a help in classification, and are of the utmost importance in fleas.

Flies are usually modest in colour, being often yellowish, brownish, or blackish, but some of the Culicidæ, e.g., *Megarhina*, are brilliantly coloured. The colours depend partly upon pigments and partly upon interference with or reflection of light.

Life-History. The female generally lays eggs; more rarely a larva is produced directly, as in *Glossina*. The eggs are laid in some material which will be useful to the larva—e.g., the eggs of Culicidæ in water and the eggs of Muscidæ often in decomposing matter. The larva is generally a very active, vigorously feeding little grub, which may or may not have a distinct head. The pupa may either remain in the old larval skin which forms the puparium (such a pupa, as seen in the Muscidæ, belongs to the coarctate type), or it may not be so enclosed, but the body and appendages being closely united, it forms the obtectate type. The imago escapes from its pupal skin by a T-shaped slit (Orthorrhapha), or by a circular opening (Cyclorrhapha).

Collection of Flies.—Mr. Austen has asked us to invite the reader's attention to certain remarks of his taken from the second report of the Wellcome Research Laboratories, which are as follows:—

1. Specimens of blood-sucking and other Diptera intended for determination should be in *the most perfect condition possible*.
2. Specimens collected by *natives* seldom fulfil this condition.
3. Flies should, if possible, always be transfixed by a pin through the thorax and pinned to a small piece of cardboard, and should be drawn up *near the head of the pin*, and not left close to the point.
4. If pinning is impossible, specimens are best placed *in three-cornered envelopes* of soft paper.
5. Flies should *never* be placed in contact with *dry cotton-wool*.
6. *A plug of soft paper* must always be pressed down on top of specimens placed in spirit, in order to fix them in the tube.
7. Several specimens *of each species* should be sent if identification is desired.
8. Specimens should always be *labelled*, with the name of locality, and date of capture, and notes of interest forwarded at the same time.

Classification.—The Diptera may be classified as follows, according to the characters of the pupa, larva, and antennæ.

SUBORDER I. ORTHORRHAPHA.

Definition. Diptera without lunula or ptilinum. Larva with a distinct head. Pupa obtectate. Imago escapes by T-shaped opening.

Section 1: Nematocera. Orthorrhapha with antennæ composed of more than six joints, with the joints, except the first two, similar, without arista. Palpi four- or five-jointed.

Families. Culicidæ, Corethridæ, Chironomidæ, Psychodidæ, Simuliidæ, Blepharoceridæ, etc.

Section 2: Brachycera.—Orthorrhapha with antennæ in which the joints differ from one another, with or without arista, which, when present, is usually terminal.

TRIBE I: *Brachycera homœodactyla*.—Orthorrhapha brachycera with three well developed pulvilli. Larva with a projecting posterior stigma.

Families.—Tabanidæ, Leptidæ.

TRIBE 2: *Brachycera heterodactyla.*—Orthorrhapha brachycera with two or three pulvilli. In the last case the middle is different from the two other pulvilli. Some species without pulvilli. Posterior stigma of the larva in front of the body-end.

Families.—Asilidæ, Empidæ.

SUBORDER II. CYCLORRHAPHA.

Definition.—Diptera with a lunula and usually a ptilinum. Antenna with always three joints and an arista. Palpi one-jointed. Mandibles absent. Maxillæ rudimentary. Discoidal cell bounded by the media and cubitus. Abdomen with seven segments at the most, often with less.

Section 1: Aschiza.—Cyclorrhapha with a clearly defined lunula, but a rudimentary ptilinum. Arista poorly developed.

Families.—Not of interest in tropical medicine.

Section 2: Schizophora.—Cyclorrhapha with lunula; at times absent, but the arched suture over the antennæ is well defined. Ptilinum usually well developed. Antennæ lie in separated hollows. Arista well developed.

TRIBES: *Muscidæ acalyptratæ* and *Muscidæ calyptratæ*.

SUBORDER III. PUPIPARA.

Definition.—Diptera with well-developed rudimentary or no wings; parasitic on vertebrates. The fully-developed larvæ are passed directly from the body of the imago without a free-living egg stage.

SUBORDER ORTHORRHAPHA.

SECTION NEMATOCERA.

FAMILY CULICIDÆ.

Definition.—*Orthorrhapha nematocera* with a long piercing proboscis, and a body more or less clothed with scales and hairs. Antennæ with whorls of hairs or plumes, which may be dense and long in the male, though scanty in the female. Wings with six to seven longitudinal veins, with scales and two distinct fork cells. The costa passes all round the wing, and carries scales, which form a fringe. Metamorphosis complete.

The Culicidæ include the flies which we call mosquitoes, a word which is derived from the Spanish, meaning little flies, and are the same as gallinippers in America. The genus *Culex* was formed by Linnæus in 1790 for the gnat *Culex pipiens*; the genus *Anopheles*, from a Greek word meaning harmful, by Meigen in 1818; the genus *Stegomyia* by Theobald in 1901. A great many other genera have also been described, but are not so important in tropical medicine as these three. Among the early workers in this field of research special prominence must be given to the names of Arribalzaga and Ficalbi.

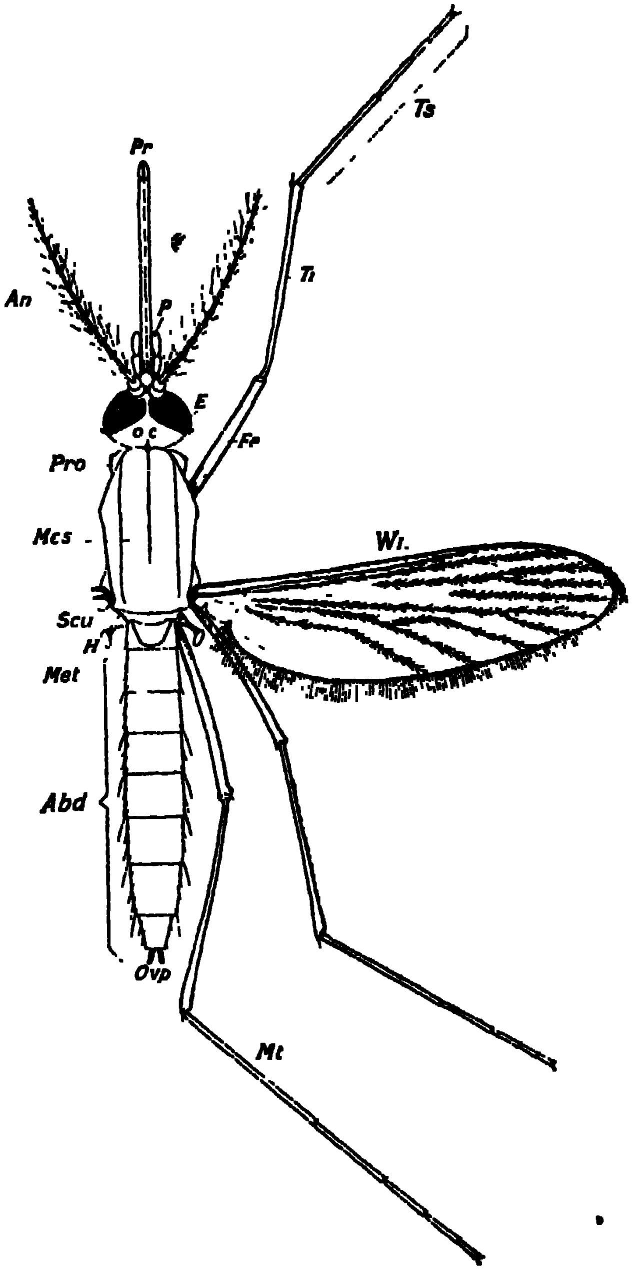


FIG. 379. DIAGRAM OF A MOSQUITO.

(After Theobald, from 'The Culicidæ of the World.')

Pr., proboscis; *P.*, palp; *An.* antenna; *E.*, eye, *Oc.*, occiput; *Pro.*, prothorax; *Mes.*, mesothorax; *Scu.*, scutellum, behind which is seen (*Met.*) the shield-like post-scutellum; *H.*, halter; *Abd.*, abdomen; *Ovp.*, ovipositor; *Wi.* wing; *Fe.*, femur; *Ti.*, tibia; *Mt.*, metatarsus; *Ts.*, tarsus: the line indicating the tarsus is made to include the metatarsus, which is sometimes regarded as the first tarsal joint.

In our description of the classification of the Culicidæ we have followed Theobald, but a simpler system is urgently required and may be evolved during the next few years, as there are already signs that such a system may be possible.

Careful dissections of *Anopheles* have been made by Nuttall and Shipley, and of *Culex* by Christophers, while the larva and pupa of *Anopheles* have been studied in detail by Imms.

As the *Anopheles* is, without doubt, of the greatest importance to medical men, its anatomy will be described.

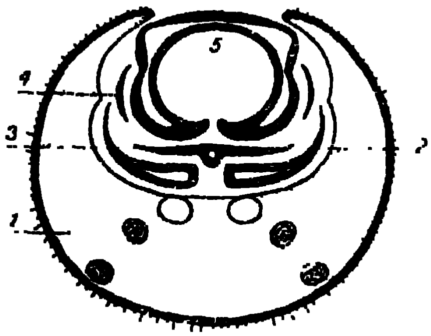


FIG. 350.—TRANSVERSE SECTION OF THE PROBOSCIS OF *Anopheles maculipennis* MEIGEN.

(After Nuttall and Shipley, from the *Journal of Hygiene*.)

1. Labium, 2, maxilla, 3, hypopharynx with salivary duct; 4, mandible, 5, labrum-epipharynx with the figure (5) placed in the blood tube.

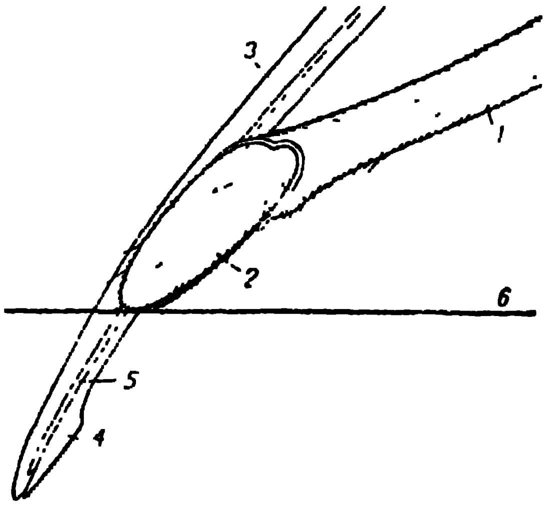


FIG. 351.—DISTAL END OF THE PROBOSCIS OF *Anopheles maculipennis* MEIGEN.

1, Labium; 2, labellæ; 3, labrum-epipharynx; 4, maxillæ, 5, mandibles; 6 skin line. (The labellæ should be divergent to the plane of the paper.)

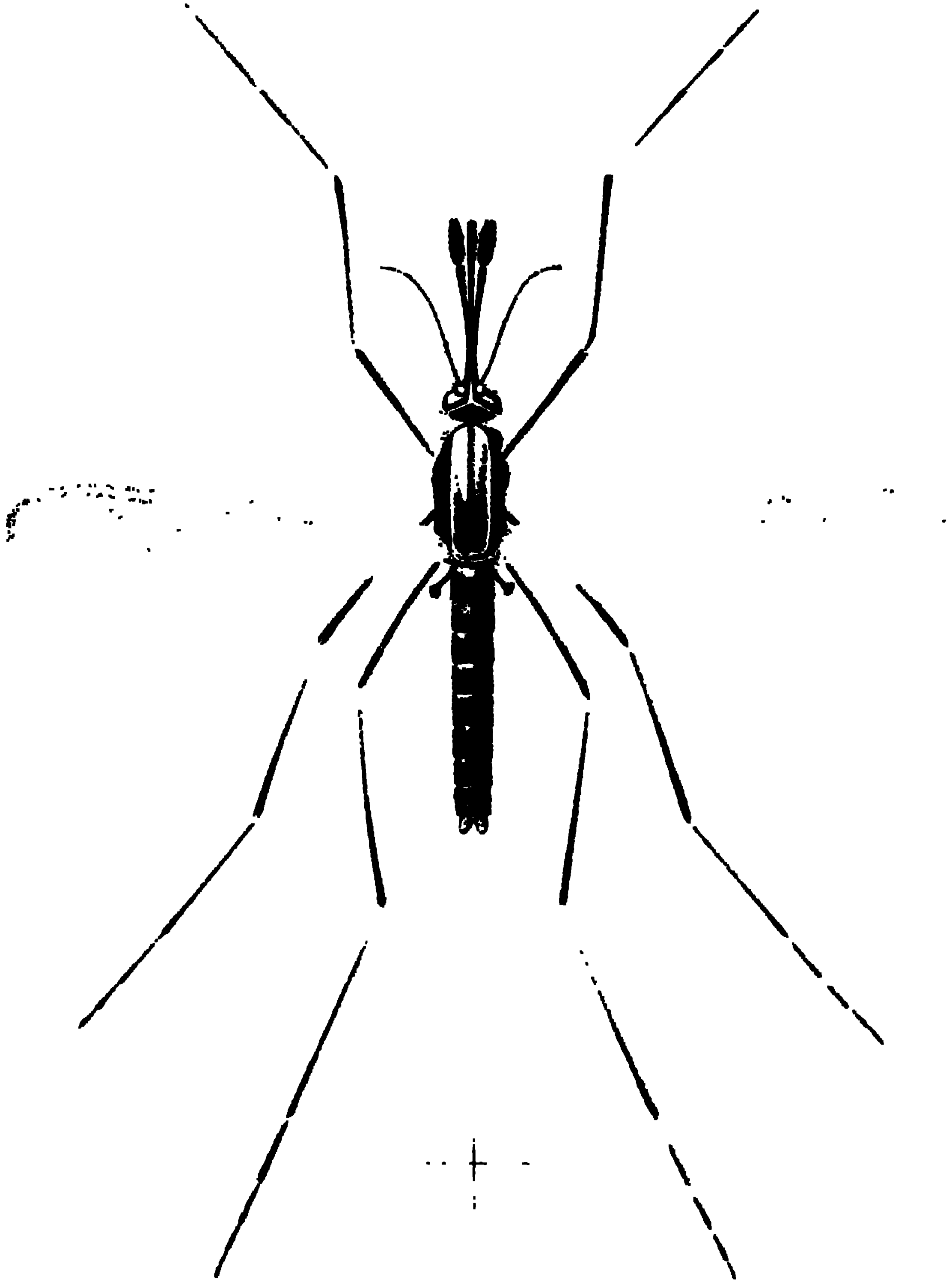
Morphology. *Anopheles maculipennis* Meigen has been studied by Nuttall and Shipley, whose account is followed in the description given below.

The body of a mosquito is divided into (*a*) head, (*b*) thorax, (*c*) abdomen.

Head. The most conspicuous objects on the head are the two large reniform, often brilliantly coloured eyes, which lie on a piece of exoskeleton, called the 'epicranium,' which covers the whole head, except in the ventral median line where the gula can be seen. Dorsally the eyes nearly meet, being separated by a piece called the 'vertex,' in front of which is the frons, which carries a pair of antennæ, different in male and female. The male antenna has sixteen segments, of which the first segment is very small; the second is globular, and contains an auditory organ, the third is long, and the fourth to the fifteenth carry twenty-five to thirty hairs in whorls at the proximal end of each segment. The sixteenth segment is about half as long as the penultimate. So dense are the whorls of verticillate hairs in the male that the term 'plumose' is applied to the whole antenna. The base of the sixteenth segment carries six hairs, and the tip is rounded. The female antenna consists of fifteen segments. The first is very small, merely a ring of chitin; the second is deeply hollowed for the third segment, which is the longest. The proximal ends of the fourth to the fifteenth carry six large hairs. The tip of the fifteenth segment bears fine hairs. These few hairs produce quite a different appearance in the antennæ, which are called 'pilose.'

In front of the frons a sclerite called the 'clypeus,' belonging to the exo-

PLATE II.



ANOPHELES MACULIPENNIS MEIGEN.

MALE.

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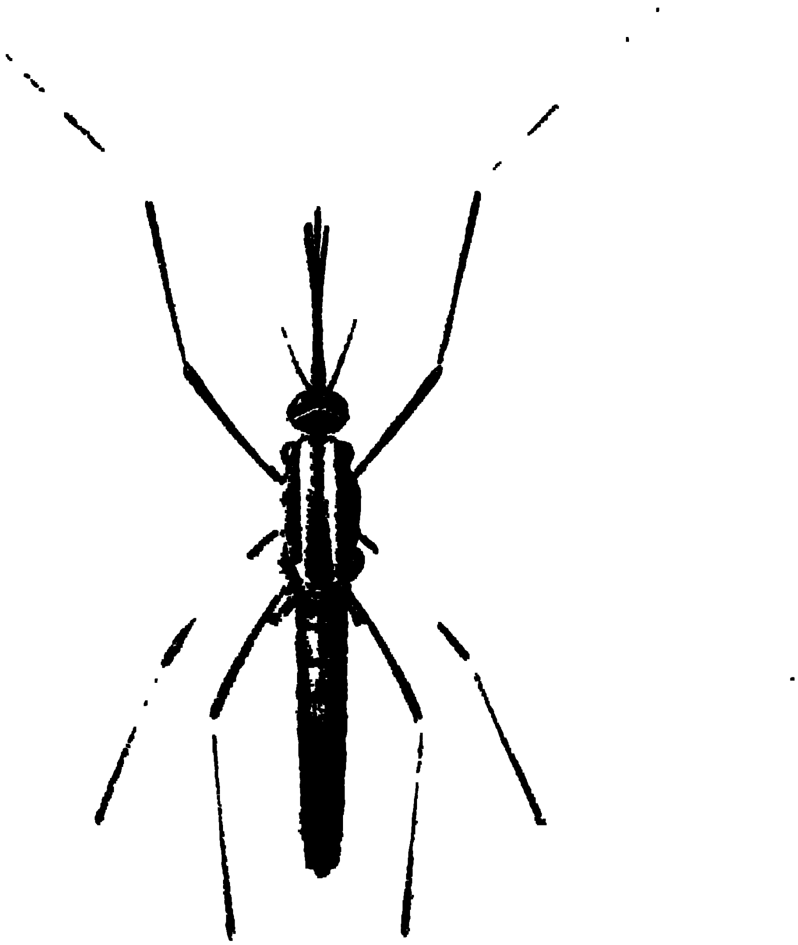
To face Plate III

PLATE III.



ANOPHELES MACULIPENNIS MEIGEN.

FEMALE.

(After Austen, by kind permission of the Trustees of the British Museum.)

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skeleton of the head, projects forwards, under cover of which the mouth appendages appear as a median proboscis and two lateral palpi.

These mouth parts are made up of the following (*vide* Fig. 22, p 224). -

1 Labrum, or upper lip, with which is combined the epipharynx to form the labrum epipharynx.
2. The mandibles.
3. The first pair of maxillæ, to which the palpi belong.
4 The hypopharynx.
5 The second pair of maxillæ, which have united together to form the lower lip or labium.

The labrum epipharynx commences at the head end as two separate chitinous structures: the more dorsal, continuous with the clypeus, is the labrum, and the more ventral, continuous with the chitinous lining of the mouth cavity, is the epipharynx, the part in the proboscis forms a deep groove, open ventrally. In the female its free end is sharp and pointed; in the male it is truncated

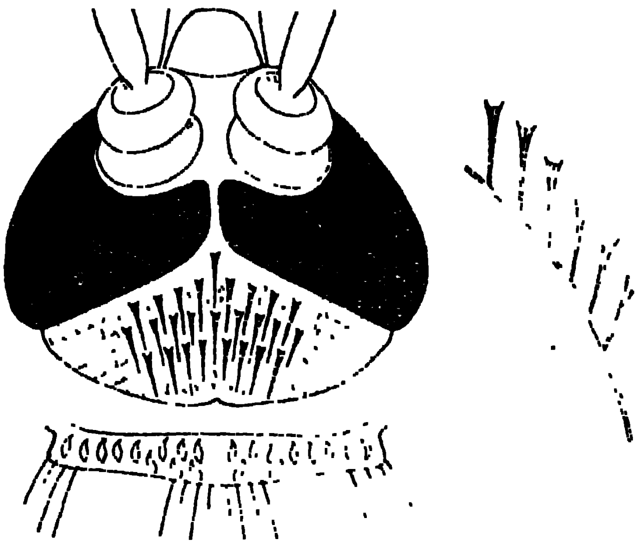


FIG. 25. THE OCCIPUT AND SCUTELLUM OF AN ANOPHELINE MOSQUITO TO SHOW THE SCALE CHARACTERS.

At the side is seen the lateral aspect of the ventral side.

(After Theobald, from 'The Culicidæ of the World.')

The mandibles are absent in the males, while in the female they appear as yellow delicate chitinous blades the base of which is attached to the sides of the labium and the apex is knife shaped with its edge serrated by thirty-one fine teeth (*vide* Fig. 23).

The first maxillæ are chitinous rods attached posteriorly to the side of the base of the labium, which is here swollen, and carries on its outer angle the palp It is continuous posteriorly with a chitinous bar, which runs backwards into the head and affords attachment to several muscles. The free extremity of the maxilla has thirteen teeth (*vide* Fig 24, p 225).

The maxillary palps project on either side of, and dorsal to, the proboscis. They are five-jointed, and covered with scales In the male the distal end of the third segment is broadened, and the whole fourth and fifth segments are broad and flat, giving a spatulate appearance to the tip. The length of these palpi varies in the different genera of the Culicidæ, as will be mentioned under the heading of Classification

The hypopharynx takes its origin just above the base of the labium in a solid mass of chitin, which is pierced by the salivary duct, which is a canal 3 to 50 μ in diameter. In the male the hypopharynx is fused with the labium

The second maxillæ are united together to form a lower lip, or labium, which is curved dorsally so as to form a deep groove in which the first maxillæ lie ventrally and laterally, with the hypopharynx situated dorsally and mesially, and the labrum epipharynx dorsally with the mandibles on either side. The distal end carries two short segments called 'labellæ,' which are movable on hinge joints. Between these labellæ there is a projection of the labium connected with them by a thin membrane (Dutton's membrane) which is stretched during the act of biting. Through this membrane filarial embryos escape from the interior of the labium. The labium itself is composed of a double cuticular wall carrying scales on its exterior, and enclosing internally a cavity containing muscles, etc., among which the filarial embryos can lie. There are, therefore, two tubes in the proboscis: the first, large, formed by the labrum-epipharynx and the hypopharynx, is the blood-tube, up which the blood is sucked into the pharynx; while the other, small, lying in the hypopharynx, is the salivary duct. The first is afferent, the second efferent.

Behind the eyes there is an area of the head called the 'occiput,' which carries different kinds of scales in different genera, as is seen by the following diagram (Fig. 383). These scales may be differentiated into narrow curved scales, upright forked scales, and flat scales, the presence and character of which have been made the means of classification. The upright forked and the curved scales occupy the middle area of the occiput, and alone are met with in this species, but quite different arrangements are met with in other genera. The extreme posterior area of the head is the nape. Below the eye laterally is the area of the head called the 'gena.' At the back of the head is the occipital foramen, through which the soft structures pass to the neck.

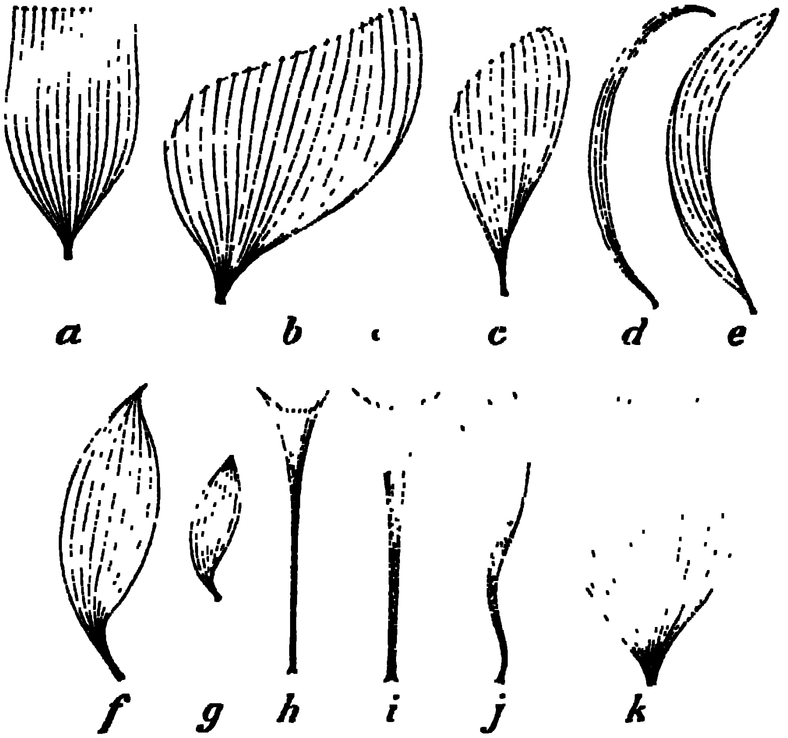


FIG. 383.—VARIOUS FORMS OF SCALES FOUND ON DIFFERENT PARTS OF A MOSQUITO.

(After Theobald, from 'The Culicidæ of the World')

a, Flat scale from abdomen; *b*, broad wing scale; *c* another broad wing scale; *d*, curved hair-like scale; *e*, narrow curved scale; *f*, flat spindle-shaped scale; *g*, small form of *f*; *h* and *i*, upright forked scales; *j* twisted upright scale; *k* inflated scale.

Neck.—The neck is the soft connection of the head with the thorax. It is strengthened with chitinous rods.

Thorax.—The thorax shows the usual three divisions into pro-, meso-, and meta-thorax, but of these the mesothorax is much the largest, and is often called 'the thorax'; in fact, the pro and meta-thorax are hard to see. It will be remembered that a typical thoracic segment should show dorsally a notum, composed of præscutum, scutum, scutellum, and post-scutellum; ventrally a sternum, and laterally a pleuron, consisting of episternum and epimerum.

On the posterior portion of each side of the neck may be seen a small sausage-shaped sclerite, called the patagium, in front of which is the neck sclerite while posteriorly there is another sclerite reaching as far as the first thoracic spiracle. Below these, and reaching to the coxa of the first leg, is still another sclerite. These four sclerites make up the prothorax. The patagium may represent a pronotum, the neck sclerite an episternite, and the posterior sclerite an epimerum, while the sclerite connected with the coxa of the first leg is undoubtedly a prosternum. This segment of the thorax carries the first pair of legs, and perhaps the first spiracle.

The interpretation of the parts of the prothorax presents considerable difficulty. Some authorities believe that there is no pronotum. The mesothorax is well developed, and presents dorsally a præscutum and scutum fused together, behind which is a trilobed area, the 'scutellum.' Behind this, again, is a shield shaped area, looked upon by some observers as a metanotum, but more probably representing the post-scutellum of the mesothorax. Laterally behind the first spiracle lies the episternum of the mesothorax, below and behind which is the mesosternum, wedged in between the second and third legs on each side. The two mesosterna are bound together by a chitinous bar.

Between the post-scutellum and the first abdominal segment lies the minute true metanotum. The metasternum is easily seen between the second and third pairs of legs and the episternum of that segment lies just dorsal to the third coxa, and contains the second thoracic spiracle as well as carrying the halter. The thorax is covered with hair-like curved scales, and its appendages are the legs and wings. There are three pairs of legs, one for each division of the thorax, which have the usual number of segments -- coxa, trochanter, femur, tibia, metatarsus and tarsus, the latter being four-jointed. The last joint of the tarsus carries the two claws or ungues, which may be toothed. In the first leg in the male the claw is single, and the first terminal tarsal segment is hollowed out. In the female all the legs terminate in a double hook, and the first tarsal segment is not hollow., The empodium, a median process projecting between the ungues is in *Anopheles maculipennis* reduced to a tuft of hairs. The arrangements of the ungues, however, vary very much in different genera and species.

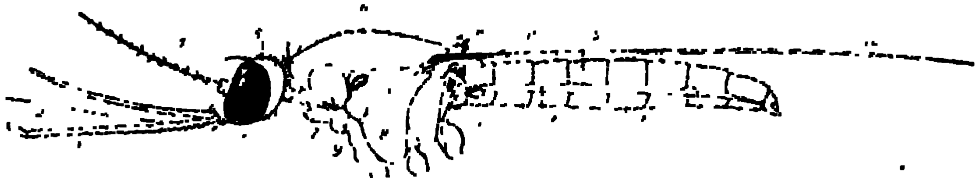


FIG. 384.--LATERAL VIEW OF *Anopheles maculipennis* MEIGEN.
(After Nuttall and Shipley, *Journal of Hygiene*.)

1, Labium; 2, labrum epipharynx; 3, palp; 4, antenna; 5, occiput; 6, mesothorax (præscutum and scutum); 7, prothorax; 8, mesosternum; 9, first thoracic spiracle; 10, metasternum; 11, second thoracic spiracle; 12, scutellum; 13, post-scutellum; 14, wing. 15, tergum; 16, pleural membrane; 17, sternum.

The wings arise by their bases from the side of the mesothorax, between the scutum and the episternum. The anterior border of the wing is straight and thick, while the posterior is curved and near the base is folded or indented twice to form squama and alula The area of the wing, bounded by the squama and alula, is broken up by a series of thickenings and ridges from which the nerves take their origin. The base of the wing has a socket which fits on to a knob on the episternum. The veins of the wings are: -

1. *The Costa.*

2. *The Subcosta*, which joins the Costa some distance from the apex of the wing.

3. *The Radius 1* (*First Longitudinal*).--Runs from base to apex of the wing.

4. *The Radius 2 + 3 (Second Longitudinal)*.—Commences in the middle of the wing, and shortly divides into two branches (Radius 2 + 3), enclosing a piece of the wing called the first submarginal cell.

5. *The Radius 4 + 5 (Third Longitudinal Vein)*. Commences in the middle of the wing and runs to the margin.

6. *The Media (Fourth Longitudinal Vein)*. Runs from the base of the wing to the margin, but forks (Media 1 + 2) to enclose the second posterior cell.

7. *The Cubitus (Fifth Longitudinal Vein)*. Runs from the base and forks (Cubitus 1 + 2) to enclose the third posterior cell.

8. *The Anal 1 + 2 (Sixth Longitudinal Vein)*. Runs a curved course from its margin.

In some mosquitoes there is a second anal vein (seventh longitudinal vein), but more often this is only indicated by a fold or incrassation. There may be a vena spuria or marking between the cubitus and the anal vein.

9. *Transverse or Cross Veins.*

- (*a*) The Humeral, between the Costa and Subcosta.
- (*b*) The Radial, between Radius 2 + 3 and Radius 4 + 5 (second + third longitudinal veins).
- (*c*) The Radio medial, between the Radius and Media (third + fourth longitudinal veins).
- (*d*) The Medio cubital, between the Media and the Cubitus (fourth + fifth longitudinal veins).

These veins mark out the following cells:

1. The Costal cell, between Costa and Subcosta, but subdivided by the humeral vein.
2. Subcostal (Mediastinal) cell, between Subcosta and Radius 1.
3. Marginal cell, between Radius 1 and Radius 2 + 3.
4. First Submarginal cell between Radius 2 + 3.
5. Second Submarginal cell between Radius 2 + 3 and Radius 4 + 5.
6. First Posterior cell, between Radius 4 + 5 and Media.
7. Second Posterior cell, between Media 1 + 2.
8. Third Posterior cell, between Media and Cubitus.
9. Fourth Posterior cell, between Cubitus 1 + 2.
10. Anal cell, between Cubitus and Anal 1.
11. Axillary cell, between Anal 1 + 2 and Anal 3, when present.
12. Spurious cell, behind Anal 3, when present.
13. Anterior Basal cell, bounded anteriorly by the Radius 1, posteriorly by the Media, and externally by the Radial transverse vein.
14. Posterior Basal cell, bounded anteriorly by the Media, and posteriorly by the Cubitus, and externally by the Medio cubital vein.

The wing has scales on all its veins, except the cross and the spurious veins, which are arranged in two ways: (1) Two rows of flat scales on each vein; (2) lateral scales along each vein.

Generally these scales in the Anophelinæ are lanceolate or long and narrow, but one genus, *Cycloleppteron*, has large inflated scales. It will be found that scales vary much in the different genera and species, the principal forms of which may be gathered from the following: The posterior margin of the wing carries a fringe consisting of scales arranged as follows: (1) Flat scales; (2) long lanceolate scales; (3) short lanceolate scales alternating with the long lanceolate scales.

Abdomen. There are eight segments in the abdomen, each of which consists of a dorsal plate, the tergum, and a ventral plate, the sternum, joined together by a pleural membrane on which lie the abdominal spiracles, said to number six or eight by different observers.

On the posterior end of the terminal segment are the external genital organs. In the male these consist of a pair of large basal lobes, each terminating in a clasp segment armed with a claw, thus forming the clasper. The arrangements of the male genitalia vary so much that they have been used as a method of classification. Therefore it is necessary to explain in a general way the terms used with regard to the various parts which may be found.

On the ventral surface of the basal lobe is the tubercle or lobe, called the claspette, while from their inner margin, near the base, a pair of claspers called harpagones, and more distally another pair, the harpes, project. Just at the junction of the two basal lobes are another pair of lobes—the setaceous lobes—which are believed to be the rudimentary ninth segment. The unci are absent in the Anophelinæ, but present as a pair of ventral processes in the Culicinæ. In the female there are the flap-like ovipositors.

The flat abdominal scales of the other Culicidæ are absent in the Anophelinæ, except in one genus.

Internal Anatomy.—A few points with regard to the internal anatomy of the mosquito may be mentioned.

ALIMENTARY CANAL.—The alimentary canal consists of: (1) Mouth; (2) buccal cavity; (3) pharynx, or pumping organ; (4) œsophagus and its pouches; (5) œsophageal valve, or proventriculus; (6) mid-gut; (7) ileum; (8) colon; (9) rectum; (10) anus (*vide* Fig. 385).

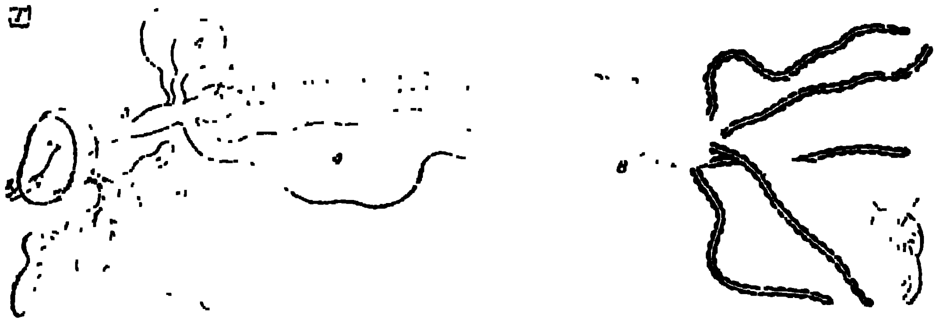


FIG. 385.—THE ALIMENTARY CANAL OF *Anopheles maculipennis* MEIGEN.
(After Nuttall and Shipley, *Journal of Hygiene*.)

1, Mouth and buccal cavity; 2, pharynx; 3, œsophagus; 4, dorsal and ventral œsophageal diverticula; 5, proventriculus; 6, salivary glands; 7, narrow portion of ventriculus; 8, so-called stomach; 9, Malpighian tubules; 10, intestine; 11, rectum; 12, anus.

1. *Mouth.*—The mouth is the place where the maxillæ, mandibles, labrum-epipharynx, hypopharynx, and palps fuse together.

2. *Buccal Cavity.*—This extends from the mouth to the valve between it and the pharynx, and is lined with chitin, and has an upward and backward direction until it approaches the pharynx, when it turns suddenly upward. There is a portion of its roof which possesses a thinner cuticle than the rest of the buccal cavity, and has been called the soft palate. This structure possesses two spines directed downwards into the lumen of the cavity, and has attached to it five pairs of palatal muscles. It is thought that as this membrane is wrinkled and has muscles attached to it, it may indicate that it is used for suctorial purposes. Posteriorly there is a valve between the buccal cavity and the pharynx, lying on a level just behind the posterior end of the clypeus. This prevents the return of fluids to the mouth during pumping. Annett and Dutton described a complicated sense organ at the junction of the buccal cavity and the pharynx, but this has not been confirmed.

3. *Pharynx.*—The pharynx extends from the posterior end of the buccal cavity to nearly the posterior end of the head, where it ends in the œsophagus. It is considerably larger in the female than in the male, because the former sucks blood, while the latter does not. The anterior portion is tubular, and passes through the nerve ring between the supra- and infra-œsophageal ganglia. The posterior portion is triangular, and has a chitinous wall arranged into three plates, one dorsal and two latero-ventral.

Posteriorly, near the œsophagus, the triradiate pharynx is surrounded by a sphincter muscle, and the chitin of this portion is marked by ridges, which end in very fine spines, making a comb-like appearance, and possibly acting as a strainer. The three chitinous plates have powerful muscles attached to them, of which the two posterior dorsal dilators run from the occiput to the dorsal plate, the two anterior dilators (two pairs in the female) taking their origin from the vertex are inserted also into the dorsal plate, and the five-paired latero-ventral dilators arising from the lateral posterior angle of the head pass upwards and a little forwards to the latero-ventral plates. When these muscles contract the triradiate pharynx becomes nearly circular, and when they relax the walls come together.

In this way the pharynx pumps the blood from the victim up the blood tube in the proboscis into the alimentary canal.

4. *Œsophagus.*—The short œsophagus runs from the pharynx to the œsophageal valve. Anteriorly it is narrow, but posteriorly it expands so much that this portion is sometimes called the crop. It is lined with thin chitin, and has many bands of muscles attached to it. Its posterior end lies on a level with the origin of the first pair of legs, and at this situation it gives off three pouches, two dorsal and one ventral. The large ventral pouch opens into the œsophagus by a single opening in the middle line, and extends backwards under the alimentary canal to the level of the fifth, sixth, or seventh abdominal segment, when fully distended. In shape it is fusiform. The two small latero-dorsally placed pouches open into the sides of the œsophagus. All these sacs are lined with thin chitin and have some slight musculature.

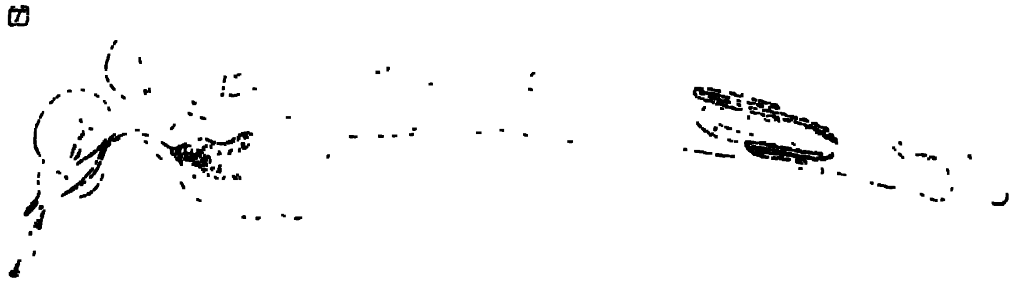


FIG. 386.—THE ALIMENTARY CANAL OF *Anopheles maculipennis* IN SITU.
(After Nuttall and Shipley, *Journal of Hygiene*.)

1, Proboscis, 2, buccal cavity, 3, pharynx, 4, œsophagus, 5, œsophageal pouches, 6, salivary glands, 7, proventriculus, 8 and 9, mid gut; 10, Malpighian tubes, 11, ileum, 12, colon, 13, rectum, 14, rectal papillæ; 15, anus.

5. *The Œsophageal Valve or Proventriculus.*—The œsophageal valve is an annular thickening of the intestinal wall, due partly to circular muscles, which are capable of closing the lumen of the gut when they contract, and partly to an invagination of the more anterior portion of the gut into the more posterior, thus forming a valve. Projecting from it are six small protuberances, more marked in the larva than in the adult insect. Christophers considers that this portion of the alimentary canal is the proventriculus of other insects. It is not lined with chitin.

6. *Mid Gut or Chylific Ventricle.*—The mid gut is a straight tube running from the œsophageal valve at the level of the first pair of legs to the posterior limit of the sixth abdominal segment; but this varies as to whether it is filled with food or not. It consists of two parts: an anterior narrow, and a posterior more distended, often called the 'stomach,' which begins on a level with the second abdominal segment, and is the receptacle for the food. The wall of the stomach is composed of the following layers:—

(1) A delicate internal cuticle.

(2) A single layer of large cylindrical or cubical epithelial cells with large nuclei; their condition varies with the state of distension of the stomach.

(3) An elastic basement membrane.

(4) Muscular fibres, circular and longitudinal, forming a loose network.

In this last layer there are numerous air-tubes or tracheæ, which probably help to keep the gut in position in the cœlom.

7-10. *Hind-Gut.*—This runs from the end of the mid-gut to the anus, being divided into the following regions:—

(1) A dorsally bent portion, the ileum, lined by flattened epithelium.
(2) A ventrally bent portion, the colon, lined by cubical epithelium.
(3) A dilated portion, the rectum, which has six large ovoid papillæ.

The rectum narrows just before the anus, which opens on the last segment of the body.

Malpighian Tubes.—There are five Malpighian tubes opening at the junction of the mid- and hind-gut.

Salivary Glands.—The salivary glands consist of two groups, each containing three acini, lying on each side of the body, in the anterior portion of the thorax, close against the prosternum, and extending almost as far back as the proventriculus. The ducts from each of these acini unite together to form a single duct on each side, which passes forwards through the neck into the head, where it unites beneath the subœsophageal ganglion, with its fellow of the opposite side, to form a common salivary duct. This duct passes forwards to end in the salivary pump, which is continuous with the salivary groove or canal of the hypopharynx. The duct of the salivary gland, therefore, is not in any way connected with the alimentary canal. These glands, which are much larger in the female than in the male, are composed of acini, surrounded by a basement membrane which is very delicate and structureless, and upon which rests a single layer of epithelial cells surrounding a central lumen. The whole acinus lies in a cleft in the fat-body.

Space does not permit of descriptions of the vascular, nervous and muscular systems being included.

Reproductive Organs. The female reproductive organs consist of ovaries, oviducts, and a common oviduct, a mucous gland and its duct, and a spermatheca and duct, while the male organs are testes and vasa deferentia, which after receiving the ducts of the receptacula seminis, run to an ejaculatory duct, which ends in a short penis.

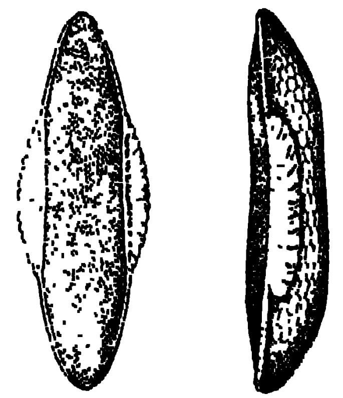


FIG. 387.—EGG OF *Anopheles maculipennis*.

(After Nuttall and Shipley.)

On the left the egg is seen from above, and on the right from the side.

Life-History. A mosquito passes through a complicated life cycle, consisting of an egg, a larval, and a pupal stage, the last-named giving rise to the perfect insect or imago.

Soon after a female insect is hatched it probably becomes fertilized, though some authorities believe that this does not take place until after the first meal of blood, which in any case precedes the oviposition, which takes place in the early morning.

The eggs, which number about one hundred, are laid upon the surface of the water, on which they may be seen arranged in stars, rows, or triangles.

The eggs of *A. maculipennis* are boat-shaped, about 0·5 to 1 millimetre in length, with a flat upper and convex lower surface, and with one end somewhat broader than the other. The head of the larva will be found at this broader anterior end. The upper surface is granular and reticulated, while the lower is smooth. On each side of the middle third the chitinous capsule is thrown into folds, called floats, while the margin projects as a chitinous frill.

The duration of the egg stage has not been well defined. Nuttall and Shipley give two to three days for *Anopheles maculipennis*, but it is probable that it is shorter in the tropics. The appearance and grouping of the eggs are quite different in the Culicinæ, as will be mentioned later.

The larva escaping from the blunt anterior end of the egg by the shifting off of a piece like a cap from the rest of the shell is seen to consist of head, neck, and abdomen.

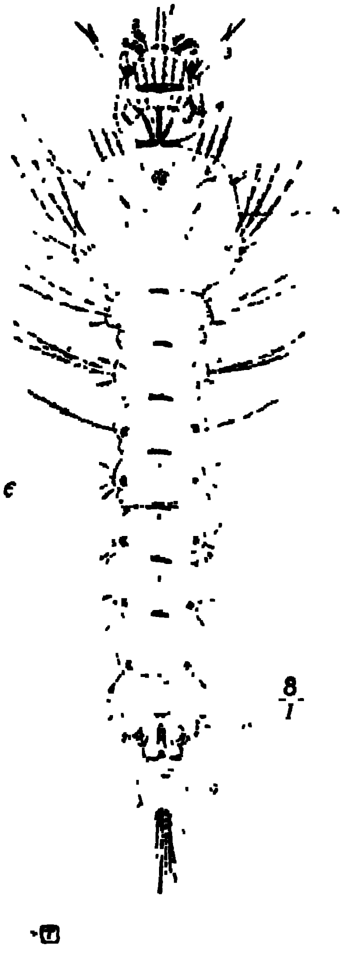


FIG. [illegible]. LARVA OF *Anopheles maculipennis*.

(After Nuttall and Shipley, *Journal of Hygiene*.)

1, Internal clypeal hairs; 2, external clypeal hairs; 3, antennæ; 4, head markings; 5, thorax; 6, abdomen; 7, palmate hair; 8, stigmatic aperture on last segment.

When first hatched the head is very black, but later on it becomes lighter in colour, and shows characteristic markings. At the back of the head there is a little notch, and from this a V-shaped dark line opens forwards, formed by two diverging bands of chitin, arranged along which are patches of pigment, which give rise to the characteristic markings. There are two large compound eyes, behind each of which lies a single eye-spot, or ocellus.

The antennæ are conspicuous rod-like bodies ending in two leaf-shaped appendages, between which is a branched hair, while another hair of specific importance arises from a papilla situated at the junction of the proximal and middle thirds.

Between the roots of the antennæ and projecting forwards there is a smooth shield-like area, the clypeus, which carries four or six hairs, which are also of specific importance. Two of these hairs (internal clypeal hairs) arise anteriorly near the middle line; external to these lie the external clypeal hairs, which arise from the outer angle of the clypeus, and behind them lie the posterior clypeal hairs. Sometimes there is a basal hair external to the antennæ.

The mouth parts consist of two large feeding-brushes, two maxillary palps, two mandibles, and on the ventral median line the under lip of Meinert, a conical chitinous structure, and a snout-like process covered with hairs projecting between the brushes.

The thorax is large, increasing in size as the larva grows older. It has numerous hairs, and sometimes a pair of the palmate hairs presently to be described.

There are nine segments in the abdomen, of which the eighth is characterized by possessing the openings of the tracheæ, and the ninth by possessing four large papillæ, and hair projecting downwards and backwards. The first two segments possess a pair of large feathered hairs on each side, the third a single hair on each side. The others do not possess these hairs. Certain of the abdominal segments have small fan-shaped hairs, called 'palmate hairs,' fixed by a short stalk on the outer side of the dorsum of the segment. Each of these consists of nineteen to twenty leaflets, which are capable of closing and opening upon the stalk like a fan. These hairs are rudimentary in the freshly hatched larva, but in the adult they are well marked, and have been used for purposes of classification, according to the variations in their number and position, and the characters of the leaflets and their terminal hairs, if present. These hairs are of use in helping to keep the larva in its horizontal position when it comes up to breathe on the surface of the water.

The stigmatic siphon is placed, as already mentioned, on the eighth segment, forming by means of raised, toothed, chitinous processes a quadrilateral space.

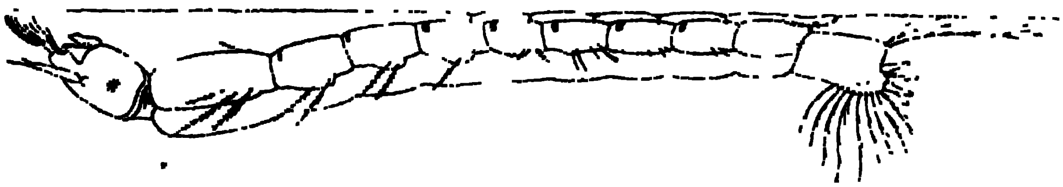


FIG. 389.—LARVA OF AN ANOPHELINE MOSQUITO LYING PARALLEL TO THE WATER

(Modified after Howard.)

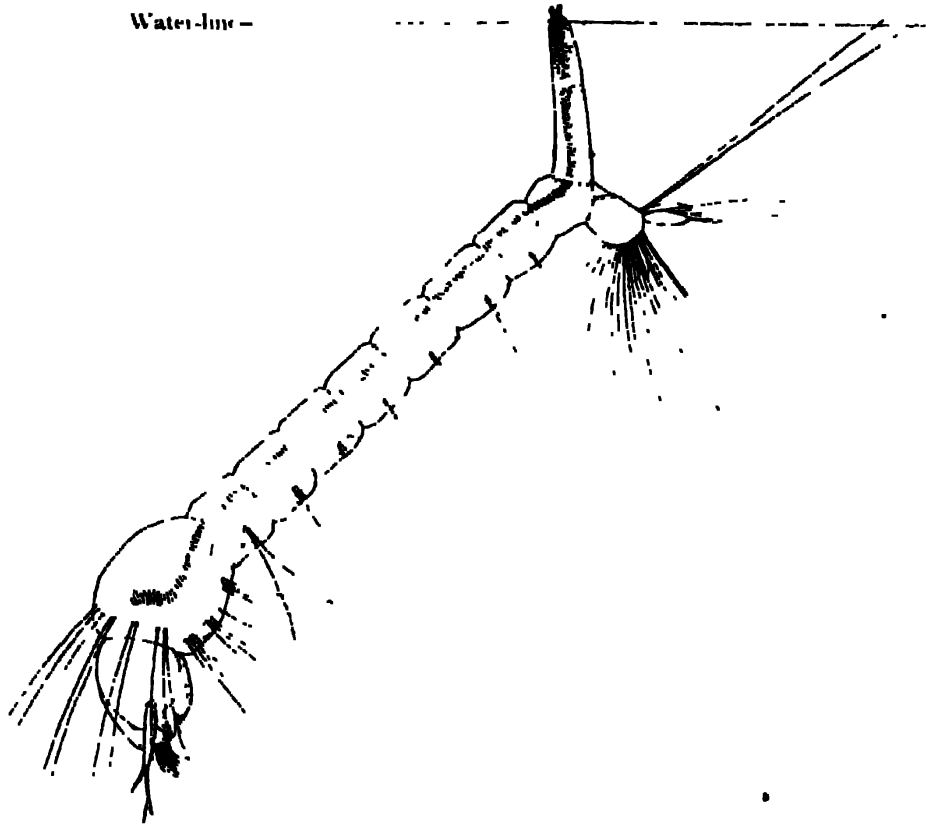


FIG. 390.—LARVA OF A CULICINE MOSQUITO HANGING DOWN FROM THE SURFACE OF THE WATER.

(After Howard.)

The teeth are of great importance, being capable of being approximated so as to close the cavity, and thus protect the two openings of the tracheæ which lie in the anterior portion of the siphon. From these openings the long tracheæ can be seen running from back to front along the larva

The duration of the larval stage varies with food and temperature, being longer in the temperate zone than in the tropics. According to Stephens, it is twelve days in *Cellia argyrotarsis* and eleven days in *Myzomyia rossi*, while it may be eighteen to twenty-one days in *Anopheles maculipennis* in the temperate zone. The larva grows by moulting several times.

Culicine larvæ are easily distinguished from Anopheline larvæ by the fact that the spiracles are carried on a long respiratory siphon, formed by a prolongation of the dorsum of the eighth abdominal segment, which has been used to distinguish the different species (Fig. 390).

Below the siphon on the eighth segment there are spines, forming a comb, while along the length of the siphon there is another comb, distal to which is a tuft of hairs. The variations in these structures, together with those in the length and breadth of the siphon, associated with those of the antennæ and clypeus, afford means of classifying the Culicine larvæ. For further information, consult either Theobald's Monograph, vol iv., p. 6, or Felt's paper, Bulletin 97 of the Division of Entomology of the New York State Museum. The Megarhininæ, Ædinæ, and Uranotæninæ possess larvæ belonging to the Culicine type.

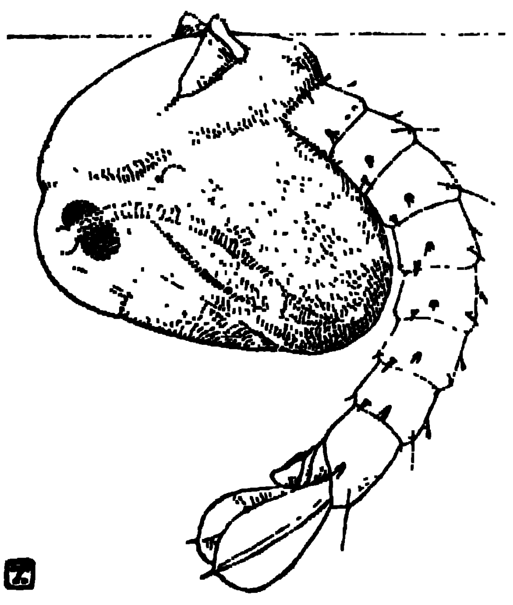


FIG. 391.—PUPA OF *Anopheles maculipennis*.

(After Nuttall and Shipley, *Journal of Hygiene*.)

The pupal stage lasts about forty-eight hours. Towards the end of an afternoon the pupa comes up to the surface, and the dorsal portion of the thorax splits with a T-shaped fissure, and the adult insect or imago emerges. Pupæ do not eat.

Differences between the Anophelinæ and Culicinæ.—The difference between these two important families may popularly be described as follows:

The Anophelinæ, as a rule, project from any plane surface on which they may be resting at a sharply defined angle, owing to their head, thorax, and abdomen forming a more or less straight line; while the Culicinæ, on the other hand, do not make such a well-defined angle, owing to the fact that the abdomen is not in the same straight line as the long axis of the thorax. The eggs of the Anophelinæ are laid singly, while those of the Culicinæ are laid in rafts. The larvæ of the Anophelinæ have no drawn-out siphons, and therefore lie more or less parallel to the surface of the water, while the larvæ of the Culicinæ hang downwards. There are, however, exceptions to these rules—thus, *e.g.*, *Myzomyia culicifacies* rests on a surface like a Culex, not like an Anopheles.

Bionomics.—The imago emerges from the pupa during the late afternoon, after which the females are ready for fertilization by the males. These latter can sometimes be seen in large numbers, while but few females are observed, which is supposed to be characteristic of the breeding period.

The female alone bites man and animals, apparently for the purpose of obtaining rich food for the eggs, while the male feeds on the juices of plants and fruits. The female can also be seen feeding upon vegetable juices, though this is more common in the females of the Culicinæ than in those of the Anophelinæ. It is believed that a female feeds on blood once a day in nature, but this is a difficult matter to be certain about. The mechanism of the bite has already been described in page 223, to which reference should be made. It will also be noted that the structure of the female mouth-parts is adapted for piercing, while that of the male is not. It will also be remembered that only the stylets pierce the skin, and that the labium never does so. Infection of the victim by the malarial germ takes place during the act of biting, as the sporozoites pass down the hypopharyngeal or salivary tube, while the infection of the mosquito is effected by the blood, which passes from the victim along the labial or blood-tube into the mouth. So much blood may be sucked that it may appear *per anum*.

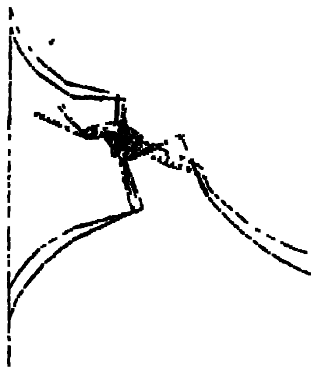


FIG. 392.—DIAGRAM TO SHOW THE POSTURE OF AN ANOPHELINE MOSQUITO ON A WALL.

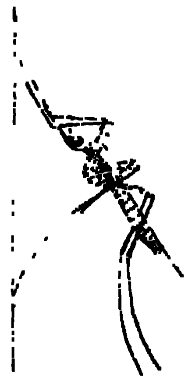


FIG. 393.—DIAGRAM TO SHOW THE POSTURE OF ANOTHER ANOPHELINE MOSQUITO ON A WALL.

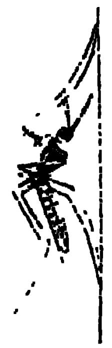


FIG. 394.—DIAGRAM TO SHOW THE POSTURE OF *Culex pipiens* ON A WALL.

(After Sambon, from the *British Medical Journal*.)

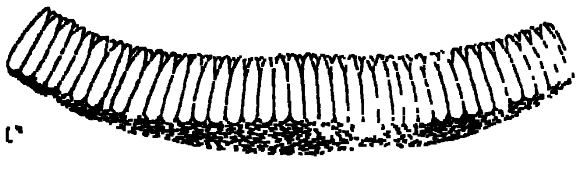


FIG. 395.—RAFT OF CULICINE EGGS. (After Sambon.)

Usually the mosquitoes bite at night, and preferably in the dark, as, for example, they will attack the ankles of people while sitting at dinner at night.

After feeding, the mosquitoes usually retire to a dark portion of the room to digest the food. It is noticeable that they avoid white areas during the daytime, and prefer dark-coloured regions away from the light, and hence are very difficult to find in ill-lighted native huts.

In the early morning the female flies to the nearest water and lays her eggs. Usually she does not travel far, but is believed to be capable of going at least half a mile in case of need.

The females of the Culicinæ do not appear to concern themselves as to the nature of the water in which they lay their eggs, but the female Anophelinæ prefer clean water with a certain amount of weed. This water may be the back eddies of a river, where there is the protection of weeds, or the margins of large lakes, where dense surface vegetation is to be found, or any collection of water which contains green vegetal matter, or, failing these, any collection of fresh or moderately salt water. Small and large wells are a prolific source of mosquitoes, as are puddles, and water in broken bottles, shells, and especially in plants like bamboos, etc. Having laid the eggs, they retire to some dark corner during the daylight, and emerge at night for another feed of blood. How long they live is not known with certainty, and will be discussed, together with other features of their bionomics, in Chapter XL., under Malaria.

Mosquitoes can hibernate during the cold weather of the temperate zone, and æstivate during the dry hot weather of the tropics.

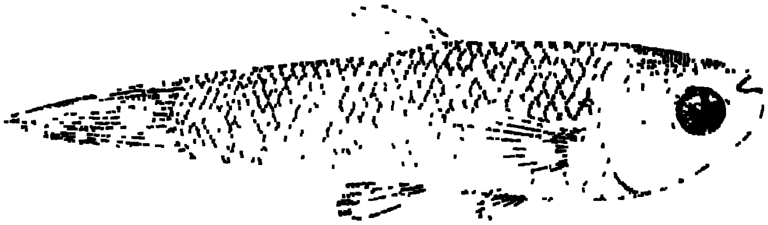


FIG. 300. *Girardinus poeciloides*, DE FILIPPI.
(The tail should have been drawn expanded.)

In this latter condition they bite and suck blood, but apparently do not lay eggs, even if water is provided. The eggs are kept afloat on the surface of the water by their structure, and in due course give rise to the larvæ, which are great eaters, living not merely upon unicellular organisms, such as algæ and diatoms, but also upon their fellows. For purposes of obtaining air they are compelled to come to the surface of the water. The Anopheline larva, not possessing a siphon, has to lie more or less parallel with the surface of the water in order to enable the air to enter the spiracles, and this it is able to do by the aid of the palmate hairs already mentioned: while the Culicine larvæ have merely to bring the apex of the siphon to the surface of the water, from which they apparently hang downwards. Larvæ are certainly able to hibernate, and perhaps eggs also. The pupa does not feed.

Mosquitoes have many enemies and parasites, but the most important from a point of view of the prophylaxis of malaria are those which eat the eggs, the larvæ, and the pupæ, of which fish are the most important.

In 1905 C. K. Gibbons pointed out that a small fish, popularly termed 'millions,' which lived in shallow water, was a voracious feeder on eggs, larvæ, and pupæ of mosquitoes. These fish, which belong to the species *Girardinus pœciloides* de Filippi, are found in Barbados, which is very free from malaria. They are very small, the full-grown female only measuring 1½ inches in length, while the male is smaller. The female is dull in colour, while the male is distinguished by red splashes and a black circular dot on its sides. The great importance of these little fish is that they are able to live in very shallow water, and to work their way in among dense surface vegetation, and thus to gain access to the larvæ, etc., of the mosquitoes, which otherwise are protected by the weeds from attacks by the larger fish. Their classification is Teleostei, Haplomi, Cyprinodontidæ, genus *Haplochilus* McClelland, 1839. The family contains 220 species, of which only 50 live out of America. Haplochilus has 24 species in Africa and 35 in Asia and America. There is no doubt that these small fish should be introduced into malarious places as a prophylactic measure against the disease. Other closely allied species are *G. versicolor* Gunther, found in St. Domingo, and *G. formosus*, found in Florida and South Carolina. With regard to other species, *Gambusca molliensia* is said to be of great value in consuming larvæ, especially when protected by dense surface vegetation. Recently Graham has reported that *Haplochilus grahami* Boulenger, 1911, and *H. bifasciatus* Steindachner, 1881, of the Cyprinodontidæ, eat larvæ greedily, while Gowdey finds the same for *Fundulus tæniopygus* and *Haplochilus pumilus* Boulenger, 1906, in Uganda.

Certain plants, as is well known, collect water, especially the bromelias, the bamboos, and the pitcher plants. In this water Culicine and sometimes Anopheline larvæ can be found. E. E. Green, of Ceylon, has shown that the flowers of the lobster claw plant (*Heliconia brasiliensis*) can hold a considerable amount of water, in which he found Stegomyia and Desvoidea larvæ in large numbers.

Classification. Various methods of classifying mosquitoes have been brought forward. The earliest were based upon the characters of the palpi, but in 1901 Theobald showed that they were useless for anything but specific characteristics, and based his larger divisions on the variations of the scales on the head, body, and wings. Felt brought forward a classification based upon the male genitalia and the wing veins, but, as Theobald remarks, the majority of known mosquitoes being female, it is most undesirable to take only male characters for the classification. Recently Dyar and Knab have issued a classification of the Culicidæ by larval characters, and Eysell has advanced matters considerably by separating the Corethrinæ from the Culicidæ under the term Corethridæ, because the Corethridæ have an entire absence of the long piercing proboscis and of scales in the adults, both of which are marked features of the Culicidæ. It will be evident that this is useful. Lutz has brought forward a classification based upon larval and adult forms, which Theobald has modified and brought into accord with one based upon scales as generic characters, and this classification is followed below.

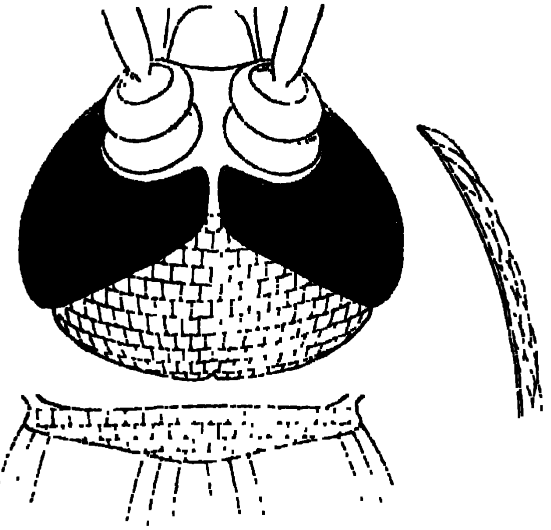


FIG. 407. HEAD AND SCUTELLUM OF MEGARHINUS, TO SHOW THE SCALES. On the right a profile view of the scales (After Theobald, 'Culicidæ of the World

THEOBALD'S CLASSIFICATION.—The Culicidæ may be divided into subfamilies, according to the characters of the scales on the head, body, legs, and wings.

A. Scutellum simple, never trilobed; proboscis straight, palpi long in male and female—*Anophelinæ.*

B. Scutellum trilobed:—

I. Proboscis strongly recurved; first submarginal cell very small—*Megarhininæ.*

II. Proboscis straight: post-scutellum nude:—

1. Wings with six longitudinal scaled veins:—

(1) Antennæ with second joint normal in length:—

(*a*) First submarginal cell as long as or longer than the second posterior cell.

Palpi in the female shorter than the proboscis, long in male—*Culicinæ.*

Palpi short in both sexes—*Ædinæ.*

(*b*) First submarginal cell very small: smaller than second posterior—*Uranotæninæ.*

(2) Antennæ with second joint very long—*Deinoceratinæ*

2. Wings with seven longitudinal scaled veins—*Heptaphlebomyinæ*

III. Proboscis straight: post-scutellum with scales or chætæ:—

1. Palpi long in male, short in female—*Trichoprosoponinæ.*

2. Palpi short in both sexes.—*Dendromyinæ.*

IV. Proboscis elbowed—*Limatinæ.*

Of these, only the Anophelinæ and the Culicinæ, and possibly the Ædinæ, contain species of importance in tropical medicine, and concerning these subfamilies a few details must be given.

ANOPHELINÆ.

Definition.—Culicidæ with straight proboscis; palpi long in both sexes; occiput mostly with upright forked scales, never with flat lateral scales. Thorax with scales or hairs, scutellum never trilobed, with scales or hairs. Postscutellum nude. Abdomen with hairs or scales. Eggs laid singly, and not in rafts. Larvæ without respiratory siphon.

This is a most important subfamily, because it contains the species which are known to carry malaria. The list of known carriers will be found in Chapter XXXV. (p. 883).

It is important for the student of tropical medicine to be able to recognize the genera and species of the more important Anophelinæ. For this purpose we give the following tables taken from Theobald's 'Manual of the Culicidæ,' vol. v., 1910. For fuller information the original work must be consulted, but it must be admitted that there is a growing opinion that Theobald's genera imperceptibly merge with one another, and are not founded on essential points; and Edwards has returned to two genera, *Anopheles* and *Bironella*, therefore in Chapter XXXV. (p. 883) we will give another classification when considering the anophelines which carry malaria.

SUBFAMILY ANOPHELINÆ Theobald, 1901.

Table of Genera.

- A. First submarginal cell very small—*Bironella* Theobald.
- B. First submarginal cell large:—
  - I. Antennal segments with dense lateral scale-tufts—*Chagasia* Cruz.
  - II. Antennal segments with outstanding scales on the second segment and more appressed ones on the first At least one abdominal segment with long flat more or less spatulate scales—*Calvertina* Ludlow.
  - III. Antennal segments without dense lateral scale-tufts:—
    - 1. Thorax and abdomen with hair-like curved scales:—
      - (*a*) No flat scales on head, but upright forked ones.
        - (A) Basal lobe of male genitalia of one segment.
          - (1) Wing scales large, lanceolate—*Anopheles* Meigen.
          - (2) Wing scales mostly small, or narrow, or slightly lanceolate costa spotted—*Myzomyia* Blanchard.
          - (3) Wings similar to (2), but with fourth longitudinal vein very near base of third Prothoracic lobes with outstanding scales—*Neomyzomyia* Theobald.
          - (4) Wings with patches of large inflated scales—*Cycloleppteron* Theobald
        - (B) Basal lobe of two segments:—
          Prothoracic lobes with dense outstanding scales—*Feltinella* Theobald.
      - (*b*) Median area of head with some flat scales; prothoracic lobes mammillated. Wing scales lanceolate—*Stethomyia* Theobald.
    - 2. Thorax with narrow curved scales; abdomen hairy:—
      - (*a*) Wing scales small and lanceolate; head with normal forked scales—*Pyretophorus* Blanchard.
      - (*b*) Wing scales broad and lanceolate; head with broad scales not closely appressed, but not forked or fimbriated—*Myzorhynchella* Theobald.

3. Thorax with hair-like, curved scales, and some narrow curved ones in front; abdomen with apical lateral scale-tufts and scaly venter; no ventral tuft. Wing scales lanceolate *Arribalzagia* Theobald

4 Thorax with hair-like, curved scales, no lateral abdominal tufts; distinct apical ventral tuft Palpi densely scaly Wing with dense, large, lanceolate scales *Myzorhynchus* Blanchard

5. Thorax with hair-like, curved scales, and some narrow, curved lateral ones; abdomen hairy, with dense, long, hair-like, lateral, apical, scaly tufts Wing scales short, dense, lanceolate; fork cells short-- *Christya* Theobald

6. Thorax with very long hair like, curved scales; abdomen with hairs, except last two segments, which are scaly Dense scale-tufts to hind femora Wings with broadish, blunt, lanceolate scales *Lophoscelomyia* Theobald.

7. Thorax and abdomen with scales: -

(*a*) Thoracic scales narrow-curved or spindle shaped; abdominal scales as lateral tufts and small dorsal patches of flat scales *Nyssorhynchus* Blanchard

(*b*) Abdomen nearly completely scaled, with long, irregular scales, and with lateral scale tufts *Cellia* Theobald.

(*c*) Similar to above, but no lateral scale tufts -*Neocellia* Theobald

(*d*) Abdomen completely scaled with large flat scales, as in *Culex* *Aldrichimelia* Theobald

(*e*) Thoracic scales hair-like except a few narrow curved ones in front, abdominal scales long, broad and irregular *Kertészia* Theobald

(*f*) Thorax with narrow hair like, curved scales, some broad straight scales, and some spatulate laterally. Abdomen with fine hairs except last three segments, which have scales Tufts of scales on hind femora Wing scales lanceolate - *Manguinhosia* Cruz

NOTE - The genus *Calodiacesis* Dyar and Knab is said by Theobald to be invalid, being based on *Anopheles barberi*, which is a true *Anopheles*.

Anopheles Meigen, 1818.

Essentially *Anopheles* are temperate zone or hill station Anophelinæ, of which the type *Anopheles maculipennis* Meigen, 1818, has been already described

Eighteen species are definitely known, but in addition there are the uncertain species of *A ferruginensis* Wiedemann, *A martini* Laveran, *A. pursati* Laveran, *A vincenti* Laveran, *A vestitipennis* Dyar and Knab, 1906, *A strigimacula* Dyar and Knab, 1906, *A apicimacula* Dyar and Knab, 1906, *A punctimacula* Dyar and Knab, 1906, etc

Theobald gives the following table by means of which the species may be recognized. -

ANOPHELES

A Wings spotted·

I Legs unbanded·

1. Wings with spots formed of collections of scales on the wing field, no costal spots *maculipennis* Meigen

2 Wings with light and dark costal markings.

(1) Costa with two yellow spots:-

(*a*) Large species: --

(A) No fringe-spots --*punctipennis* Say.

(B) Fringe-spots present--*pseudopunctipennis* Theobald.

(*b*) Small species. Wings much spotted—*franciscanus* McCracken.

(2) Costa with one spot—*perplexus* Ludlow.

II. Legs with basal pale bands:—
  1. Costa with two large dark spots—*gigas* Giles.
  2. Two large and two small basal spots—*formosus* Ludlow.
III. Legs with narrow apical bands:—
    Costa dark, with two small pale yellow spots—*wellcomei* Theobald

B. Wings unspotted:—
  I. Legs unbanded:
    1. Thorax adorned as in Corethra—*corethroides* Theobald.
    2. Thorax normal ornamentation
      (*a*) Second fork cell much more than half the length of the first.
        (1) Palpi unbanded
          (A) Petiole of first fork cell more than one third length of cell
            Abdomen with golden hairs—*bifurcatus* Linnaeus
            Abdomen with brown hairs—*algeriensis* Theobald.
          (B) Petiole of first fork cell one third length of cell—*barberi* Coquillett
        (2) Palpi banded. Dark species. Wing scales very dense—*smithii* Theobald
          Wing scales not so dense—*nigripes* Staeger
      (*b*) Second fork cell not more than half the length of the first—*aitkenii* Theobald
  II. Legs banded.
    1. Hind femora only with broad white band—*lindsayi* Giles
    2. Apices of hind tarsi pale—*immaculatus* Theobald

Myzomyia Blanchard, 1902

This *Myzomyia* includes some important mosquitoes found in West Africa, and in India and Ceylon, which are carriers of malaria.

The diagnostic table given by Theobald is as follows:

MYZOMYIA.

A. Proboscis unbanded:
  1. Legs banded:—
    (*a*) Palpi with three white rings.
      (1) Legs with faint apical pale bands
        Wing fringe spotted—*funesta* Giles
      (2) Legs with prominent apical pale bands and a broad, pale, median band to fore and mid-metatarsi—*lutea* Theobald.
      (3) Legs (hind) with apical and basal pale bands
        Wings with five to six pale costal spots, the largest T-shaped—*rossii* Giles.
        Wings with three yellow costal spots—*longipalpis* Theobald.
    (*b*) Palpi with two white rings:
      (1) Apex white—*aconita* Dönitz
      (2) Apex black—*d'thali* Patton
    (*c*) Palpi with four white rings—*p hali* Patton.
  2. Legs spotted and banded:—
    (*a*) Supernumerary cross-vein straight. Palpi with three white bands. Apical and basal pale leg banding.
      (1) Third large costal spot with two spots beneath on first vein—*ludlowi* Theobald.
      (2) Similar, but much smaller—*mangyana* Banks
      (3) Third costal spot T-shaped, as in *rossi*—*indefinata* Ludlow.
      (4) Thorax with two ocelli; wings much spotted—*tessellata* Theobald
    (*b*) Supernumerary cross-vein markedly curved—*pyretophoroides* Theobald.

- 3. **Legs unbanded**:—
  - (*a*) Apex of palpi white and ringed. Three pale palpal bands.
    - (A) Third long vein mostly yellow—*listoni* Liston.
    - (B) Third long vein dark.
      - (1) Several fringe-spots—*leptomeres* Theobald.
      - (2) Two fringe-spots—*culicifacies* Giles.
      - (3) No fringe spots—*rhodesiensis* Theobald.
  - (*b*) Apex of palpi white only—*nili* Theobald.
  - (*c*) Apex of palpi black.
    - (1) Black apex narrow—*turkhudi* Liston.
    - (2) Black apex broad—*hispaniola* Theobald.
- 4. Legs with spots only at joints. Palpi with three bands; apex black—*azriki* Patton.

B. Proboscis banded:

- I. Legs unspotted—*albirostris* Theobald.
- II. Legs spotted—*thorntoni* Ludlow.

Neomyzomyia Theobald, 1912.

This genus includes only one species, *Neomyzomyia elegans* James, 1903. It is found in India.

Pyretophorus Blanchard, 1902.

The important species is *Pyretophorus costalis*, the spreader of malaria in West Africa and Mauritius.

PYRETOPHORUS

A. Legs unbanded:—

- I. **Palpi with three pale bands; apex black**—***nigrifasciatus*** **Theobald.**
- II. Palpi with three pale bands; apex white:—
  - (*a*) Wings with four large and two small black costal spots; mid cross-vein very long—*nursei* Theobald.
  - (*b*) Wings with four large black spots; mid cross-vein normal—*minimus* Theobald.
  - (*c*) Wings with five large black costal spots:—
    - (1) First fork cell much longer than the second posterior—*sergenti* Theobald.
    - (2) First fork cell about as long as the second cell—*palestinensis* Theobald.

B. Legs banded:—

- I. Legs with apical banding. Hind legs only banded. Palpi, black apex, and three pale bands.
  - (*a*) Three dark lines on post scutellum—*myzomyfacies* Theobald.
  - (*b*) Two dark lines on post-scutellum—*chaudoyei* Theobald.
- II. All legs with apical pale bands. Palpi with three white bands.
  - (*a*) Wings with four black costal spots, fringe unspotted—*superpictus* Grassi.
  - (*b*) Wings with four large and two small costal spots; fringe spotted.
    - (A) Apical palpal band broad, other two small—*jeyporensis* Theobald.
    - (B) Apical and median palpal bands broad—*austeni* Theobald.
    - (C) Thoracic scales creamy—*pitchfordi* Power.
- III. **Fore and hind legs with apical pale bands.**
  Four white palpal bands—*cinereus* Theobald.

C. Legs spotted and banded:—

- I. **Last three hind tarsals all white.**
  Thorax golden scaled—*aureosquamiger* Theobald.
- II. **Last hind tarsal not white**:—
  - (*a*) **Femora and tibiæ spotted.** Tarsal bands apical. **Three palpal bands.**

(A) Apical one broad; others narrow:—
(1) Fringe-spots narrow—*costalis* Loew.
(2) Fringe-spots broad—*merus* Dönitz.
(B) Apical and median ones broad—*marshalli* Theobald.
(*b*) No spots on femora—*pseudocostalis* Theobald
(*c*) Femora, tibiæ, and first tarsals spotted. Tarsal bands apical. Four palpal bands—*ardensis* Theobald.

Myzorhynchus Blanchard, 1902.

These mosquitoes are usually said to only occur in the open, but we have repeatedly found *Myzorhynchus barbirostris* in houses. *M. sinensis* is known to carry the parasite of malaria in Japan. No species have so far been reported from America.

The thirteen species can be recognized as follows (it has been asserted that *Anopheles coustani*, which has never been correctly placed, is *M. coustani* Laveran, but see Chapter XXXV. on this point):—

MYZORHYNCHUS.

A. Palpi unbanded:—
I. Last hind tarsals brown Legs with pale apical tarsal bands:—
(*a*) One fringe spot
(1) Legs not spotted—*barbirostris* van der Wulp.
(2) Legs with speckled femora and tibiæ, and more numerous 'round-ended' scales on the wing—*pseudobarbirostris* Ludlow.
(*b*) Several fringe-spots—*bancrofti* Giles.
(*c*) No fringe spot.
(1) One pale costal spot; wings with light and dark scales—*umbrosus* Theobald.
(2) Two pale costal spots; wings mostly dark scaled—*strachani* Theobald
II. Last hind tarsal white—*albotæniatus* Theobald.

B. Palpi banded:—
I. Last hind tarsal brown:—
(*a*) Wing-fringe with one pale spot—*sinensis* Wiedemann.
(*b*) Wing-fringe unspotted.
(A) Palpi with four pale bands; apex white.
1. Wings with two yellow costal spots.
(1) Wings distinctly spotted—*vanus* Walker.
(2) Wings without prominent spots—*pseudopictus* Grassi.
2. Wings with two white costal spots—*minutus* Theobald.
(B) Apex of palpi black—*nigerrimus* Giles.
II. Last two hind tarsals white—*mauritianus* Grandpré.
III. Last three hind tarsals white—*paludis* Theobald.

Nyssorhynchus Blanchard, 1902.

The important member is *Nyssorhynchus fuliginosus* Giles, 1900 which is without doubt a malarial carrier Theobald's diagnostic table is as follows:—

NYSSORHYNCHUS.

A. Last hind tarsals brown:—
Legs spotted:—
(*a*) Apical pale bands to legs.
(1) Proboscis dark—*stephensi* Liston.
(2) Proboscis pale on apical half—*masteri* Skuse.
(*b*) Apical and basal pale banding—*annulipes* Walker.

B. Last hind tarsal white:—
  I. Legs spotted with white:
    (a) Palpi with three white bands *willmori* James.
    (b) Palpi with four white bands *maculatus* Theobald
  II. Legs not spotted, four palpal bands *karwari* James

C. Last two hind tarsals white. Legs with mottled femora, tibiæ, and tarsi; three white palpal bands:
    (a) Two apical palpal bands close together *theobaldi* Giles
    (b) Two apical palpal bands far apart *pretoriensis* Theobald.

D. Last two and a half to two and three quarters tarsals white—*tibani* Patton

E. Last three hind tarsals white
  I. Palpi with three white bands.—
    (a) Palpi spotted, legs spotted—*maculipalpis* Giles
    (b) Palpi spotted, hind legs not banded—*indiensis* Theobald
    (c) Palpi not spotted, legs spotted *jamesii* Theobald
    (d) Palpi and legs not spotted
      (1) Wings with four white costal spots *fuliginosus* Giles.
      (2) Wings with five white costal spots *nivipes* Theobald
  II. Palpi with four white bands *philippinensis* Ludlow

F. Legs uniformly brown *brunnipes* Theobald

Cellia Theobald, 1902

This genus which is widely distributed throughout the tropics, has two malarial carriers, *Cellia argyrotarsis* and *C. albimana* the latter being also known as a filarial carrier

CELLIA

A. Legs with last three hind tarsals white:
  I. Dark species *argyrotarsis* Robineau Desvoidy.
  II. Dark species, but with whitish grey apex to abdomen *braziliensis* Chagas.
  III. Yellowish species *pulcherrima* Theobald.

B. Legs with last hind tarsals white
  I. Femora and tibiæ mottled; apical foot bands *pharoensis* Theobald.
  II. Femora and tibiæ not mottled *bigoti* Theobald

C. Legs with last hind tarsal white except base, second and third white—*albimana* Wiedemann.

D. Legs with last hind tarsal dark
  I. Dark species, three white long lateral thoracic lines *squamosa* Theobald
  II. Pale species:—
    (a) Thorax with two eye like spots, pleuræ pale with large black spots *kochi* Dönitz
    (b) Similar, but with wings more spotted *punctulata* Dönitz

SUBFAMILY CULICINÆ Theobald, 1901.

Definition. Culicidæ with straight proboscis, long palpi in the male, short in the female. Post scutellum nude, wings with a long first submarginal cell and without a third anal vein. Larvæ with respiratory siphons.

Remarks.—There are upwards of sixty-three known genera, but of these only *Stegomyia*, *Culex*, and perhaps *Mansonia*, are of importance to medical men at present.

Stegomyia Theobald, 1901.

Definition.—Culicinæ with the head and scutellum clothed with flat scales.

Remarks.—The important species is *Stegomyia fasciata*, the tiger mosquito, which spreads yellow fever. It is peculiar in that it bites chiefly in the afternoon. It is found all over the world, which is due to the fact that it can live on board ship easily.

Unfortunately its name is about to be changed either to *S. calopus* Meigen, or *S. frater* Desvoidy. Theobald at present is not certain which will prove to be the correct term. The name as it stands at present is *S. fasciata*

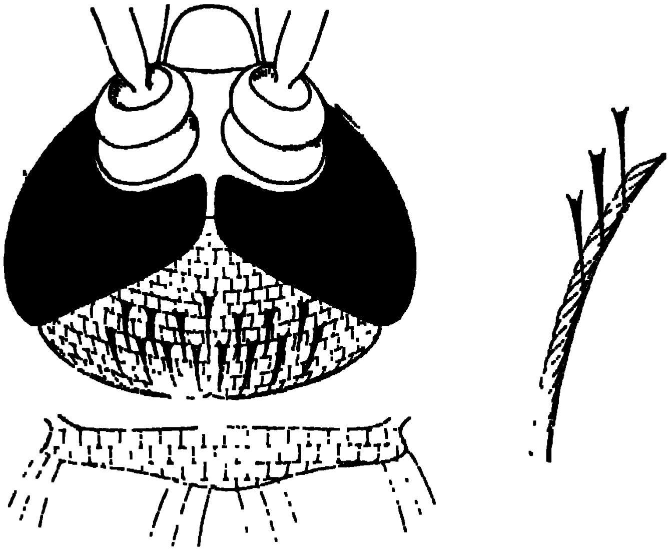


FIG. 308. HEAD AND SCUTELLUM OF STEGOMYIA, TO SHOW SCALES. (After Theobald, 'The Culicidae of the World')

Fabricius 1805, (*non* O. F. Muller, 1764) (synonyms, *Culex calopus* Meigen 1818 (?), *C. frater* Desvoidy, 1827). O. F. Muller, it appears, used the term 'fasciata' for a *Culex* in 1764.

STEGOMYIA

A. Proboscis banded.
  - I. Legs basally banded.
    - (*a*) Thorax brown, with scattered creamy white scales—*annulirostris* Theobald.
    - (*b*) Thorax black, with narrow, curved golden scales—*periskelata* Giles.
  - II. Legs with basal and apical banding. Fore legs with no bands, mid with apical and basal bands on first tarsal and second tarsal, hind with basal bands.
    - Thorax white in front, with a brown eye-like spot on each side—*thomsoni* Theobald.

B. Proboscis unbanded:
  - I. Legs basally banded.
    - (*a*) Abdomen basally banded.
      - (A) Thorax with one median silvery white line—*scutellaris* Walker.
      - (B) Thorax similar, but with two white spots near where the line ends.
      - (C) Thorax with two median yellow lines and lateral curved silvery lines—*fasciata* Fabricius.
      - (D) Thorax with two short median pale lines and a white patch on each side—*nigeria* Theobald.
      - (E) Thorax with large lateral white spots in front, smaller ones by the wings, two narrow median yellow lines, and two posterior submedian white lines—*lilii* Theobald.
      - (F) Thorax with a white W-shaped area in front, a prolongation curved on each side enclosing a brown, eye-like spot—*alba* Theobald.

(G) Thorax with white frontal median spot, two large lateral spots, one small spot on front of wings, one narrow median white line and narrow submedian lines on posterior half. Last two hind tarsi white—***wellmani*** Theobald.

(H) Thorax brown, with broad white line in front, extending laterally towards the wings, where they swell into a large patch, a white line just behind wings. Last two hind tarsi white—*albipes* Theobald.

(I) Thorax with silvery white spot on each side in front, small spot over root of wings, and a white spot over the base of the wings—***pseudonigeria*** Theobald.

(J) Thorax with two lateral white spots, the front one the largest, a small median one near the head; two yellow median lines and a short silvery one on each side before the scutellum—***simpsoni*** Theobald.

(K) Thorax with a silvery white scaled area in front, and another on each side in front of wings—***argenteomaculata*** Theobald.

(L) Thorax with a median, yellowish-white line, a silvery patch on each side in front of the wings, extending as a fine yellow line to scutellum, and another silvery spot before base of each wing—***poweri*** Theobald.

(M) Thorax with small grey-scaled area in front of roots of wings and three short creamy lines behind—***minutissima*** Theobald.

(N) Abdomen black, fifth segment with yellow basal band, sixth unbanded, (seventh) two medio-lateral white spots, (eighth) two baso-lateral white spots; second hind tarsi nearly white—***dubia*** Theobald

(*b*) Abdomen unbanded

(1) Third hind tarsal nearly all white.
Thorax with two lateral white marks directed upwards—***africana*** Theobald.

(2) First hind tarsal all white.
Thorax with one white spot anteriorly, and one in front of each wing—***apicoargentea*** Theobald
Thorax chestnut brown—*terrens* Walker.

II. Legs with white lines as well as basal bands.
Thorax brown, with white lines; abdomen with basal bands—***granti*** Theobald.

III. Fore and mid legs with apical bands; hind basal.
Fourth tarsal of hind-legs nearly all white — ***mediopunctata*** Theobald.
Base of mid-metatarsi, base and apex of hind, and base of first tarsal with pale banding—***assamensis*** Theobald.

IV. Legs unbanded:—

(*a*) Abdomen basally banded

(1) Thorax with front half silvery white, remainder bronzy-brown—***pseudonivea*** Theobald.

(2) Thorax deep brown with scattered golden scales—***albocephala*** Theobald.

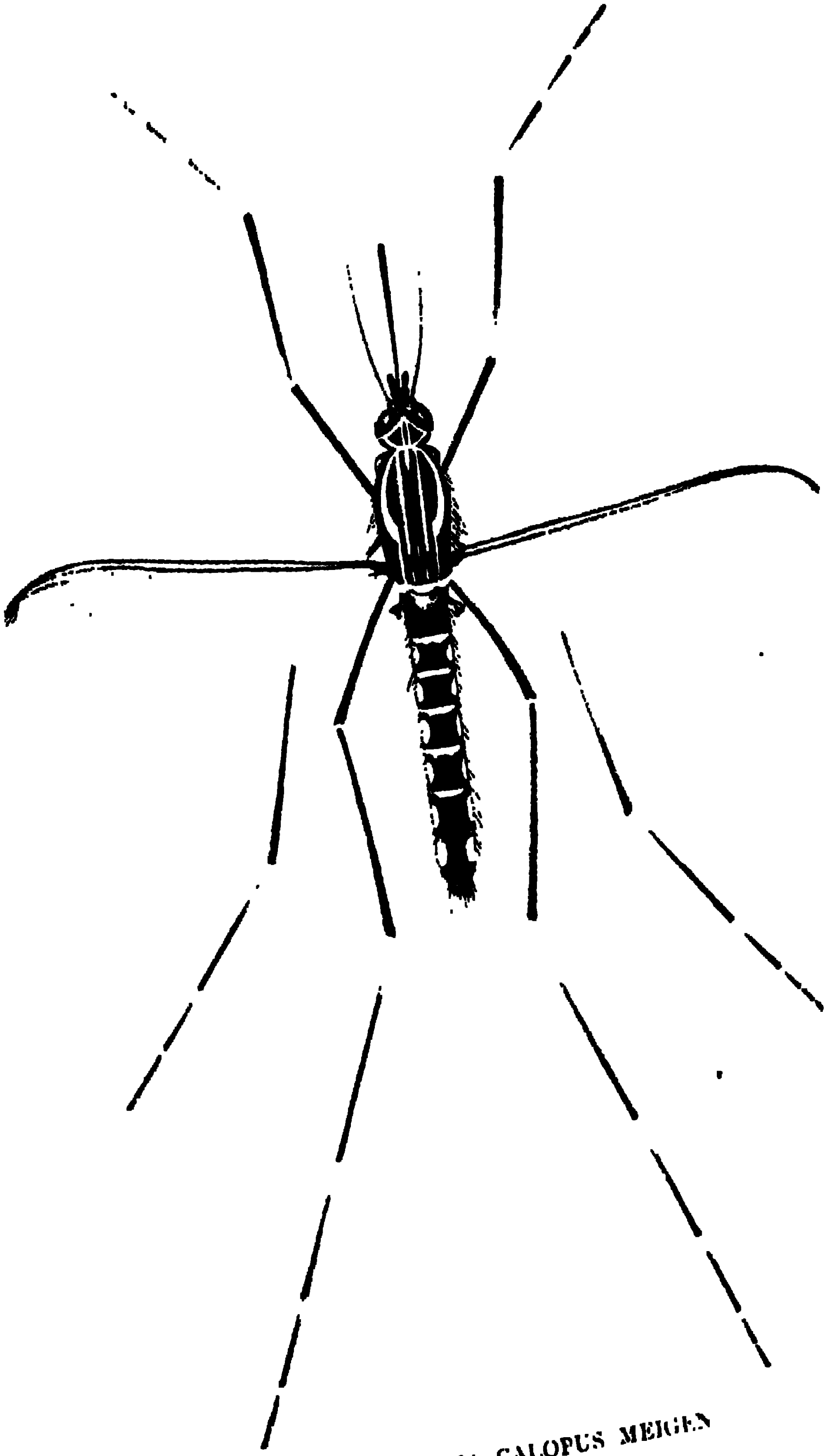
(3) Thorax brown with golden stripes—***auriostriata*** Banks.

(*b*) Abdomen banding indistinct.
Thorax with broad silvery white patch on each side anteriorly—***albolateralis*** Theobald.

(*c*) Abdomen unbanded.
Thorax with six silvery spots—***argenteopunctata*** Theobald.

(*d*) Abdomen with apical white lateral spots.
Thorax unadorned, except for pale scaled lines laterally—***punctolateralis*** Theobald.

PLATE IV.



STEGOMYIA CALOPUS MEIGEN

FEMALE.

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Geo. Waterston & Sons Ltd. Edin

(e) Abdomen with basal white lateral spots.
  (1) Thorax with two pale, indistinct, median, parallel lines, and two silvery lateral spots—*minuta* Theobald.
  (2) Thorax unadorned.
    White spot mid-head—*tripunctata* Theobald.
    No white spot—*amesii* Ludlow.

C. Proboscis yellow basally, dark apically.
  Abdomen with apical pale bands—*crassipes* van der Wulp.

D. Proboscis with median interrupted white line on basal half.
  Head black with grey margin—*albomarginata* Newstead.

NOTE.—*S. lamberti* Ventrillon; *S. leucomeres*, *S. desmotes* Giles; *S. striocrura* Giles, of uncertain position.

Culex Linnæus, 1758.

Definition.—Culicidæ with head covered with narrow, curved scales above, flat scales at the sides, and upright forked scales. Male palpi long, acuminate. Female, short. Thorax with hair-like, curved scales or narrow curved scales. Linear lateral vein-scales.

Remarks.—The important species are *Culex pipiens* Linnæus and *C. fatigans* Wiedemann.

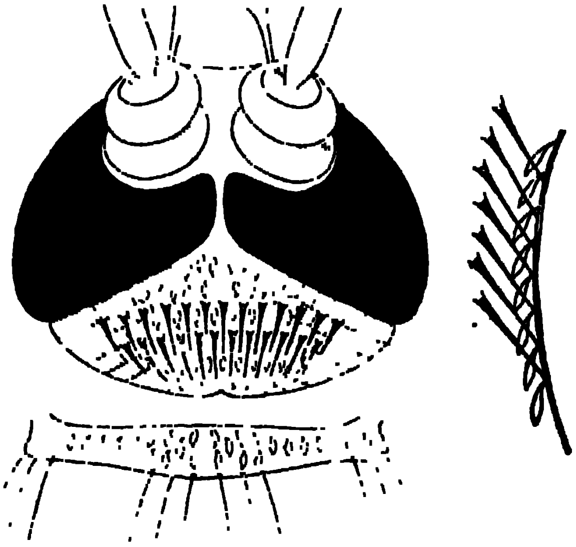


FIG. 309. HEAD AND SCUTELLUM OF A CULEX, TO SHOW SCALES

(After Theobald, 'Culicidæ of the World.')

Culex pipiens Linnæus, 1758.

Synonyms.—*Culex vulgaris* Linnæus, 1767; *C. alpinus* Linnæus, 1767; *C. agilis* Bigot; *C. ciliaris* Linnæus, 1767; *C. communis* de Geer; *C. rufus* Meigen, 1818; *C. phytophagus* Ficalbi, 1889.

C. pipiens is widely distributed in Europe, North Africa, and North America, where it is the common brown mosquito.

Its general appearance is well shown in the illustration in which the head is brownish from the golden-brown scales, as are the proboscis, palpi, and antennæ. The thorax is dark brown, with golden-brown curved scales, and with three black lines due to black bristles. Abdomen brown, with basal yellow bands. Legs are brown and unbanded.

Culex fatigans Wiedemann, 1828.

Synonyms.—*Culex æstuans* Wiedemann, 1828; *C. pungens* Wiedemann, 1828; *C. pallipes* Meigen, 1838; *Heteronychia dolosa* Arribalzaga, 1896.

This is the common brown house-mosquito of the tropics, which is believed to spread dengue fever.

It resembles the above, but has only two dark lines on the thorax as a rule, while the basal abdominal bands are white or pale cream colour, and the first fork cell is longer.

ÆDINÆ Theobald.

Definition.—Culicidæ with straight proboscis, short palpi in both sexes, usually plumose antennæ in the male, pilose in the female. Wings with six scaled longitudinal veins, and with the first submarginal cell as long as or longer than the second posterior. Post-scutellum nude.

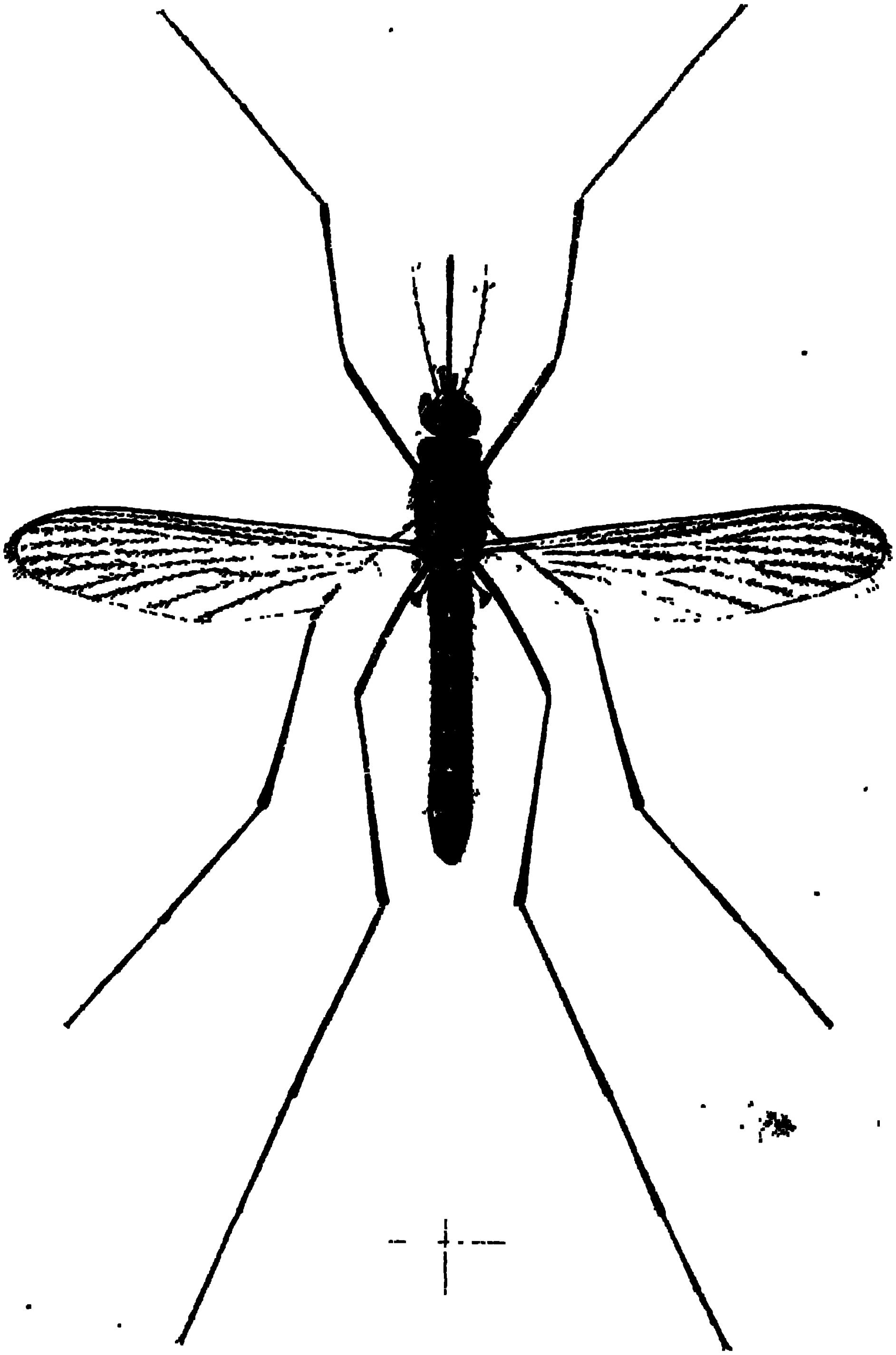


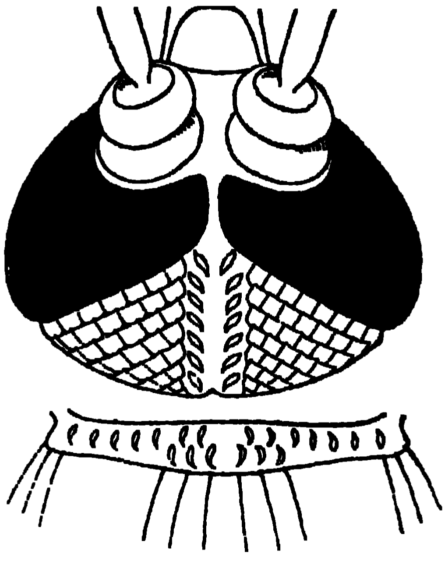
FIG. 400.—*Culex pipiens* LINNAEUS.

The mosquitoes included in this subfamily are generally found in the jungle, and not in habitations.

Daniels thinks that perhaps they may be proved to be malarial carriers (see

Chapter XXXV.). Loew suspects some of them (*Hæmogogus ?*) as possible carriers of *Filaria* (especially *F. perstans*).

The eggs are laid in rafts, and the larvæ have respiratory siphons. A number of genera are described by Theobald, whose work should be consulted if further information is desired.



[Fig. 401.—Head and Scutellum of Ædes, to show Scales.

(After Theobald, 'Culicidæ of the World.')

Limatinæ Theobald.

Definition.—Culicidæ with elbow-bent proboscis and squamæ on post-scutellum. Palpi short in both sexes. First fork cell longer than second.

Genus.—*Limatus.*

Family Corethridæ

Eysell, 1905.

Definition.—*Orthorrhapha nemocera* with short proboscis not formed for piercing, without scales in the adult condition, with transparent larvæ rather resembling those of *Chironomus.*

Remarks.—The only reason why this family, which includes the genera *Corethra* and *Mochlonyx*, is mentioned here is that it has only cently been separated from the Culicidæ, of which it formed subfamily—Culicinnorphæ.

Family Chironomidæ.

Synonyms. –*Tipulariæ culiformis*, *Culicites* Newman, *Tipiladæ* Leach, *Chironomii* Zelt, *Chironominæ* Rondani

Definition.—*Orthorrhapha nematocera* with head small, often retracted under and covered by the thorax. Ocelli absent. No transverse suture on thorax; eyes reniform. Antennæ from six to fifteen joints: pectinate in male, simple and composed of fewer joints in female. Wings without veins along the posterior margin; costal vein ending near the tip of the wing.

Remarks.—The Chironomidæ include over 800 species of very delicate and often quite minute flies, popularly called 'midges,' which are found all over the world, especially near water.

Kieffer classifies the family into three subfamilies, as follows:—

A. Media and cubitus united by a cross vein—*Tanypinæ.*

B. Media and cubitus united only at the base.

- I. Thorax humped over the head—*Chironominæ.*
- II. Thorax not humped over the head—*Ceratopogoninæ.*

Of these three subfamilies only the last concerns us.

SUBFAMILY CERATOPOGONINÆ Kieffer, 1899.

Definition.—Chironomidæ with the thorax not prolonged over the head, antennæ with fourteen, rarely thirteen, joints in both sexes, and the last joint never longer than the two preceding taken together, while the last five are longer or almost the same as the preceding joint.

Life-History.—The eggs may be laid on land or water. If they are laid on land the larvæ and pupæ resemble those of *Phlebotomus*, presently to be described; while if they are laid in water they occur in small clusters of thirty to sixty eggs. The larva is snake-like and transparent, and lives on the surface of stagnant water, or slowly flowing streams, along which it wriggles and finally develops into a dark coloured inactive pupa, with usually breathing organs on the thorax, which floats on the surface of the water.

Genera.—The subfamily has been especially studied by J. J. Kieffer, who recognizes the following genera: *Leptoconops* Skuse, 1889, *Ceratopogon sensu stricto* Kieffer, 1899; *Culicoides* Latreille, 1809; *Ecacta* Poey, 1851; *Bezzia* Kieffer, 1899; *Brachypogon* Kieffer, 1899; *Ceratolophus* Kieffer, 1899, *Palpomyia* Meigen, 1818. Of the other genera usually mentioned he considers *Tersesthes* Townsend, 1893, and *Mycterotypus* Noé, 1905, to be simply synonyms of *Leptoconops* Skuse, 1889; and *Psychophæna* Philippi, 1865, *Tetraphora* Philippi, 1865, and *Didymophleps* Weyenbergh, 1883, to be identical with either *Ceratopogon* or *Culicoides*, but which it is impossible to say, as the descriptions are too imperfect.

Key of Genera.

- (*a*) Wings absent or rudimentary.
- (*aa*) Wings present.
  - (*b*) Median cubital cross vein present (*i.e.*, cell enclosed by a vein).
  - (*bb*) Median-cubital cross vein absent.
    - (*c*) Wing with four to five very indistinct longitudinal veins, wing club shaped, the anterior margin with a long, curved seta; the antennæ with about twelve joints.
    - (*cc*) Wing margin without long, curved seta.
      - (*d*) Proboscis and palpi rudimentary.
      - (*dd*) Palpi not rudimentary.
        - (*e*) Antennæ with not more than ten joints.
        - (*ee*) Antennæ with thirteen to fifteen joints.
- (*f*) Antennæ fifteen jointed (European and tropical genera).
  - (*g*) Wings hyaline.
  - (*gg*) Wings spotted—(1) *Ecacta*.
- (*ff*) Antennæ fourteen or less joints.
  - (*g*) Thorax rounded and not produced over the head. Antennæ thirteen to fourteen joints, legs of moderate length.
    - (*h*) Antennæ thirteen joints—(2) *Leptoconops*.
    - (*hh*) Antennæ fourteen joints, plumose in the male, sparsely paired in female. Typical wing venation.
- (*i*) Wings hairy; last joint of tarsus with an empodium.
  - (*j*) Empodium well developed, almost as long as the claws, which are without setæ—(3) *Ceratopogon*.
  - (*jj*) Empodium not so distinct, less than half as long as the claws, which have setæ on the underside—(4) *Culicoides*.

(*ii*) Wings bare; pulvilli and empodium wanting.
  (*j*) Wing with R_1 distinctly separated from R_{2+3}, and not connected with it by the cross vein like R_2 (5) *Bezzia.*
  (*jj*) Wing with R_2 present, cells sometimes indistinct.
    (*k*) Media wanting--(6) *Brachypogon.*
    (*kk*) Media present.
      (*l*) Femora unarmed -(7) *Ceratolophus.*
      (*ll*) Some of the femora spinose beneath - (8) *Palpomyia.*

Leptoconops Skuse, 1889.

Synonyms.--*Tersesthes* Townsend, 1893; *Mycterotypus* Noé, 1905.

The flies of the genus are found in Egypt, Australia, New Mexico, and Italy.

The various species are *L. kertészi* Kieffer, 1908; *L. stygius* Skuse, 1889; *L. torrens* Townsend, 1893; *L. bezzii* Noé, 1905; and *L. irritans* Noé, and they can be recognized as follows:

A. Antennæ of the female, twelve joints, with verticillates twice as long as the thickness of the joint. Palpi three jointed. Costal nervure stops at the cubitus. Legs without spines, except four anterior: metatarsi tarsal hooks simple (Egypt- *L. kertészi* Kieffer).

B. Antennæ of the female thirteen articles.

  I. Palpi with four joints, legs without spines, tarsal hooks simple, costal nervure stops at the cubitus, flagellum with dense verticillates (Australia *L. stygius* Skuse).

  II. Palpi with three joints.
    (*a*) Legs without spi[illegible] tarsal hooks simple, costal nervure nearly to the extremity of the wing, verticillates of flagelli a little shorter than thickness of joints (New Mexico- *L. torrens* Townsend).
    (*b*) Legs armed with spinules, especially the tibias.
      (1) Tarsal hooklets of the female with one large basal tooth: those of the male unequal; the anterior with one long, curved, S shaped tooth: the posterior with a short, arched tooth (Italy *L. bezzii* Noé).
      (2) Tarsal hooklets of the female with one strong basal tooth, flagellum with some verticillates, spinose, and stronger than in *L. bezzii* (Italy *L. irritans* Noé).

New species are *L. lauræ* Weiss, 1912, Tunisia; and *L. interruptus* Enderlein, 1907, South Africa.

Ceratopogon *sensu stricto* Meigen, 1803.

Definition.- Ceratopogoninæ, with long haired wings, especially in the female, and with a very apparent and hairy empodium on the last joint of the tarsus.

Type. *Ceratopogon bipunctatus* Linnæus.

Kieffer has subdivided this genus into the subgenera *Ceratopogon*, *Atrichopogon*, and *Forcipomyia*, but none of the species of these genera are definitely known to suck the blood of vertebrates.

although Austen states that in the type specimen of the species *C. castaneus* Walker, 1848, the abdomen is apparently distended with blood as far as can be judged by external examination.

Culicoides Latreille, 1809.

Synonyms.—*Ceratopogon* Meigen, 1803, *pro parte*; *Cheironomus* Fabricius.

Definition.—Ceratopogoninæ with body small, pilose, or bare. Head depressed in front, prolonged into a short rostrum. Proboscis, which is markedly longer than the head, with fleshy labium; labrum horny, seated on base of labium. Maxillæ long and horny. Antennæ filiform, fourteen-jointed, hairy, with the second to eighth joints cylindrical, ovate, and the next four or five more elongate and subcylindrical, and the last joint ovate and cylindrical. Subcostal vein ending much beyond half the length of wing: radial ending near tip; cubital ending by the tip. Abdomen composed of eight segments. Legs almost equal in length; femora armed beneath with spines.

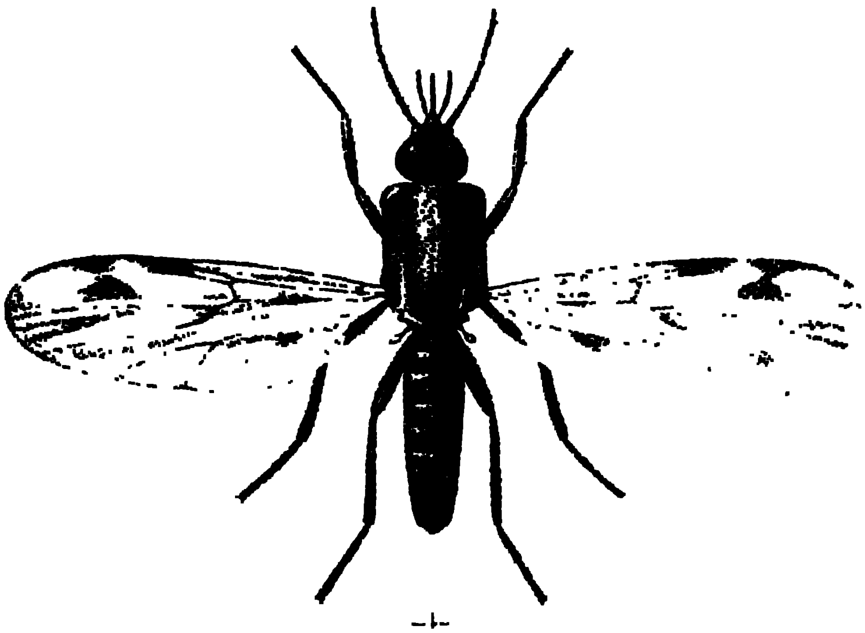


FIG. 402.—*Culicoides pulicaris*: FEMALE.
(After Austen, 'British Blood-Sucking Flies.')

Type.—*Culicoides pulicaris* Linnæus.

There are over one hundred known species of this genus (and many more have been described since this statement was first written), in which only the females suck blood, which they do most viciously, and though they are not known to cause disease, still they give rise to much irritation, especially as, being very small, they can get through any ordinary mosquito-netting. The eggs of the naked species are laid in water, attached to floating algæ, and give rise to white worm-like larvæ and small pupæ, with prominent respiratory horns. The eggs of the hairy species are laid in decaying vegetal matter, and give rise to small larvæ.

Culicoides grahami Austen, 1909.

Synonyms.—*Culicoides habereri* Becker, 1909; *Œcacta hostilissima* Pittaluga, 1910.

This minute fly appears to be extremely common, and to be almost the most troublesome of these blood-thirsty insects in tropical Africa. It is known in the Spanish Guinea, Ashanti, Congo Free State, Uganda, Kamerun, Southern Nigeria, Angola For fuller particulars see Austen's 'African Blood-Sucking Flies,' p. 7, Plate I., Fig. 3, and Pittaluga's works.

Culicoides varius Winnertz, 1867.

This is the blood-thirsty species in Europe.

Œcacta Poey, 1851.

This genus is closely related to *Ceratopogon* and *Culicoides*. The antennæ have fifteen and the palpi five joints. Ocelli are present. The wings have few cells. The tibial spurs and the pulvilli are absent. The sexes are similar, but the antennæ of the male are more hairy than those of the female.

Species.—*Œcacta furens* Poey, 1851, found in America, but according to Austen *Œcacta hostilissima* Pittaluga, 1912, is the same as *Culicoides grahami* Austen, 1912.

Œcacta furens Poey, 1851.

This is the jejen of Cuba, which is said to be very irritating. Its length is 2 millimetres from the head to the end of the abdomen. Frons and antennæ rufous. Thorax bronze-coloured with fuscous spots; abdomen fuscous; legs with whitish articulations and a ring upon each femur; tibia fuscous. Wings broad, whitish, with fuscous spots. They are covered with minute scales and possess conspicuous marginal fringes.

Bezzia Kieffer, 1899.

Synonym.—*Ceratopogon* Meigen, 1803, *pro parte*. *Ceratopogoninæ* with bare wings and tarsi without empodia. Radius with three branches.

Type.—*Bezzia ornata* Meigen, 1803.

Brachypogon Kieffer, 1899.

Ceratopogoninæ with bare wings, media coalescent with R_1; pulvilli absent.

Type.—*Brachypogon vitiosus* Winnertz, 1852 (?) 1846 (?).

Ceratolophus Kieffer, 1899.

Synonym.—*Johannseniella* Williston. *Ceratopogoninæ* with bare wings, simple R_1 and R_3 connected by cross vein, tarsal claws without teeth.

Type.—*Ceratolophus femoratus* Fabricius. *C. fulvithorax* Austen, 1912, is the first *Cerotolophus* to be described in Africa.

Palpomyia Mergele.

Synonym. *Xylocrypta* Kieffer.

Ceratopogoninæ with bare wings and five radial cells R present, media simple; some or all the femora spinose underneath; pulvilli and empodia wanting.

Four subgenera: *Alasion* Rondani, 1857; *Sphæromyas* Stephens, 1829, *Serromyia* Mergele, 1818; *Heteromyia* Say, 1825.

FAMILY PSYCHODIDÆ.

Definition. *Orthorrhapha nematocera* without ocelli, and with body densely covered with coarse hairs. Thorax without transverse suture. Antennæ long, sixteen-jointed. Wings very broad and hairy. No discoidal cell. Legs long, tibiæ without spurs.

Remarks. – The members of this family are small, sometimes very small midges, with the bodies and wings thickly covered with hairs and scales, which give them a most characteristic appearance. They are found all over the world, and have a preference for damp, shady places, while their larvæ have been found in damp places – in cracks in rocks, old walls, etc.; in rotting vegetation, liquid filth, and water. The blood-sucking genera are: *Phlebotomus* and *Sycorax* belonging to the Phlebotominæ, and possibly one in the Psychodinæ.

The Psychodidæ are classified into two subfamilies:—

(1) *Psychodinæ* – Psychodidæ, in which the second longitudinal vein gives off its first branch in the root of the wing. The female has a horny ovipositor, while the male has two claspers.

(2) *Phlebotominæ* Psychodidæ, in which the second longitudinal vein branches after it has passed well into the body of the wing. The female has not got a horny ovipositor, while the male has three claspers.

SUBFAMILY PSYCHODINÆ.

The genera *Pericoma* and *Psychoda* and their allies belong to this subfamily. As a rule it is stated that these flies are not blood-suckers, but Howlett states that an Indian species occasionally sucks blood.

SUBFAMILY PHLEBOTOMINÆ.

This subfamily is of importance not merely because it contains blood-sucking flies, but because the genus *Phlebotomus* is accused of spreading the 'Three Days' Fever.' The two blood-sucking genera may be distinguished as follows:–

(1) Two simple veins between the forks of the second and fourth longitudinal veins– *Phlebotomus*.

(2) One simple vein between the forks of the second and fourth longitudinal veins. Seventh longitudinal vein very short.– *Sycorax*.

Phlebotomus Rondani, 1840.

Morphology.– Phlebotominæ, with mouth parts formed for piercing and sucking, palpi of five joints, antennæ long, filiform, composed normally of sixteen segments. The thorax is mainly mesothorax, the prothorax being very diminutive, but the scutellum and post-scutellum are well developed. Wings hairy, narrow, with second longitudinal vein twice forked, thus forming one of the two simple veins between the forks of the second and fourth longitudinal veins, the other simple vein being the third longitudinal. The cross veins are placed near the basal fourth of the wing. Legs very long and slender, and densely clothed with scales. Ungues simple. The abdomen has ten segments, the last being modified for the genitalia, which in the female are flattened, leaf-like structures, and in the male very complex structures composed of superior claspers, inferior claspers, submedian lamellæ, and intermediate appendages, and a penis.

The buccal cavity is wide in front and narrow behind, where it leads via the pharynx into the œsophagus, which divides posteriorly into two tubes, one leading to the sucking and the other to the mid-gut, at the posterior extremity of which are situate the four Malpighian tubules, after which come the small and large intestines. Attention is invited to the presence of the sucking stomach, and to the number of the Malpighian tubules.

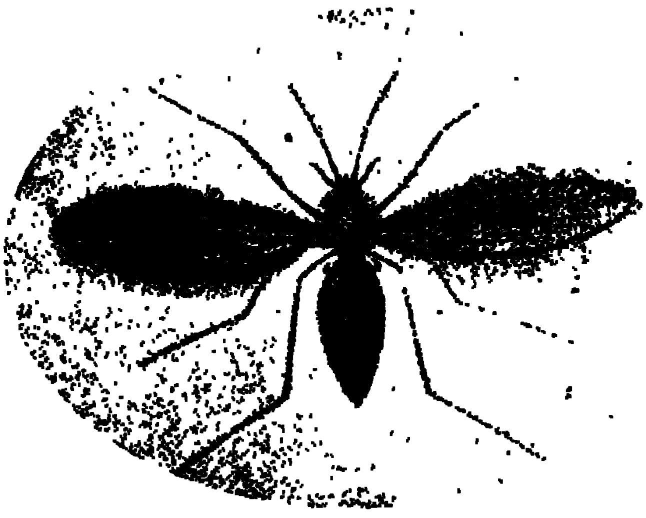


FIG. 403.—*Phlebotomus duboscquii* NEVEU-LEMAIRE, 1906.
(From a photograph by J. J. Bell.)

The female organs consist of ovaries, from which the tubular oviducts pass to unite before reaching the base of the inferior claspers. There are two spermathecæ.

The male organs are testes, seminal vesicles, ejaculatory duct, pompetta or little pump—which regulates the exit of the spermatozoa—and penis.

Life-History.—After fertilization the female takes a meal of blood, even though she may have previously sucked blood. She then lays some thirty to eighty eggs in damp places, usually cracks in rocks, stones, or bricks, and in doing so is apparently much exhausted, and in captivity may soon die. The eggs vary in size in different species from 0·15 to 0·5 millimetre in length. They are elongate oval in shape, marked with longitudinal dark marks, connected at places by means of cross lines. The eggs are laid singly, and require four to six days in warm, and fourteen days in cold, weather before hatching. The larvæ measure some 2 to 5 millimetres in length, and are composed of a head without eyes, but with well-developed mouth-parts and a Y-shaped mark, and cylindrical body of twelve segments, each with a transverse row of spinous hairs, and with spiracles on the first and penultimate segments. The characteristic point about the larvæ is the presence of two very long bristles situate on two tubercles on the ultimate segment. These bristles may be as long as the head and body taken together. The length of the larval stages depends upon the air temperature, and may last from two to fourteen days.

The pupa, 2 to 5 millimetres in length, is motionless, lying in the wrinkled, brownish larval skin which envelops its last three segments, and by which it is attached to the stone on which it lives. The duration of the pupal stage varies from eight or nine to twenty-eight days. The whole development, therefore, requires about one month in warm and two months in cold weather.

Habits.—These little flies are essentially nocturnal in their habits, but are attracted by light. During the day they lie up in cool, shady places in houses, etc., under bricks, in hollow trees, behind shutters, books, pictures, etc., often in bathrooms, and more often in latrines. They are very small, and can easily pass through the meshes of an ordinary mosquito curtain and fill themselves with human blood; or, failing this, they will content themselves with animal blood—*e.g.*, that of cattle, dogs, frogs, geckos, serpents, lizards, etc. They fly quite silently, and only the female bites, and that only at night. She appears to be stimulated in her biting propensities by an increase of humidity and temperature, and will even crawl under the bed-clothes to get at her victim. During the act of biting the posterior end of the abdomen is raised, while the whole abdomen becomes much distended with blood and reddish in colour, except at the posterior tip.

The originally replete female becomes half empty in sixteen, and quite empty of blood in thirty-six to forty hours. When first gorged, she cannot fly easily; and may be unable to escape from the mosquito curtain, where she may be caught while quietly digesting her enormous meal. During the day, as already stated, the flies remain resting in cool, shady places in houses and other buildings, under bricks, in hollow trees, behind shutters, pictures, books, etc., and are often found in bathrooms, and more often in latrines.

The larvæ are very difficult to find, because they are so small, while the pupæ are even more difficult to see, because not merely are they small, but they are also of a colour similar to the stones to which they are attached. Hence the habits of larvæ and pupæ are not well known, and require to be restudied. Their presence may be determined, even when they cannot be found, by placing the stones in a glass case or under fine netting, when the adult flies will appear in due course if any pupæ are present.

Pathogenicity.—*Phlebotomus papatasii* Scopoli, 1786, is the carrier of the virus of 'Pappataci fever,' and the whole genus is composed of virulent blood-suckers, whose bite is generally severe, and may be quite painful to non-immune, new arrivals, when the sensations produced by the bite is stated to resemble that which people imagine ought to be experienced by the application of a red-hot needle. The area of the bite becomes a small rose-red papule, surrounded by a reddish macula, the total result being a maculo-papule, which may persist for several days, and is associated for a day or so with a sensation of itching. Children are especially liable to be attacked.

Prophylaxis.—Newstead classifies the possible means of prophylaxis into—(1) Repellents, (2) fumigation, (3) light, (4) artificial air movements, (5) traps, (6) nets, (7) destruction of breeding-grounds, and of all these he thinks that very fine spraying with a 1 per cent. solution of formalin is the most effective, especially if performed during the day into the dark portions and angles of the sleeping-chamber, while the mosquito curtain might be sprayed towards night. He thinks that an electric fan and a modified biscuit-box trap lined with dark cloth and placed high up in dark places of the sleeping-chamber would be useful. Major Crawford recommends the following ointment for personal use: Oleum anisi, 1 drachm; oleum eucalypti, 1 drachm; oleum terebinthinæ, ½ drachm; and unguentum acidi borici, 1 ounce.

Species.—The species are fairly numerous, and may be grouped geographically as follows:—

Europe.—*Phlebotomus papatasii* Scopoli, 1786 (type species); *P. minutus* Rondani, 1840; *P. mascittii* Grassi, 1908; *P. nigerrimus* Newstead, 1911; *P. perniciosus* Newstead, 1911.

Africa.—*P. duboscquii* Neveu-Lemaire, 1906, found in Timbuktu.

Asia.—*P. papatasii* Scopoli, 1786(?); *P. argentipes* Annandale, 1910; *P. major* Annandale, 1910; *P. malabaricus* Annandale, 1910; *P. babu* Annandale, 1910; *P. himalayensis* Annandale, 1910; *P. perturbans* Meijere; *P. angustipennis* Meijere.

America.—*P. vexator* Coquillett, 1906; *P. cruciatus* Coquillett, 1906; *P. rostrans* Summers, 1912.

Newstead gives the following table for the purpose of recognizing the *Phlebotomi* of Malta:—

A. *Abdominal Hairs Recumbent:*—
  (*a*) Integument black. Large species. Palpi with second segment slightly longer than the third—*P. nigerrimus.*
  (*b*) Integument ochreous. Small species. Palpi with second segment one-half the length of the third—*P. minutus* and *P. minutus* var. *africanus* Newstead.

B. *Abdominal Hairs more or less Erect:*—
  (*a*) Legs in both sexes relatively short; average length of hind-leg 3 millimetres—*P. perniciosus.*
  (*b*) Legs in both sexes relatively long; average length of hind-leg 4 millimetres—*P. papatasii.*

Other species are:—*P. squamiplairis* in Khartoum; *P. antennatus*, Gold Coast; *P. vexator*, *P. legeri* Mansion, 1914, Corsica; *P. duboscquii*, Mauritania.

Phlebotomus verrucarum Townsend, 1913, is believed by Townsend to be the carrier of *Verruga peruviana*, but Strong, Tyzzer, Brues, Sellards, and Gastiaburu consider that the observations need confirmation before they can be accepted.

Phlebotomus papatasii Scopoli, 1786.

Synonyms.—*Cyniphes molestus* Costa, 1840; *Hemasson minutus* Loew, 1844.

Newstead reports that there are two distinct colour varieties of this insect—viz.: (1) A uniformly pale variety which is to be considered typical: and (2) a variety with a dark fringe to the costa and hind margin of wing. These two varieties he distinguishes as the pale variety and the dark variety.

Pale Variety.—Almost uniformly pale, translucent, ochreous; thorax with a long, dull, red-brown median stripe and a single spot of the same colour on either side near the front: wing fringe not markedly darker than the hairs on the disc of the wing.

Dark Variety.—Female with general colour of pale form, but with wing fringes smoky grey, and some of the hairs on the veins also dark grey or smoky grey. The male was not observed.

Life-History.—Ovum when first expelled shows the oolemma (interior) and a micropyle at anterior end. The first instar of the larva is caterpillar-like. Two pairs of caudal bristles, one much longer than the other, the other pair very short. Length, 2 to 3·28 millimetres. Pupa with abdomen curved upwards in varying degree. The eggs hatch in six to nine days, and the larvæ, which live in the earth, become pupæ in about eight weeks. The total item of development is about ten to eleven weeks, and the life of the fly is about eight days.

Pathogenicity.—It is the carrier of Pappataci fever.

FAMILY SIMULIIDÆ.

Synonyms.—*Melusinidæ*, *Tipulariæ* Meigen, *Simulides* Zelt, *Simulites* Newman, *Simulinæ* Rondani.

Orthorrhapha nematocera without ocelli: without transverse suture on the thorax; with short legs, in which the posterior tibiæ and the first joint of the hind tarsi are dilated: with short, straight, cylindrical, eleven jointed antennæ without setæ. Eyes of the male are large, and meet in the middle line, while those of the female are smaller and separate. Size, 1·5 to 4 millimetres in length.

The *Simuliidæ* or *Melusinidæ* are the sand-flies, also called 'brûlots' or 'potu' flies, and have a wide distribution, being particularly found in the tropics, but are also well known in Europe. Though small in size, they are great blood-suckers, attacking man and beast, and also other insects, but only the females suck blood.

Though there is only one genus, *Melusina* Meigen, 1800, more correctly known as *Simulium* Latreille, 1802, there are very many species—*i.e.*, about seventy—of which *Simulium reptans* Latreille and *S. hirtipes* Fries are known in Scotland. *S. columbaczense* Schonberg, locally known as the 'banat,' is the cause of much destruction of cattle in South Hungary. *S. indicum* Becher is the 'dam din' of Assam, which is a cause of irritation to tea-coolies. *S. damnosum* Theobald in Uganda, where it is called 'mbwa,' and in the Sudan, where it is called 'kunteb'; and *S. griseicollis* Becker, of Dongola, locally called 'nimetta,' are very virulent. Austen says that the 'potu' flies were accused of having caused the death of coolies while constructing an Indian road. The effects of the bite of these small insects is most irritating, and the appearance of a person after a severe attack is most peculiar, the face and hands—*i.e.*, the exposed parts—being covered with papules.

Life-History.—The eggs are deposited on stones or plants in running water. The larva is broad posteriorly, where it possesses a sucker, capable of attaching it to any convenient object Anteriorly it has two fan like organs. It moves about in the water after the manner of a leech, and also by the aid of a silken thread which it spins. It feeds on water plants. The larval stage lasts about a month, when a cocoon is spun, inside which the pupa is formed. The pupa breathes by means of branched filaments, and at the end of a week becomes the imago, which is carried to the surface of the water in an air-bubble.

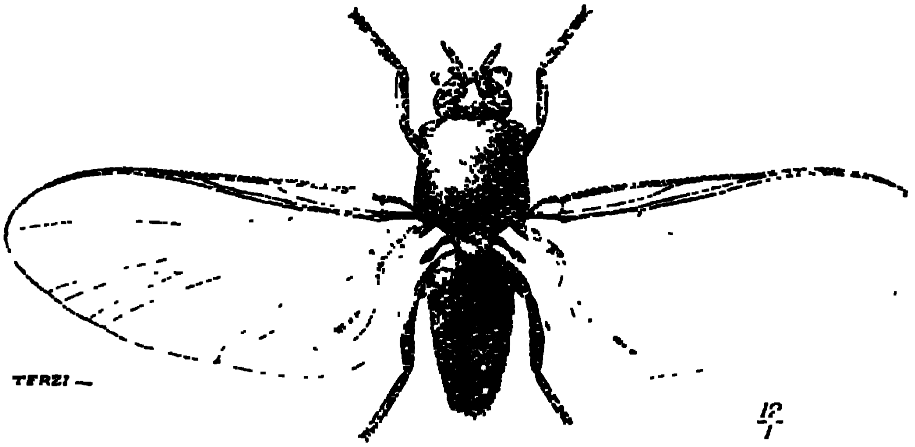


FIG. 304.—*Simulium reptans* LATREILLE: FEMALE.

Habits.—The *Simuliidæ* live in the open country, and very rarely enter houses. They can be found in the early morning, or, better, in the late afternoon, flying in clouds. During the daytime they can be found on trees, grasses, etc. It is common to find the males quite close to the streams in which the eggs, larvæ, and pupæ abound; but the female can apparently travel for considerable distances in search of food, and can quite easily be caught on the wing. They may also be found in the ears of cattle, donkeys, etc., where they feed. They are not all vicious, blood-thirsty insects. Thus, for example, *S. venustum* Say is said to be quite peaceably disposed. It is quite possible that in some instances mistakes have been made with regard to the blood-thirsty propensities of some species, and it is possible that the real culprit was one of the Ceratopogoninæ, and therefore it is necessary to be quite certain that the insect in question is really a *Simulium*, and this can only be done by careful examination. For purpose of quick field examination, it is as well to inspect the antennæ carefully, as they are fairly characteristic.

Enemies.—The *Simuliidæ* have many enemies, among which may be mentioned the larvæ of the May- and that of the Caddis-fly, and many kinds of fish which prey upon the larvæ, pupæ, or flies.

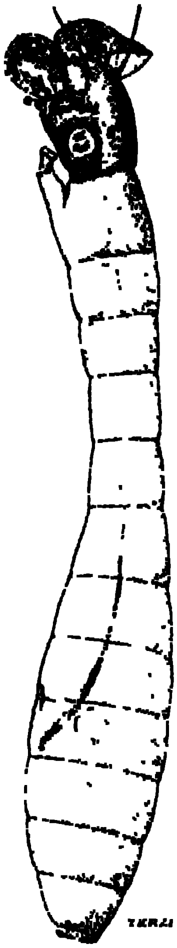


FIG. 405.—SIMULIUM LARVA. (× 8.)

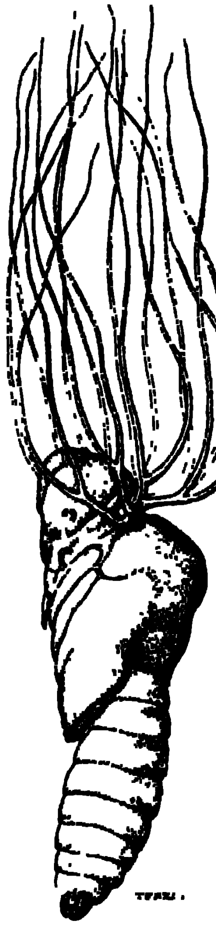


FIG. 406.—SIMULIUM PUPA. (× 8.)

Classification.—The genus has been divided into two subgenera by Roubaud—*i.e.*, *Prosimulium* and *Eusimulium*, but the differentiation of the species is very difficult. In fact, the family urgently requires revision.

Pathogenicity.—Although sand-flies are very irritating, and cause the death of cattle, it is not known whether they are the carriers of any definite disease of cattle or man, though it seems possible that they may be associated with the spread of pellagra, as Sambon has suggested; but more will be said on this subject when discussing pellagra in Chapter LXXIII.

Marchoux and Borret have suggested that sand-flies may play a rôle in the transmission of leprosy.

FAMILY BLEPHAROCERIDÆ Loew, 1860.

Orthorrhapha nematocera, without discal cell and with a secondary set of crease-like lines on the wings.

In this family the genus *Curupira* Osten-Sacken is said to contain species which suck blood. The larvæ live in rapid streams. *C. torrentium* (Muller) is found in Brazil.

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CHAPTER XXXIII

DIPTERA (*concluded*)

MUSCIDÆ AND ALLIED FAMILIES

Flies—Orthorrhapha—Brachycera—Tabanidæ—Leptidæ—Asilidæ—Phoridæ—Scenopinidæ—Empidæ—Cyclorrhapha—Œstridæ—Sarcophagidæ—Muscidæ—Anthomyidæ—Pupipara—References.

BITING AND PARASITIC FLIES.

This chapter deals with all those insects which come under the term 'biting and parasitic flies.' In medicine they are of importance because of their blood-sucking habits, through which they are able to disseminate animal parasites. Further, the larvæ of certain species may enter the skin or the alimentary canal, and cause irritation and disease in this way (*Myiasis* Hope, 1837).

Continuing the classification of the Diptera already given, the first section included in this chapter is that known as the Brachycera.

SUBORDER I. ORTHORRHAPHA.

SECTION BRACHYCERA.

The principal Orthorrhapha Brachycera may be divided into two groups:—

GROUP 1: *Brachycera Homœodactyla.*—Imago with pulvilliform empodia. Larvæ with a terminal posterior stigma. Families: Tabanidæ, Leptidæ, Stratiomyidæ.

GROUP 2: *Brachycera Heterodactyla.*—Imago with empodia undeveloped or bristle like. Posterior stigma of the larva not terminal. Families: Asilidæ, Empididæ.

BRACHYCERA HOMŒODACTYLA.

The families with which we are concerned may be recognized as follows:—

A. Antennæ composed of more than five joints, or third joint complex.
    I. Squamæ large—*Tabanidæ*.
    II. Squamæ small.
        Tibia with spurs—*Leptidæ* in part.
B. Antennæ composed of three joints or third joint simple—
    Leptidæ in part.

FAMILY TABANIDÆ.

Orthorrhapha Brachycera with bulky bodies and often large heads. The eyes usually meet in the males, but are separate in the females. Antennæ with third joint marked by four to eight annuli, but without a terminal bristle. Proboscis strong and prominent. Thorax narrower than the head. Wings with large basal cells and five posterior cells. Third longitudinal vein bifurcate. Legs moderately stout. Empodia large.

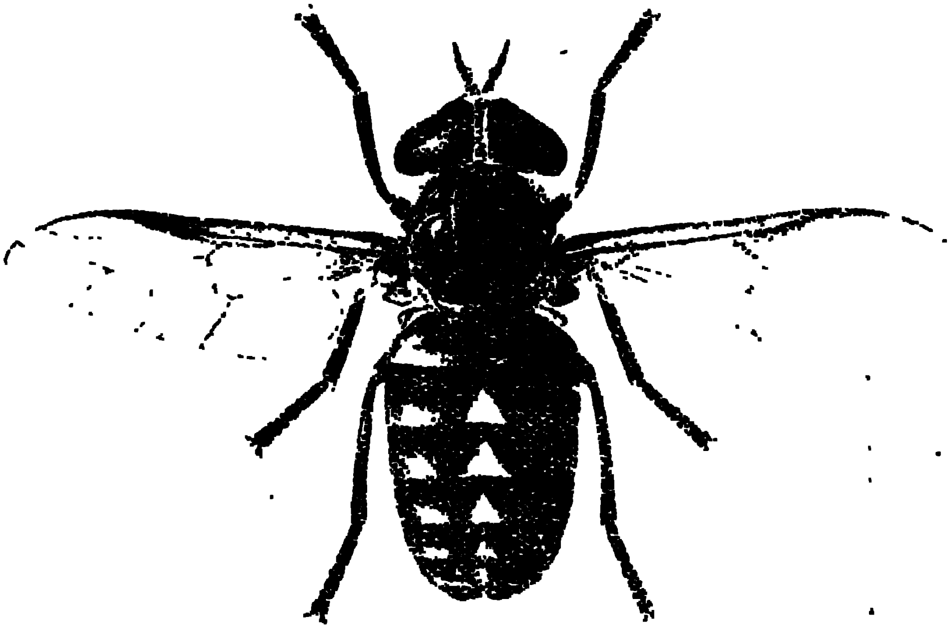


FIG. 407. *Tabanus bovinus* LINNÉ FEMALE.

Remarks. -The Tabanidæ are blood-sucking flies, of which some 2,000 species are known. The blood-sucking habit is confined to the females, while the males live on the juices of plants. They are variously known as horse-flies, breeze-flies, gad-flies, serut-flies (Nile), and mangrove-flies (West Africa), and are distributed widely over the world. They are in the habit of coming to water for drinking purposes, and this has enabled them to be killed in large numbers by sprinkling the water with kerosene, which probably prevents them escaping from the surface of the water, and partially kills them by its poisonous effects.

Morphology.—As a rule the head is as wide or wider than the thorax, convex anteriorly, and concave posteriorly, with very large, brilliantly coloured eyes, with golden-green or purple markings.

The antennæ are very distinct, but the proboscis varies, being very short in some genera and enormously long in others. In the genera in which it is short it hangs vertically downwards from the head. It consists of a labrum, two maxillæ with palps, two mandibles, a hypopharynx, and a thick labium with well-marked labial palps (labella). The wings have a large discoidal cell and very elongate basal cells. When at rest the wings diverge at the tips. They may be mottled. The legs are large and strong. The body is brown, whitish, or yellowish in colour, but there may be markings on the abdomen.

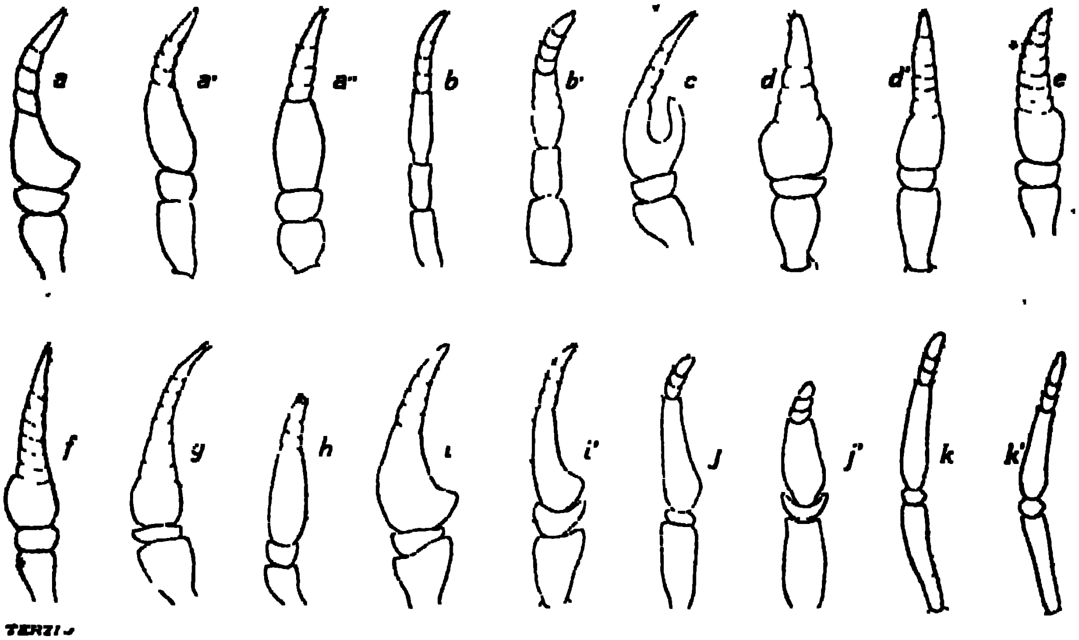


FIG. 408.—ANTENNÆ OF THE TABANIDÆ.

a, a', a", Silvius; *b, b'*, Chrysops; *c*, Rhinomyza; *d, d'*, Cadicera; *e*, Dorcalæmus; *f*, Pangonia; *g*, Erephopsis; *h*, Lepidoselaga; *i, i'*, Tabanus; *j, j'*, Hæmatopota; *k, k'*, Hippocentrum.

Life-History.—The eggs, which are spindle-shaped, and whitish in colour, are laid in raft- or flask-shaped masses attached to water-plants. The larvæ live either in water or damp earth, and feed upon small animal organisms. They are spindle-shaped and segmented, with knobs or protuberances on the rings, either all round or only ventrally. The pupa, which is free, is found in water or damp rubbish.

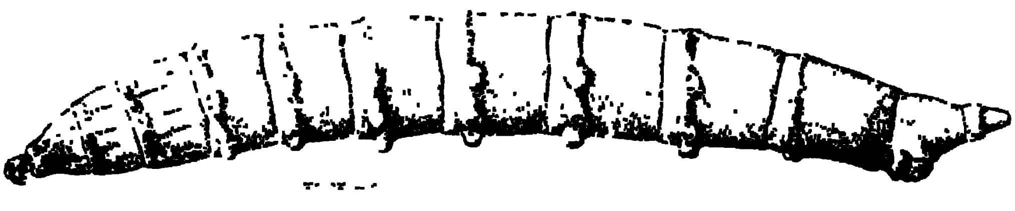


FIG. 409.—LARVA OF A TABANUS. (×2½.)

Pathogenicity.—It is possible that they may disseminate trypanosomes. The diseases m'bori in dromedaries in Timbuktu and souma in Segon are believed to be spread by *Tabanus ditæniatus*, while the dromedary disease of Algeria is spread by *T. nemoralis* Meigen and *T. nigritus* Fabricius. *T. glaucopis* Meigen is infected with *Herpetomonas subulata*. According to Leiper, Chrysops is the carrier of *Loa loa* Cobbold, 1864.

Prophylaxis.--Kerosene spread on water appears to be the best method of dealing with these pests.

Classification.--The family is divided into two subfamilies: Tabaninæ and Pangoninæ.

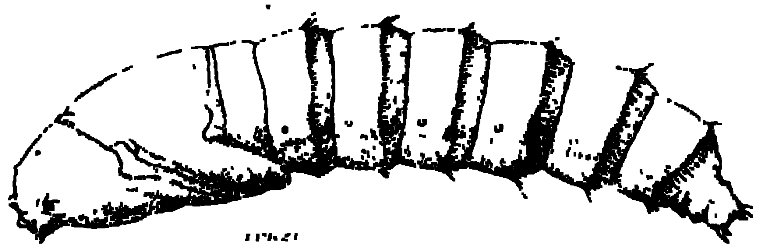


FIG. 410. PUPA OF *Tabanus kingi* AUSTEN. (AFTER KING.)
(From the Fourth Report of the Wellcome Tropical Research Laboratories, Khartoum.)

TABANINÆ.

Tabanidæ without spurs on the hind tibiæ.

The important genera of the Tabaninæ may be recognized by the following table:--

I. Thorax and abdomen with iridescent tomentum--*Lepidoselaga*.
II. Thorax and abdomen without iridescent tomentum.
  1. Eyes bare.
    (*a*) Third joint of the antenna without basal tooth.--
      (1) Antennæ extremity slender, and first joint elongate--*Hippocentrum* (Fig. 408, *k*, *k'*).
      (2) Antennæ not remarkably slender and first joint not remarkably elongate--*Hæmatopota* (Fig. 408, *j*, *j'*).
    (*b*) Third joint of the antenna with well developed basal tooth--*Tabanus* (Fig. 408, *i*, *i'*).

Lepidoselaga Macquart, 1838.

Synonym.--*Hadrus* Perty.

Lepidoselaga lepidota Wiedemann, 1828, the motúca fly of Brazil, is a well-known biter. (Antennæ: *vide* Fig. 408, *h*.)

Hæmatopota Meigen, 1803.

Synonym.—*Chrysozona* Meigen, 1800.

The number of species comprised in this genus is rapidly increasing. About 130 have already been described, and Austen informs us that many more still await description from Africa alone. The characteristics of a species belonging to this genus are--The elongate antennæ, the peculiar wing markings (Fig. 412), and the peculiar arrangement of the wings when at rest, when the bases meet together, while the rest of the wings diverge slightly and slope backwards and outwards. The species of *Hæmatopota* are very blood-thirsty, and are a terrible pest in the wet season to man and beast alike. They are said never to bite in the early morning or after sunset, but, on the contrary, Mayer states that *H. decora* is most troublesome in the early morning and late evening. Neave

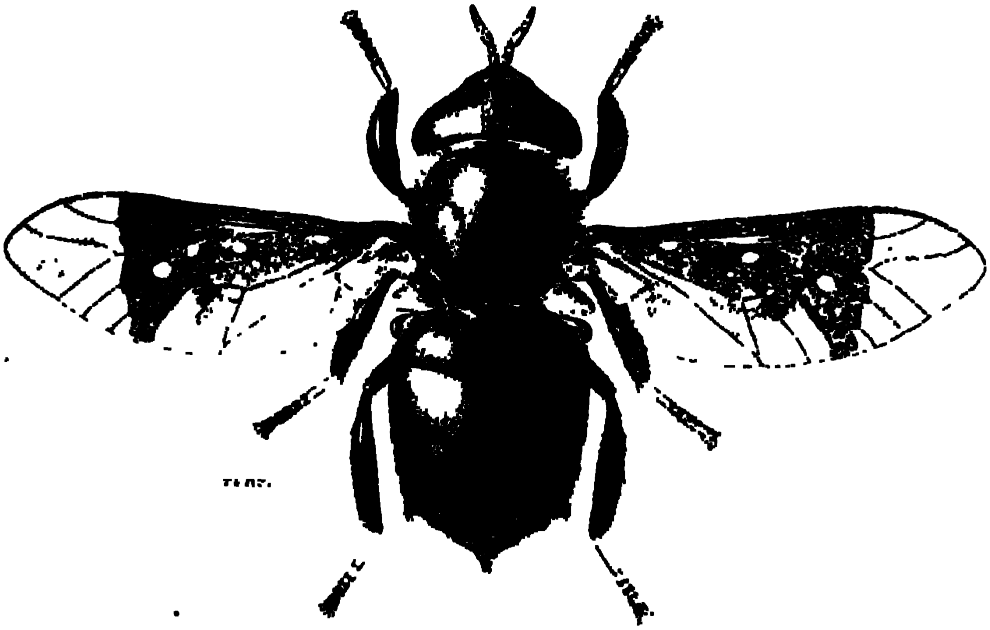


FIG. 411.—*Lepidoselaga lepidota* WIEDEMANN: FEMALE. (×6.)

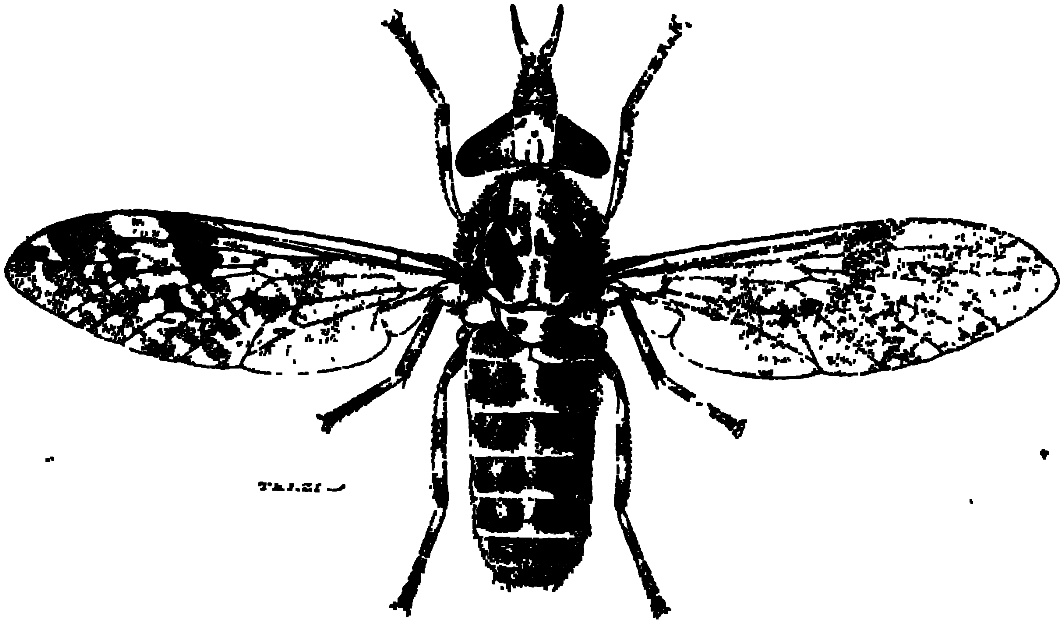


FIG. 412.—*Hæmatopota vittata* LOEW. (×4.)

states that the females bite in rather dull, damp weather, and rarely in the heat of the sun, being mostly in evidence from about 8 to 10 a.m. and from 4 p.m. to sunset in sunny weather, but in the shady, damp forest they may be troublesome all day. The life-history of the tropical species is but little known, but Neave thinks that the majority of the species may have two broods. The life-history of *H. pluvialis* Linnæus is partially known. The egg stage has not, so far as we know, been observed. The larva and pupa are of the Tabanid type, as described above. With regard to pathogenicity, Balfour reports El Takasha (' the attacking fly'), probably *H. taciturna* Austen, is believed to cause swelling of the lungs in sheep and goats.

With regard to individual species, *H. pluvialis* Linnæus is common in Europe, while *H. grahami* Austen, 1912; *H. daveyi* Austen, 1912; *H. rubens* Austen, 1912; *H. beringeri* Austen, 1912; *H. crudelis* Austen, 1912; are some new species recently described by Austen from tropical Africa. Other species are *H. obscura* Loew, 1875, in South Africa; *H. vittata* Loew in tropical Africa; and *H. bullatifrons* Austen in Northern Nigeria.

Hippocentrum Austen, 1908.

This genus is nearly allied to *Hæmatopota* Meigen, 1803, but is, according to Austen, distinguished by the fact that the head is for the most part shining, the antennæ extremely slender, and the first joint elongate (Fig. 408, *k*, *k'*), and the terminal joint of the palpi in the female very large and shining on the outer side, which is strongly convex, while the inner side is flattened; the wings are more or less suffused with dark colour, interrupted with pale streaks or blotches without the peculiar light markings of *Hæmatopota*.

Species.—*H. versicolor* Austen, 1908, in Uganda and the Lado, *H. trimaculatum* Newstead in West Africa, *H. strigipennis* Karsch, which may be identical with *H. trimaculatum*, has only been found in Gaboon, and *H. murphyi* Austen, 1912, in West Africa. The females bite man and animals. The life-history is unknown.

Tabanus Linnæus, 1761.

There are over 900 known species of *Tabanus*, of which *Tabanus bovinus* Linnæus, 1761, is found in Europe, Asia, and South Africa. In the Sudan these flies are called serut-flies: *T. ditæniatus* Macquart, *T. gratus* Loew, *T. tæniola* Palisot de Beauvois, *T. fasciatus* Fabricius, *T. africanus* Gray, may be noted. In West Africa they are known as mangrove flies. Recently Patton has described the life-cycle of a Crithidia (*C. tabani* Patton, 1909), which is a true parasite of *T. hilarius* and another species.

Subgenus Therioplectes Zeller, 1842.

A number of species of this genus are known in Europe. *Therioplectes micans* Meigen, *T. borealis* Meigen, *T. montanus* Meigen, and *T. tropicus* may be mentioned.

Subgenus Atylotus Osten Sacken, 1876.

Atylotus fulvus Meigen and *A. rusticus* Fabricius are met with in Europe.

Other Genera.

In 1906 Grünberg described three genera, with one species in each, as belonging to the Tabaninæ—viz., *Thaumastocera*—*T. akwa* in West Africa; *Holocera*—*H. nobilis*—in Tropical East Africa; *Parhæmatopota*—*P. cognata*—in Tropical East Africa and Zanzibar; while other genera are *Hexatoma* Meigen in Europe, *Dasybasis* Macquart in South America and Australia, *Bolbodimyia* Bigot in South America, *Udenocera* Ricardo in Ceylon, *Diachlorus* Osten Sacken in America, *Stibasoma* Schiner in South America, *Acanthocera* Macquart in South America, *Dichelacera* Macquart in South America, and *Selasoma* Macquart in South America.

PANGONIINÆ.

Tabanidæ with hind tibiæ armed at the tips with spurs.

I. Proboscis short.
    1. Antennæ longer than the head—*Chrysops*.
    2. Antennæ shorter than the head—*Silvius*.
II. Proboscis long.
    1. Proboscis little longer than the head—*Cadicera*.
    2. Proboscis usually much longer than the head, often longer than the body—*Pangonia*.

Chrysops Meigen, 180

This genus has become of greater importance since Leiper has shown that it includes the carrier of *Loa loa* Cobbold, 1864, which in its turn is suspected to be the cause of Calabar swellings.

The genus is world wide in its distribution, and is said to contain more than 100 species, of which some seventeen or more have been found in the Ethiopian region. The African flies belonging to the genus are of medium size, not exceeding 10·5 millimetres in length according to Austen. The wings of the majority show a conspicuous black band (Fig. 413) running across the surface. There are three ocelli on the crown of the head. The characters of the antennæ are shown in Fig. 408, *b*, *b′*; in the latter the first joint is shown to be conspicuously swollen. During life the eyes are of a golden-green

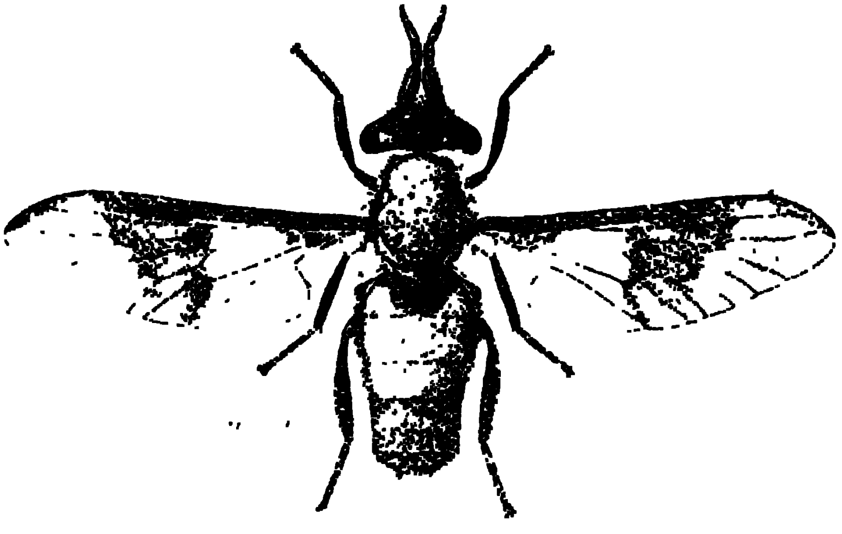


FIG. 413.—*Chrysops wellmani* AUSTEN: FEMALE. (× 4½.)

colour, and are marked with purplish spots and streaks, which Austen considers present useful specific characters. When resting, the wings are kept half open.

The females inflict a very severe bite, which causes pain, inflammation, and even at times œdema and fever.

The eggs, which at first are white and later turn brown or black, are deposited upright in a single layer upon leaves and stems of plants near water, in which, or in the mud in the vicinity, the larvæ live. The larvæ and pupæ resemble those of *Tabanus*, but in the larva the last antennal joint is longer than the penultimate, and in the pupæ the antennæ project beyond the head. With regard to pathogenicity, the genus is now known to contain the carrier of *Loa loa*.

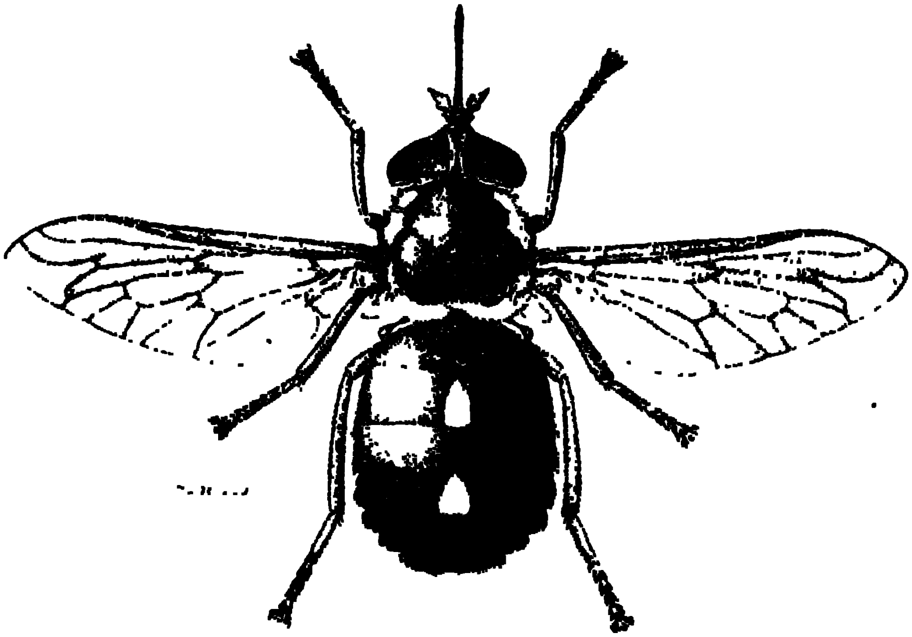


FIG. 414.—*Cadicera chrysostigma* WIEDEMANN: FEMALE. (× 2½.)

As examples the following species may be mentioned. *C. dimidiata* van der Wulp, 1885, in West Africa; *C. distinctipennis* Austen, 1906, in tropical Africa generally; *C. bicolor* Cordier, 1907, in Tropical East Africa; *C. silacea* Austen, 1907, in West Africa; *C. magnifica* Austen, 1911, in Tropical East Africa; *C. centurionis* Austen, 1911, in Uganda; *C. cana* Austen, 1911, in East Africa; and *C. dispar* Fabricius in the Oriental region.

Silvius Meigen, 1820.

This widely distributed genus may be exemplified by *Silvius fallax* Austen, 1912, found in North-Eastern Rhodesia, and *S. decipiens* Loew. The characters of the antennæ are illustrated in Fig. 408, *a*, *a′*, and *a″*.

Cadicera Macquart, 1854.

Over a dozen species of this genus are now known in the Ethiopian region, of which the following may be mentioned: *C. melanopyga*

Wiedemann, 1819; *C. chrysostigma* Wiedemann, 1828; *C. rubramarginata* Macquart, 1885; *C. quinquemaculata* Austen, 1908; *C. biclausa* Loew, 1860; *C. chrysophila* Macquart, 1834; *C. distanti* Austen, 1912; *C. speciosa* Austen, 1912; *C. flavicoma* Austen, 1912; and *C. obscura* Ricardo, 1908. The females have been observed to bite man, but very little is known as to the habits or life-history of the species of this genus.

Pangonia Latreille, 1802.

This widely distributed genus used to contain a very large number of species, but has of late been split up into several subgenera, as may be shown in the following table taken from Miss Ricardo's paper in *The Annals and Magazine of Natural History*, Series 7, vol. v., January, 1900:—

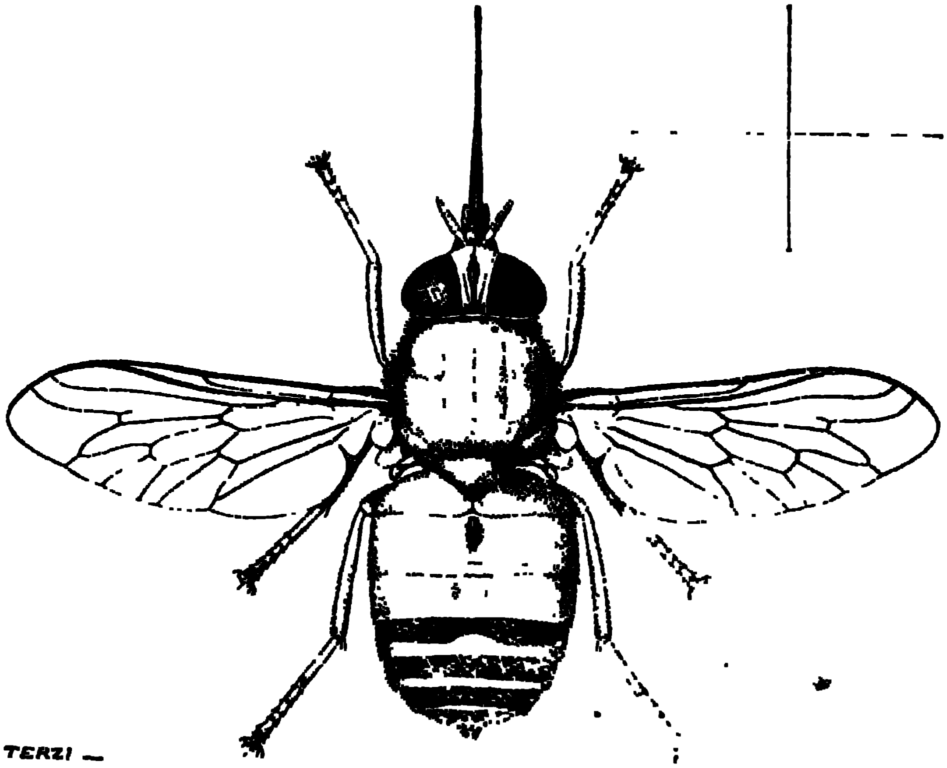


FIG. 415.—*Pangonia ruppellii* JAENNICKE, 1867: FEMALE. (×3.)

I. Wings with first posterior cell closed.
  (*a*) Eyes bare -*Pangonia* Latreille (subgenus *Pangonia*).
  (*b*) Eyes hairy -*Pangonia* Latreille (subgenus *Erephopsis* Rondani).

II. Wings with first posterior cell open.
  (*a*) Eyes hairy—*Dialomineura* Rondani (subgenus *Dialomineura*).
  (*b*) Eyes bare—*Dialomineura* Rondani (subgenus *Corizoneura* Rondani).

The characteristic of the genus is the extremely long proboscis. The antennal characters of ***Pangonia*** are shown in Fig. 408, *f*, and of ***Erephopsis*** at *g* in the same figure. The females are known to be very blood-thirsty and to bite while on the wing, a feat which they can readily perform owing to the length of the proboscis. At the present time the life-history is unknown, and the pathogenicity is also unknown.

As examples the following may be mentioned: ***P. rostrata*** Linnæus, 1764; ***P. varicolor*** Wiedemann, 1828; ***P. gulosa*** Wiedemann, 1828, in Africa; ***P. beckeri*** Bezzi, 1900, in Somaliland; ***P. rüppellii*** Jaennicke, 1867, in the Anglo-Egyptian Sudan and British East Africa: ***P. comata*** Austen, 1912, in East Africa: ***Diatomineura suavis*** Loew, 1858, in South Africa; ***D.*** (***Corizoneura***) ***lineatithorax*** Austen, 1912, in Northern Rhodesia; ***D.*** (***Corizoneura***) ***penetrabilis*** Austen, 1912, in Northern Rhodesia; and ***D.*** (***Corizoneura***) ***hasta*** Austen, 1912, in Portuguese East Africa.

Rhinomyza Wiedemann, 1820.

In this genus the first and second segments of the antennæ are short, while the third segment is composed of five rings (Fig. 408, *c*). Moreover, the third segment has a well-marked tooth. The proboscis is short. *R. fusca* Wiedemann, 1820, is known in Java, and ***R. denticornis*** Wiedemann, 1828, in South Africa. ***R. costata*** Loew, ***R. edentula*** Wiedemann, and ***R. pusilla*** Schiner may also be noted, as may *R. umbraticola* Austen, 1911, in North-Eastern Rhodesia and Kalanga, while ***R. maculata*** Surcouf is found in Madagascar.

Other Genera.

Other genera of the Pangoniinæ are *Dicrania* Macquart in Brazil, *Apocampta* Schiner in Australia, *Pityocera* Tos in Central America, *Goniops* Aldrich in North America, *Pelecorhynchus* Macquart in Australia and South America, *Apatolestes* Williston in California, *Dorcalæmus* Austen in South Africa, *Scione* Walker in South America, *Pronopes* Loew in South Africa, *Gastroxides* Saunders in India, and *Subpangonia* Surcouf in West Africa.

FAMILY LEPTIDÆ.

Orthorrhapha brachycera with brownish, medium-sized, or long narrow bodies and small heads. The third antennal joint is short, and carries either a terminal brush or bristle. The proboscis resembles that of the Tabanidæ, as does the wing venation.

Three genera are accused of blood-sucking: *Leptis*, *Symphoromyia*, and *Trichopalpus*.

With regard to *Leptis*, the species *L. scolopacea* Linnæus and *L. strigosa* Meigen are said to bite persons in France, but this is rare. *Symphoromyia* (species uncertain), characterized by a single spur on the hind tibia and a kidney-shaped third antennal joint, is found in California. *Trichopalpus obscurus* Phil. is known in Chili.

The life-history of the blood-sucking species is not known, but the other larvæ of the Leptidæ live upon decaying vegetable matter.

BRACHYCERA HETERODACTYLA.

A. Antenna apparently two-jointed with a three-jointed arista. Small hunch-backed, quick-running flies - *Phoridæ.*

B. Antenna always three-jointed.
Empodia wanting, vestigial or linear.

- I. Radial 4 and 5 separate.
  - (*a*) Arista dorsal - *Empidæ* (in part).
  - (*b*) Arista terminal.
    - (1) Front hollowed out between the eyes. Males never holoptic. Proboscis without fleshy labellæ at tip - *Asilidæ.*
    - (2) Front plane or convex. Males often holoptic. Not more than four posterior cells. Third antennal joint without bristle or style - *Scenopinidæ.*
- II. Radial 4 and 5 not separate.
  Wings not lanceolate, anal cell short; second basal cell confluent with distal cell. Not brilliantly coloured *Empidæ* (in part).

The orders Therevidæ, Midasidæ, and Dolichopodidæ, while containing species predatory on other insects, do not appear to attack man.

FAMILY ASILIDÆ.

Orthorrhapha brachycera with long narrow body, short broad head, prominent eyes, third joint of the antennæ simple. Thorax narrow in front. Wings with elongate basal cells, third longitudinal vein bifurcate, two intercalary veins present. Empodium with a horny bristle.

It is not known whether the Asilidæ are really blood-sucking flies or not. It is suspected that they bite in the tropics, but there is no definite information.

FAMILY PHORIDÆ.

Phora femorata occurs occasionally in houses. *Aphiochæta ferruginea* Brunner causes intestinal myiasis.

FAMILY SCENOPINIDÆ.

Scenopinus fenestralis Linnæus is the so-called window fly, which is probably the only household fly which is not injurious to health.

FAMILY EMPIDÆ.

Orthorrhapha brachycera with medium or small bodies and small heads. Antennæ with the first two joints very small and hardly distinct, the third joint annulated, often with terminal bristle. Wings with three large complete basal cells, of which the third is shorter than the second. The posterior basal transverse vein is parallel to the border of the wing. Empodium membranaceous.

It is doubtful whether these insects attack man. As a rule they live on the juices of other insects and plants.

SUBORDER II. CYCLORRHAPHA.

Section 1: Aschiza.—This group includes the family Syrphidæ, of which no species is known to bite man.

Section 2: Schizophora.—This group includes the true flies characterized by a distinct frontal lunula and a frontal suture: antennæ with three simple segments, and an arista which is generally dorsal. They may be classified into

Muscoidea.

Synonym.—*Eumyidea.*

This superfamily is divided into:

TRIBE 1: *Muscoidea acalyptratæ,* without squamæ covering the halteres (see Chapter XXXV.).

TRIBE 2: *Muscoidea calyptratæ,* with squamæ covering the halteres.

MUSCOIDEA CALYPTRATÆ.

1. Œstridæ.
2. Sarcophagidæ.
3. Muscidæ.
4. Anthomyidæ.

DIAGNOSTIC TABLE.

A. First posterior cell of the wings not widely open.
  - I. Antennæ small, more or less hidden in round pits; arista single or plumose; body very hairy—*Œstridæ.*
  - II. Antennæ well marked, not hidden; arista more or less plumose; body not very hairy.
    - (*a*) Arista plumose for only half its length, bare in the terminal half, which is hair-like—*Sarcophagidæ.*
    - (*b*) Arista plumose or pectinate along its whole length—*Muscidæ.*

B. First posterior cell widely open—*Anthomyidæ.*

FAMILY ŒSTRIDÆ.

Muscoidea calyptratæ with very hairy bodies, which cause them to resemble bees. Antennæ inserted into round pits, with a terminal bristle on the third joint. Mouth-parts rudimentary.

Remarks.—The Œstridæ are commonly known as the bottle or warble flies, and are of interest because the larvæ become parasitic, either under the skin, in the nasal or pharyngeal cavities, or in the alimentary canal.

Classification.—The genera may be grouped into two subfamilies—(*a*) ***Œstrinæ*** with rudimentary proboscis, including the genera *Gastro-*

philus, *Œstrus*, *Hypoderma*, etc.; and (*b*) *Cuterebrinæ*, with a well-developed retractile proboscis, including *Dermatobia*, etc. The four genera of interest to us may be recognized as follows:—

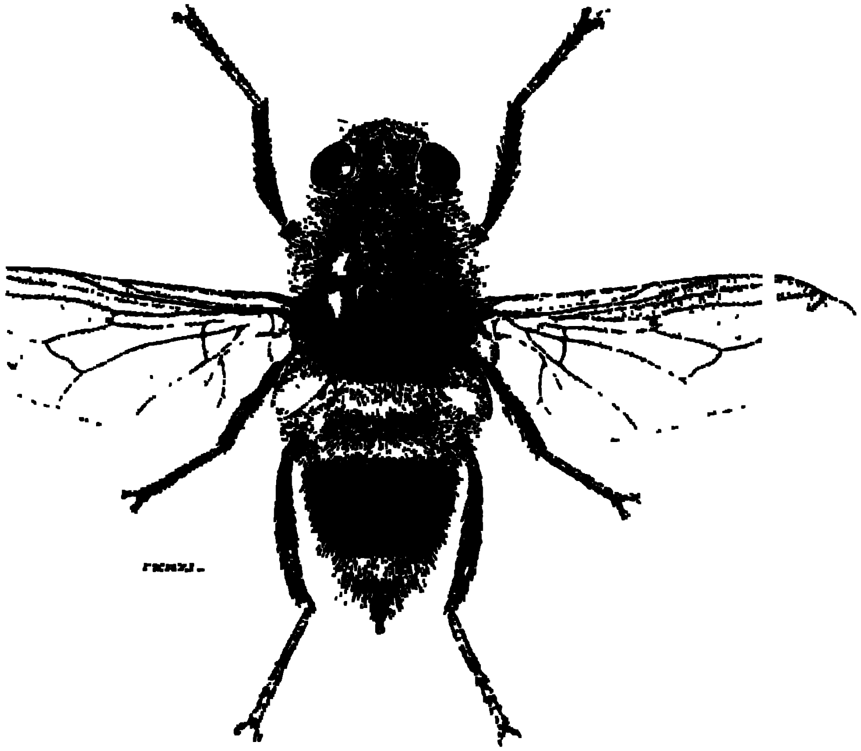


FIG. 416.—*Hypoderma bovis* DE GEER. (×2½.)

Wing without posterior transverse vein; the media runs towards the posterior border. First posterior cell is partly open. Arista naked—*Gastrophilus* Leach, 1817.

II. Wing with posterior transverse vein. The media at its end is bent towards the radius, and the first posterior cell is either open, partially open, or closed.

A. Facial grooves approximated below. First posterior cell closed and petiolate body nearly bare—*Œstrus* Linnæus, 1758.

B. Facial grooves remote.

(*a*) Proboscis straight, capable of being extended, or entirely rudimentary. Antennal groove with small angular dividing wall. Palpi absent—*Hypoderma* Latreille, 1825.

(*b*) Proboscis bent and capable of being drawn into a deep cavity on the under surface of the head, and generally hidden therein. Arista with hairs on the upper side. Third antennal joint much longer than the first two—*Dermatobia* Brauer, 1860.

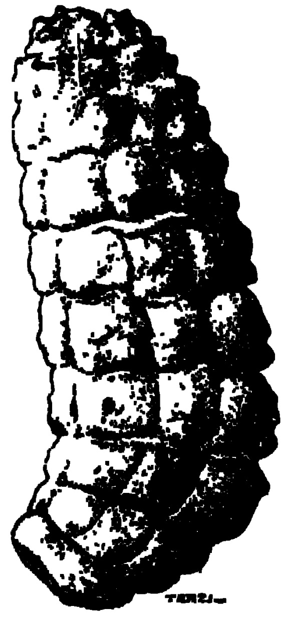


FIG. 417.—LARVA OF *Hypoderma bovis* DE GEER. (×2½.)

Hypoderma.—A good example of dermal infection is *Hypoderma bovis* de Geer, which infests cattle. The eggs are laid on the skin of the animal, and are probably transferred to the mouth by licking, whence they pass via the œsophagus to the skin, in which they form tumours. It is found in Europe and America, and Peiper has gathered together histories of several cases in which *Hypoderma bovis* and *H. diana* Brauer have occurred in man, but this is very rare. The larva which is commonly found in man belongs to *Dermatobia cyaniventris*, which is described below.

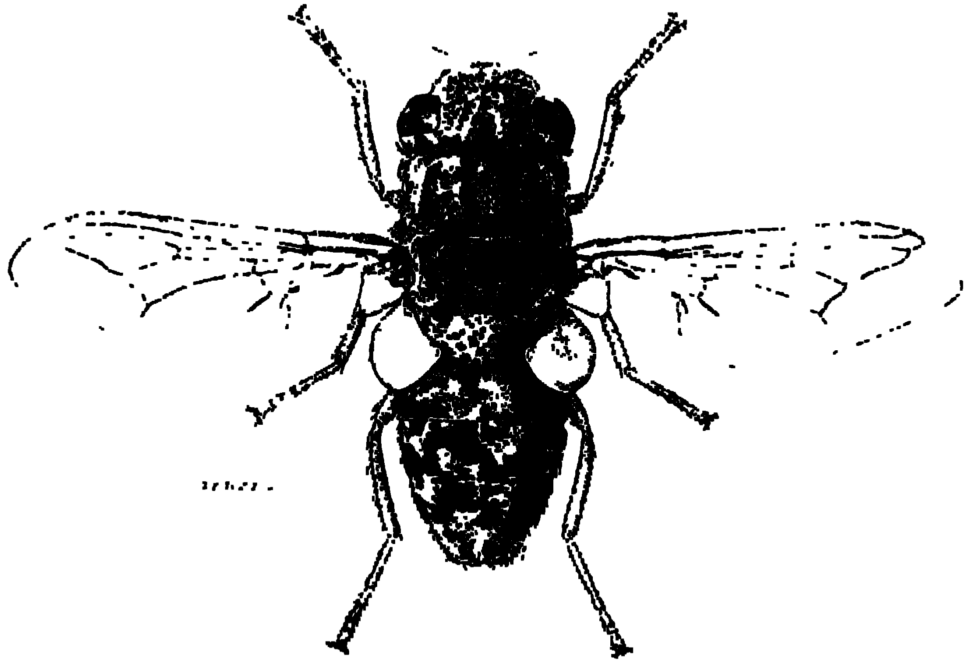


FIG. 418.—*Œstrus ovis* LINNÆUS: FEMALE. (× 4.)

Œstrus.—Rhinal myiasis is exemplified by *Œstrus ovis* Linnæus, 1761, which has been found several times in the nasal cavities of man, though usually found in sheep. The egg is laid in the nasal cavity, in which the larvæ live until they become pupæ.

Gastrophilus.—Intestinal myiasis is exemplified by *Gastrophilus equi* Fabricius. The eggs are laid on the skin, often about the knees, and transferred to the mouth, and so to the stomach, by licking. In this organ they live on the secretions and contents; but though they do not bite the mucosa, they cause irritation. In due course they pass out of the alimentary canal with the fæces, and then

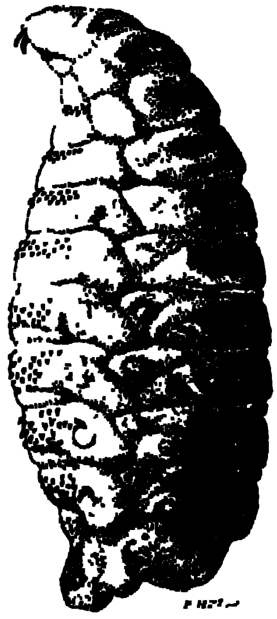
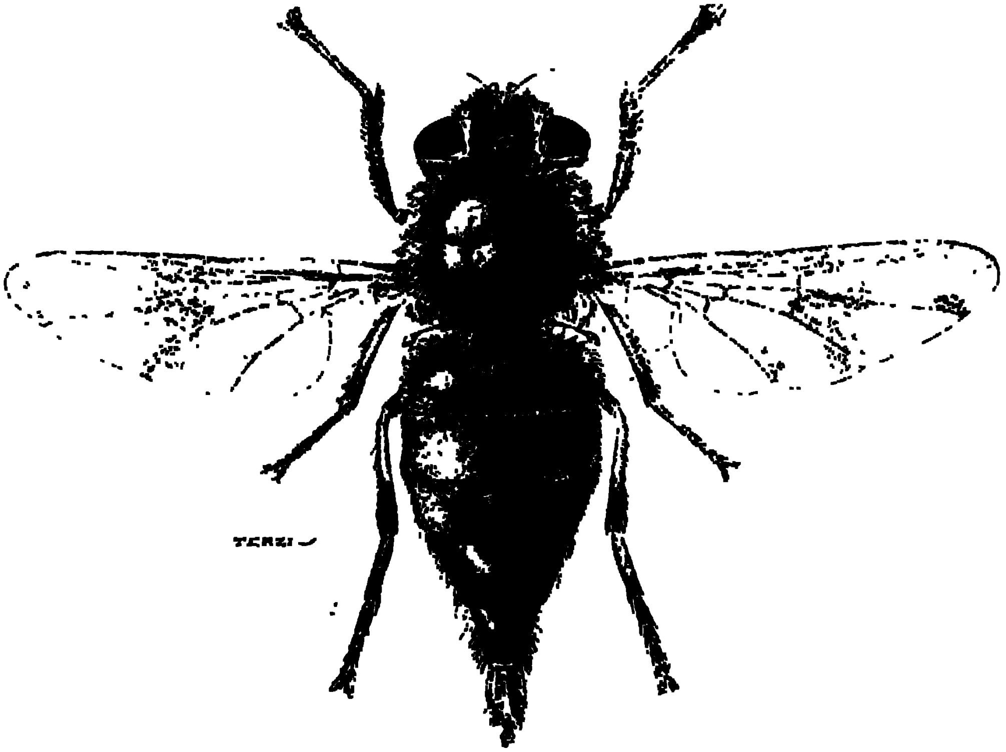


FIG. 419.—LARVA OF *Œstrus ovis* LINNÆUS. (× 4.)

proceed to pupation. *G. pecorum* Fabricius, 1794, is stated to frequently attack man in Siberia.



Fi[illegible] .— *Gastrophilu*[illegible] Fa[illegible] 3½.)

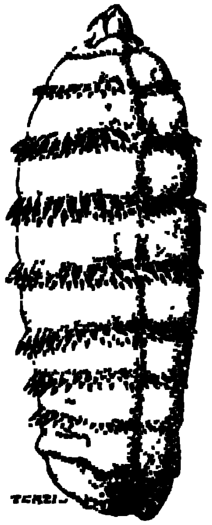


FIG. 421.—LARVA OF *Gastrophilus equi* FABRICIUS. (× 3.)

Dermatobia Brauer, 1860.

Dermatobia cyaniventris Macquart, 1843.

Synonyms.—*Cuterebra noxialis* Goudot, 1845; *Dermatobia noxialis* Brauer, 1860; *Dermatobia hominis* Say, 1822; *Œstrus hominis* Gmelin, 1788.

There appears to have been great doubt as to whether *D. noxialis* is the same as or different from *D. cyaniventris*. At present, on the strength of R. Blanchard's observations, it is usual to look upon them as the same. The larva of this species is found in the skin of man in tropical America at times, and is known by various local names: 'Ver moyoquil' in Mexico; 'ver macaque' in Cayenne; 'torcel' in Venezuela; 'nuche' in Colombia; 'ura' and 'berne' in Brazil; 'cormollote' and 'anal coshol' in British Guiana; 'nuche' or 'gusano' in New Granada.

The fly, which has a yellowish head and dark blue abdomen, is supposed to lay its eggs on the skin of domestic and wild animals and man. The larvæ from these eggs are supposed to enter the skin. The usual areas affected are the head or trunk.

The larva presents two quite different appearances. In the first they are club-shaped, white in colour, with a thick anterior and a

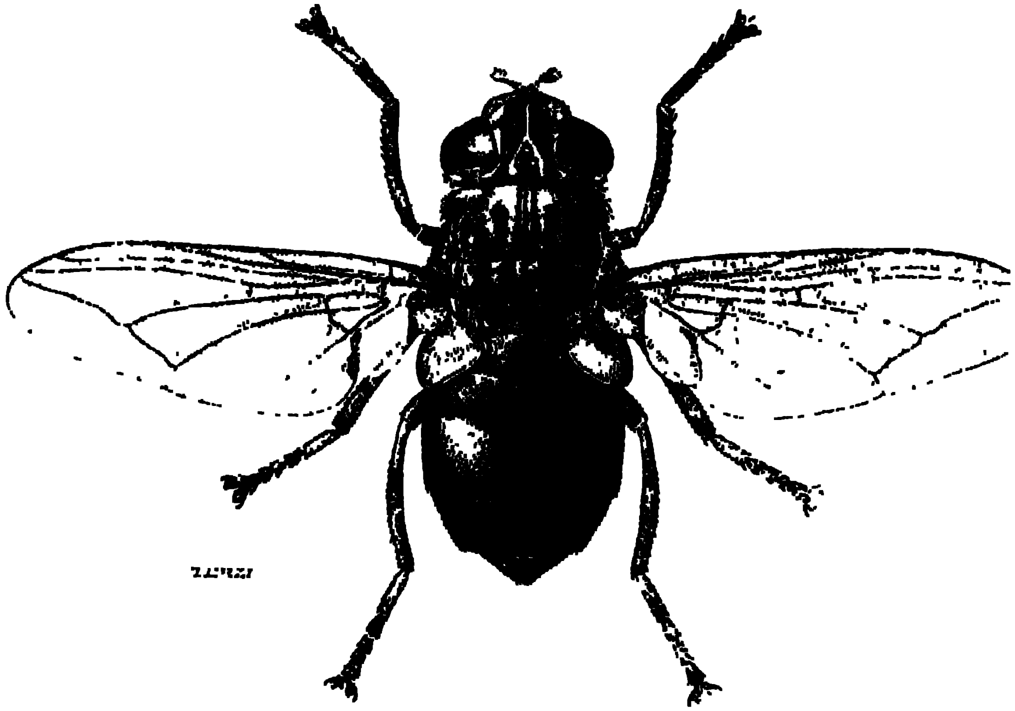


FIG. 422. *Dermatobia cyaniventris* MACQUART. (× 3)

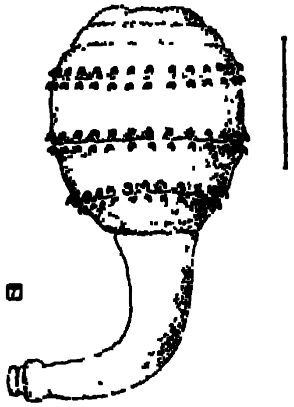


FIG. 423.—YOUNG LARVA OF *Dermatobia cyaniventris*. (× 3.) (After Blanchard.)

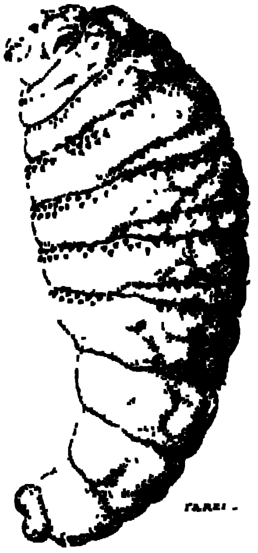


FIG. 424.—OLDER LARVA OF *Dermatobia cyaniventris* MACQUART. (× 2½.)

thin posterior end. The anterior portion is beset with booklets, and has two strong oral hooks. The posterior end carries the stigmata.

If left to themselves, the larvæ will remain in the skin for some time, after which an abscess forms, and they are thrown out, drop on to the ground, and become pupæ, and finally imagos.

We have seen larvæ resembling these in the skins of Europeans in Africa, and similar observations have been made by Plehn, Strahan, Kolb, Nagal, Arnold, and Smith and others, but whether these are *D. cyaniventris* or some other species has not been determined.

Pathogenicity.—They cause pain and itching at the infected spot, with swelling and œdema of the surrounding region, giving rise to a boil-like swelling, rather hard, of a deep red colour, with a central opening. Berne or ura of Brazil is the disease.

Treatment.—On inspecting the region, a small opening will be seen, and the larva may be noted, showing its stigmata at times, and at other times disappearing and reappearing like a jack-in-the-box. There is no difficulty in seizing this parasite with a pair of forceps and forcibly removing it, and then treating the wound antiseptically. The Brazilians try to asphyxiate the larva by tobacco-smoke, or apply some animal fat to the opening in the little tumour. The fat is said to act by preventing the larva from breathing and compelling it to leave the tumour. Some authors advise the application of calomel to the opening.

Dermatobia (?) **keniæ** Kolb.

Kolb described a reddish-brown fly in East Africa under this term.

The fly behaved like *D. cyaniventris* in laying its eggs on the skin of people when bathing. The larvæ entered the skin, forming nodules. The natives called the fly 'ngumba.' It is, however, possible that this is not a true *Dermatobia*, which is a New World genus, but a *Cordylobia*.

FAMILY SARCOPHAGIDÆ.

Muscoidea calyptratæ with large bodies, and antennal bristles feathery at the base, but hair-like and very fine at the tip. Legs stout. First posterior cell closed or only slightly open.

The Sarcophagidæ are the blow-flies, of which *S. carnaria* is common.

Genera.—*Sarcophaga, Wohlfahrtia, Sarcophila, Cynomyia.*

Sarcophaga Meigen, 1826.

It is by no means uncommon in the tropics to find ulcers, and especially syphilitic erosions of the nose, infected with larvæ of flies, which may belong to *S. carnaria* Linnæus, 1758. The larvæ have also been found in several cavities of the human body, and those of the former in the alimentary canal. The following are causes of intestinal myiasis: *S. affinis*, *S. carnaria* Linnæus, 1761; *S. hæmor-*

rhoidalis Fallen, 1810; *S. hæmatodes* and *S. chrysostoma* Wiedemann, 1830. *S. lambens* and *S. ruficornis* cause cutaneous myiasis in South America. *S. plinthopya* and *S. lambens* have been found in ulcers.

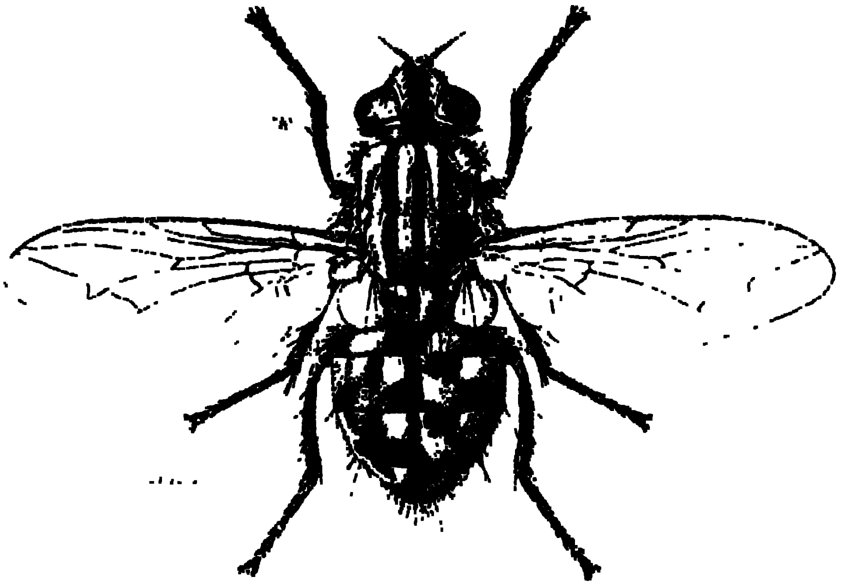


Fig. 425.—*Sarcophaga carnaria* Linnæus: Female. (×3)

Wohlfahrtia Brauer and Bergenstamm, 1889.

The larvæ of *Wohlfahrtia magnifica* Schiner, 1862, have been found in cavities in man's body, and also in cattle, sheep, dogs, and domestic fowls.

Sarcophila Rondani, 1856.

The larvæ of species of this genus *e.g.*, *S. meigeni* Schiner, *S. latifrons* Fall., and *S. ruralis* Fall.--may also be found in ulcers, etc., in Germany, Austria-Hungary, and France.

Cynomyia Robineau-Desvoidy, 1830.

Cynomyia mortuorum Linnæus, 1761, is believed to infect ulcers with its larvæ.

FAMILY MUSCIDÆ.

Muscoidea calyptratæ with stout bodies and short thoraces. Arista either entirely plumose or pectinated. The first posterior cell is either only slightly opened, or else closed at the border of the wing.

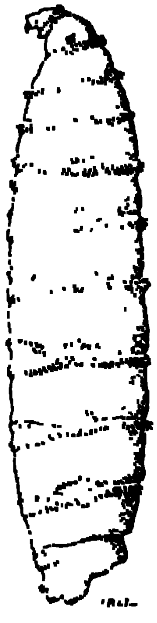


Fig. 426.—Larva of Sarcophaga sp.

The Muscidæ include a number of important genera, which may be recognized by the following table:—

- A. Proboscis long, adapted for biting—***Philæmatomyinæ.***
  - I. Proboscis partly chitinous, partly fleshy, with large fleshy labellæ—*Philæmatomyia.*
  - II. Proboscis entirely chitinous, with attenuated labellæ—*Stomoxydinæ.*
    - (A) Arista feathered dorsally only.
      - (*a*) Palpi thin, much shorter than the proboscis. Third longitudinal vein with bristles proximally; first posterior cell open—*Stomoxys.*
      - (*b*) Palpi thickened, as long as or nearly as long as the proboscis.
        - (1) Proboscis long and tapering; first posterior cell widely open; third longitudinal vein without bristles—*Lyperosia.*
        - (2) Proboscis short and stumpy; first posterior cell narrowly open; third longitudinal vein with bristles proximally—*Stygeromyia.*
      - (*c*) Palpi strongly built everywhere, not thickened. Proboscis thin, more than twice the head length, swollen at the base. Arista with many branched hairs. Media (fourth longitudinal) with two sharp bends—*Glossina.*
    - (B) Arista feathered dorsally and ventrally.
      - (*a*) First posterior cell narrowly open; third longitudinal vein without bristles—*Hæmatobosca.*
      - (*b*) First posterior cell widely open.
        - (1) Third longitudinal vein with bristles proximally—*Hæmatobia.*
        - (2) Third longitudinal vein without bristles proximally—*Bdellolarynx.*
- B. Proboscis short, not adapted for biting—*Muscinæ.*
  - (*a*) Mid tibia without bristle on inner side—*Musca.*
  - (*b*) Mid tibia with bristles on inner side.
    - (1) Thorax and abdomen bluish-black, not lustrous—*Calliphora.*
    - (2) Thorax and abdomen green or greenish, lustrous.
      - (*a*) Scutum longitudinally marked—*Chrysomyia.*
      - (*b*) Scutum not so marked.
        - (A) Thorax metallic green or bluish-green—*Lucilia.*
        - (B) Thorax brassy green or purplish-blue—*Pycnosoma.*
    - (3) Thorax and abdomen dirty brownish-yellow.
      - (*a*) Eyes wide apart in both sexes, second abdominal segment of the female more than half the length of the abdomen—*Auchmeromyia.*
      - (*b*) Eyes of male not wide apart, and second abdominal segment without the above character—*Cordylobia.*

PHYLÆMATOMYINÆ.

Philæmatomyia Austen, 1909.

Stomoxydinæ resembling *Musca domestica* Linnæus, being grey flies with remarkable proboscis. Front in male narrow, its width in centre being from one-eleventh to one-fifteenth of total width of head; width of the front in the female, one-third of total width of head. Proximal portion of proboscis shows a swollen chitinous bulb, distal portion soft and fleshy, and folded back under distal end of bulb when not in use, but when extended there is a tubular extension furnished with a circle of chitinous teeth. Distribution: India, Ceylon (very common), Cyprus, Senegal, and the Congo.

Type Species.- -*Philæmatomyia insignis* Austen, 1909.

Philæmatomyia insignis Austen, 1909.

Smoke grey or yellowish grey in colour, with dorsum of thorax with four dark longitudinal stripes. The eggs are laid in batches of fifty to sixty in cracks in dry cow's-dung. Egg is 2 to 2·2 millimetres in length by 0·4 millimetre in breadth. Larvæ hatch in eight to nine hours, and when mature measure about 1·25 centimetres. They are bright lemon yellow in colour. They burrow under the ground on the evening of the second day, and pupate. The puparium resembles that of *Musca*, 0·5 centimetre long by 0·18 centimetre broad. It is of a light mahogany colour, and has eleven segments. The life-history may be summarized: Egg-laying, five to ten minutes; egg, eight to ten hours; larvæ, two days; pupa, three and a half to four and a half days; total, six to seven days. The fly is ready to feed eight hours after hatching. Feeds usually on cattle only occasionally bites man They pass out a clear watery fluid from the anus while feeding (common in a blood-sucking fly).

Enemies.—Hymenoptera spiders, tachinids.

Other Species. *Ph. lineata* Brunetti, 1910 (synonym, *Pristirrhynchomyia lineata* Brunetti, 1910), and *Ph. gurnei* Patton and Cragg, 1912, both in India.

STOMOXYDINÆ.

Stomoxys Geoffry, 1764.

Arista of three segments, feathered dorsally only; proboscis long, tapering, chitinized in all its extent, non-retractile; palpi slender, very short, less than half the length of the proboscis. Fourth longitudinal vein curved so as to merely narrow the first posterior cell distally; third longitudinal vein bristly at its proximal end. Front narrower in the male than in the female.

Type Species.- -*Stomoxys calcitrans* Linnæus, 1758.

The genus *Stomoxys* is cosmopolitan in its distribution. The principal species are- -

European Species.- -*S. calcitrans* L., 1758.

Asiatic Species.—Twelve species known and two synonyms: *S. brunnipes* Grünberg, *S. calcitrans* L., *S. plurinotata* Bigot, *S. dacnusa* Speiser, *S. indica*

Picard, *S.* ***limbata*** Austen, *S.* ***nigra*** Macquart, *S.* ***bengalensis*** Picard, *S.* ***oblongopunctata*** Brunetti, *S.* ***prattii*** Summers, *S.* ***pulla*** Austen, *S.* ***siliens*** Rondani, *S.* ***triangularis*** Brunetti.

African Species.--Fourteen species and four probable synonyms are known: *S. calcitrans* L. (*S. korogwensis* Grunberg), *S. siliens* Rondani, *S. griseiceps* Becker, *S. nigra* Macquart (*S. glauca* Grunberg and *S. lafonti* Picard), *S. boueti* var. *clara* Roubaud, *S. inornata* Grunberg, *S. omega* Newstead, *S. varipes* Bezzi, *S. intermedia* Roubaud, *S. bouffardi* Picard, *S. bilineata* Grunberg, *S. brunnipes* Grunberg (*S. stellata* Grunberg), *S. tæniatus* Bigot, *S. ochrosoma* Speiser.

American Species.- *S. calcitrans* L.

Australian Species. *S. calcitrans* L.

For the methods of diagnosis of these species, *vide* Summers, L. M. (1912), *Journal of London School of Tropical Medicine*, July, p. 184; London.

The following table, modified from Grunberg, gives the diagnosis of a few of the species:--

A. Legs entirely yellow. Wings yellowish. *S. tæniatus* Bigot, 1887.

B. Legs either entirely black or largely black or blackish-brown. Wings clear or darkish coloured.

I. Venter brilliantly white--*S. siliens* Rondani, 1873.

II. Venter pale dusky brown, with characteristic omega mark on the thorax-- *S. omega* Newstead, 1907.

III. Venter grey or yellow.

1. Thorax without clear black stripes. Hinder part black without any markings. *S. inornata* Grunberg, 1906.

2. Thorax with clear black stripes. Abdomen with regular dark marks or spots.

(*a*) Knee, tibia, and tarsus--at all events, on the two anterior pairs of legs--entirely brown.

(1) Tibia and tarsus on the anterior and middle legs light brown, on the hind legs dark brown. Thorax with two small brown longitudinal median lines--*S. bilineata* Grunberg, 1906.

(2) Tibia and tarsus brown on all three legs. Thorax with broad black longitudinal stripes.

Wings blackish, head and thorax brown yellow--*S. brunnipes* Grunberg, 1906.

Wings glassy, head and thorax grey. *S. stellata* Grunberg, 1906.

(*b*) Legs black, with light brown knees or decidedly dark brown spots.

(1) Wing brushes yellowish-brown, with black tips. Abdomen with dark middle longitudinal line. Second and third segments with dark anterior and posterior borders. *S. glauca* Grunberg, 1906.

(2) Wing brushes black. Abdomen grey. Both middle segments with regularly arranged dark spots without dark median longitudinal line.

Second and third abdominal segments with one middle basal, one side apical dark spot, and dark anterior border, with which the basal spot unites. *S. korogwensis* Grunberg, 1906.

Second and third abdominal segments with the same dark spots, but without anterior border-lines--*S. calcitrans* Linnæus, 1761.

Stomoxys calcitrans Linnæus, 1758.

S. calcitrans is the common stable-fly, found in houses, stables, and in the open near cattle. It bites all classes of mammals, and in so doing is suspected of spreading trypanosomes, especially *T. evansi*. Manders considered *S. nigra* Macquart, 1850, to be the cause of the spread of surra in Mauritius.

It is rather like the common house-fly, but is easily recognized by the head being raised in the resting position, by the projecting proboscis, and by the closed wings, touching one another at their bases, and diverging behind.

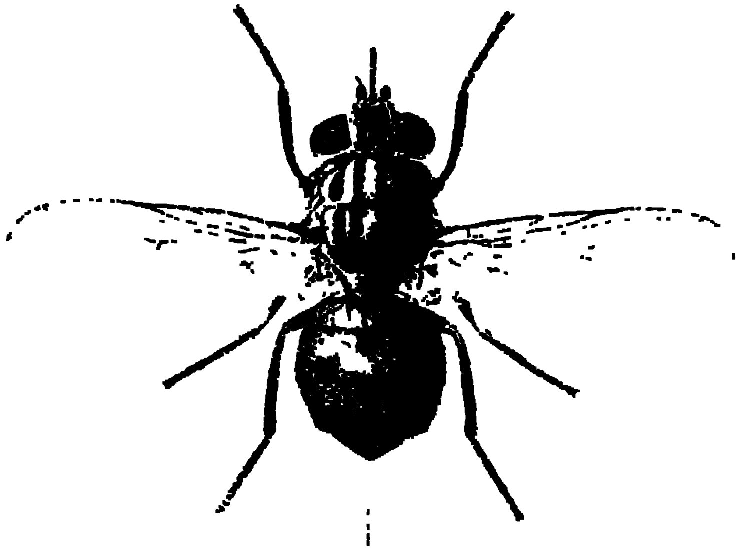


FIG. 327. *Stomoxys calcitrans*. Female.

Morphology. The mouth-parts consist of a proboscis, composed of rostrum, haustellum and labellæ, which are bent posteriorly forming an elbow-shaped joint. The posterior portion can be retracted or projected forwards, and carries the chitinous fulcrum of the pharyngeal wall, the maxillæ and their palps. It is cone-shaped and is called the rostrum.

The structure of the haustellum, or proboscis proper, is very complex. It consists essentially of a labrum, hypopharynx, and labium. The labrum is a sharp-pointed stylet, which near its apex bears a ventral ridge with four sensory hairs. Posteriorly it is attached to the head, where it forms a chitinous projection. It is horseshoe-shaped on transverse section, the ventral opening being closed by the hypopharynx, while laterally its walls, which expand and enclose a cavity containing muscles, articulate with the labium, thus keeping the hypopharynx in its place. The hypopharynx, which contains the salivary tube, starts from the labium and runs forwards, expanding laterally and closing in the labial, pharyngeal, or blood-tube mentioned above. Its lateral expansions contain a cavity. At its tip it appears to be membranous, which Stephens and Newstead think by its flaccid condition prevents ingress of fluid during blood sucking, while freely permitting the egress of saliva. The labium is stout and thick, with a swollen basal portion gradually tapering towards the proximal and distal extremities, but less so basally. Posteriorly it encloses the labrum and hypopharynx, which it carries on a sclerite, which farther forwards forms the boundary of the labial gutter and is joined dorsally by another dorsal hooked sclerite. These sclerites stop at the base of the labellæ. Ventral to the dorsal sclerites are two ventral sclerites, which

anteriorly articulate with a transverse forked sclerite whose arms run forwards. To these arms the tendons of longitudinal muscles are attached, which are capable of rotating them, causing the eversion of the labellæ. Farther forward the two labellæ are strengthened internally by dorsal and ventral sclerites, while a pear-shaped axial apophysis projects forwards freely from the labium.

The ventral plate is obliquely placed, and carries—(1) five teeth; (2) nine sets of petiolated blades; (3) six sets of rod-like hairs; (4) five sets of operculate hairs; (5) six sets of bifurcated hairs; (6) an anterior dorsal fringe of hairs; (7) a posterior ventral set of hairs; (8) ventral phalanges or lips with ventral hairs; (9) dorsal external set of hairs; and (10) latero-external set of hairs.

Internal Anatomy.—The pharyngeal tube leads into the pharynx, whose wall is formed by the chitinous fulcrum. The œsophagus, at first flattened, afterwards cylindrical, passes into the thorax and opens into the ventral surface of the proventriculus. At this point it is joined by the duct from the crop or sucking stomach, which is a large hollow blood-reservoir lying in the abdomen. The chylific ventricle has three coils. The usual Malpighian tubules, small and large intestine and rectum are present. The salivary gland resemble those of *Musca* and *Glossina*.

Method of Biting.—*Stomoxys* carefully inspects the skin, and having selected a spot, everts the labellæ, and by a rotatory motion cuts a hole through the epidermis by means of its teeth, and then, inserting the proboscis into the wound, sucks the blood.

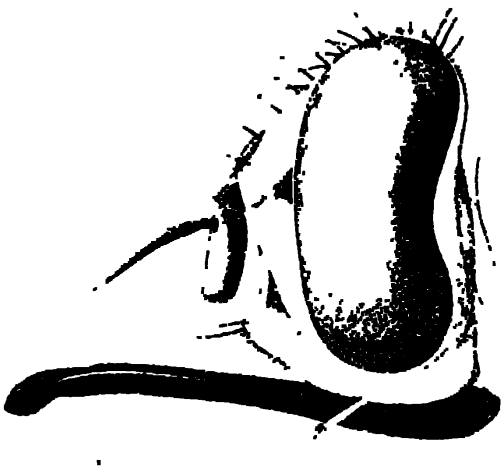


FIG. 428.—HEAD OF *Stomoxys calcitrans*: FEMALE.

Life-History.—The life-history has been studied by Newstead, who finds that the incubation period of the egg is two to three days, the life of the larva fourteen to twenty-one days, the pupal stage nine to thirteen days, making the total life-cycle twenty-five to thirty-seven days, but this may be considerably prolonged by the incubation and larval stages being lengthened in the absence of moisture, or the presence of a low temperature.

The eggs are 1 millimetre in length, white, turning later to a cream colour; coriaceous and reticulated; curved on one side and straight on the other, where there is a broad deep groove, wider anteriorly, where the larva escapes. The number of eggs varies from forty-eight to seventy-one, and they are laid in warm dung and fermenting grass.

The larva is 11 millimetres long, and tapering, yellowish in colour, with blackish mouth parts. The segmentation is not well marked. The head has two large diverging processes, which carry the four-jointed antennæ. The mouth is armed with a hook-like mandible, which carries a ventral tooth, and is attached by means of a hypostomal sclerite to two large cephalo-pharyngeal sclerites, in front of the upper arms of which is a small perforated sclerite. The posterior stigmata are two in number. The mouth-hook is used for locomotion.

Pupation is brought about in two hours by the larva shortening itself and becoming barrel-shaped, the colour turning to red. The pupa measures 5 to 5·5 millimetres in length, and possesses eleven visible segments. In a few days the pupal skin is split along lateral and median lines anteriorly, and at the fourth segment transversely, and the imago escapes.

Lyperosia Rondani, 1862.

Synonym.—*Glossinella* Grunberg, 1906.

Stomoxydinæ resembling *Stomoxys*, but with palpi as long as the long slender proboscis, around which, as they are broad, they form almost a sheath, with no bristles on the third longitudinal vein. Distribution: Europe, Asia, Africa, North America, and Australia.

Type. —*Lyperosia irritans* Linnaeus, 1761

They are dirty brown or dirty yellowish-grey, very small blood-sucking flies, with inconspicuous markings, and usually only attack animals, and do not come into houses.

European Species. *L. irritans* L., 1758, *L. titillans* Bezzi, 1911.

Asiatic Species.—*L. minuta* Bezzi, 1892, *L. schillingsi* Grunberg, 1906, *L. exigua* de Meijere, 1903; *L. flavohirta* Brunetti, 1910; *L. rufipalpis* Becker 1910 (probably *Stygeromyia maculosa* Austen, 1907).

African Species.—*L. minuta* Bezzi, 1892; *L. longipalpis* Roubaud, 1906 (= *L. pallidipes* Roubaud, 1907), *L. schillingsi* Grunberg, 1906 (= *St. maculosa* ?); *L. potans* Bezzi, 1908; *L. punctigera* Austen, 1909; *L. exigua* (Meijere, 1903); *L. thirouxi* Roubaud, 1903.

American Species.—*L. irritans* L., 1758, *L. alcis* Snow, 1891 (synonym: *Hæmatobia alcis* Snow, 1891).

Australian Species. *L. exigua* Meijere, 1903.

(For details see Summer's paper, *vide infra*.)

Stygeromyia Austen, 1907.

Stomoxydinæ with general appearance and body like *Stomoxys*, proboscis and palpi like *Hæmatobia*, arista feathered dorsally only. Head flattened from front to rear; proboscis short, stout, shiny, chitinous, not tapering, palpi as long as the proboscis; clavate at tips, curving upwards. Cell opening as in *Stomoxys*. Apical portion of fourth vein straight beyond bend—*i.e.*, not bent inwards as in *Stomoxys* and *Hæmatobia*. Distribution: Africa and Southern Arabia.

Type.—*Stygeromyia maculosa* Austen, 1907.

Stygeromyia sanguinaria Austen, 1909, is stated by Yale Massey to be a blood-sucker in the Congo Free State, while *S. maculosa* Austen, 1907, found in Little Aden, is inferred to be also a blood-sucker, and *S. woosnami* Austen, 1912, in East Africa.

Glossina Wiedemann, 1830.

Synonym.—*Nemorhina*, Robineau-Desvoidy, 1830.

Narrow bodied, elongate, greyish-brown or yellowish-brown, dull-coloured flies, with the wings closed flat over one another, and projecting considerably beyond the abdomen when at rest, with an anterior projecting proboscis, beyond which the palpi slightly extend, and in which they are ensheathed. Base of proboscis bulbous.

This is the genus of the tsetse-flies, a name probably derived from the noise which they make when flying, and now used in a generic sense. They were first named by Wiedemann from *G. longipalpis*, brought from Sierra Leone by Adam Afzelius, and in the same year Robineau-Desvoidy named another species from the Congo *Nemorhina palpalis*. Their bites have been long known to be dangerous to animals, but it was not till Bruce showed that they were the spreaders of *Trypanosoma brucei* and the cause of the disease nagana in horses, etc., that they received much attention. The interest in them became vastly greater when in 1903 Bruce and Nabarro showed that they were the spreaders of *T. castellanii* and especially when Kleine showed that the transmission was not mechanical.

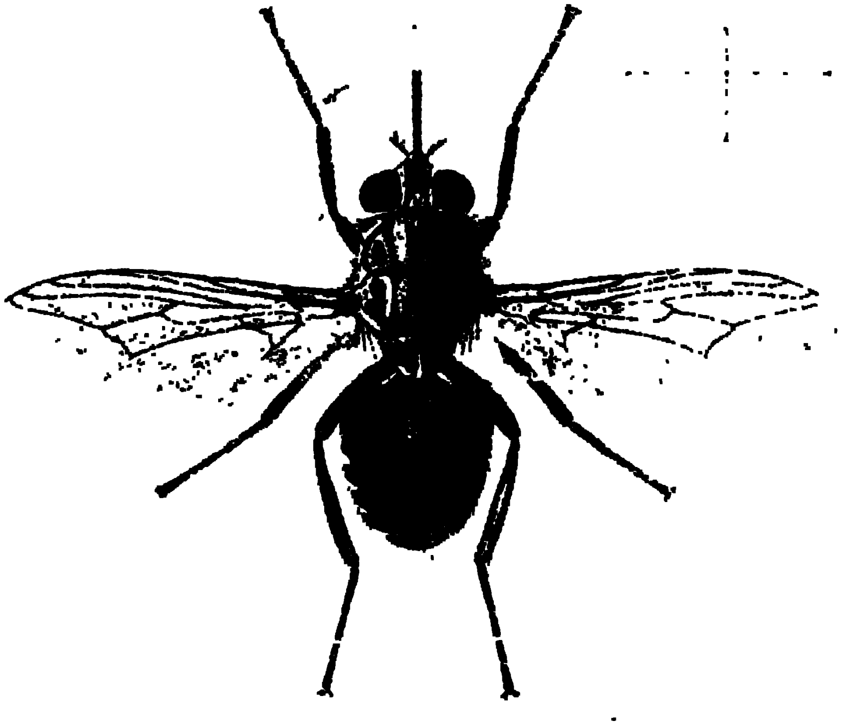


FIG. *Glossina palpalis*: FEMALE

The genus is confined to tropical Africa and Arabia.

Morphology.—The points in the morphology to which attention should be paid are as follows:—

The eyes are large and bare, and between them the vertex is depressed, and at its back carries ocelli. In front a deep facial pit is separated by a transverse impression from the gena. The proboscis projects horizontally forwards, while its bulbous posterior portion is enclosed in a fold of skin. Palpi are rod-like, and clothed with short black hairs, and enclose the proboscis. The antennæ are three-jointed, the first two being small and the third large, with its anterior external angle prominent and directed forwards and outwards. At its base is attached a two-jointed arista, of which the first segment is small, and the second long and tapering, bearing some twenty-two fine, curving, branched hairs on its upper surface only. Bristles are frontal, vertical, ocellar, and post-medial.

With regard to the thorax, the most important feature is the wing, which is brownish, with a peculiar venation. The costal vein is

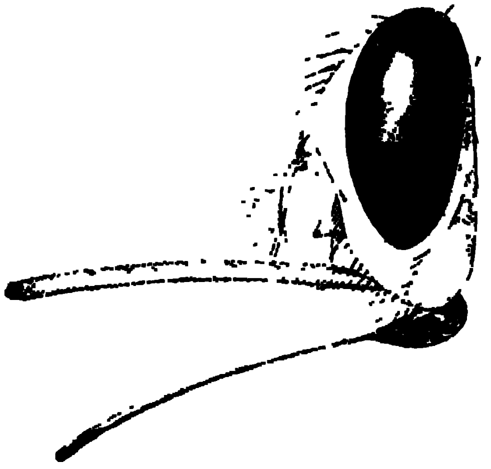


FIG. 430.—HEAD OF A GLOSSINA.

This figure shows the proboscis being lowered previously to piercing the skin to suck blood.

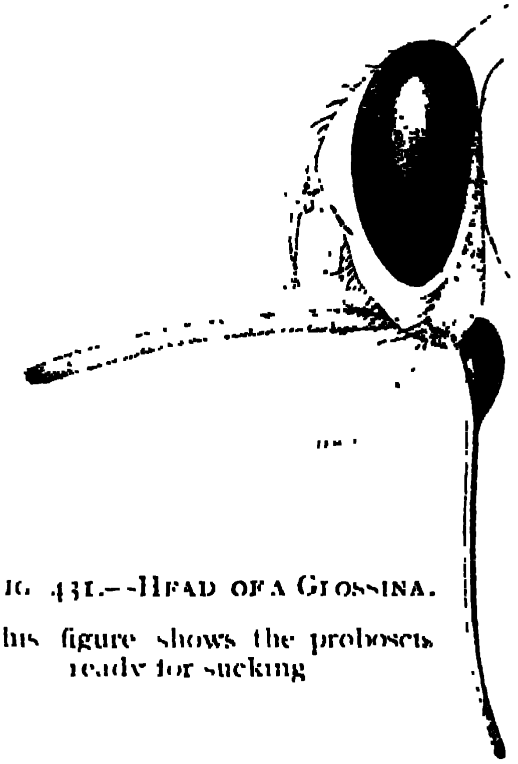


FIG. 431.—HEAD OF A GLOSSINA.

This figure shows the proboscis ready for sucking.

well marked, and the subcostal vein (auxiliary) joins it about the junction of the inner with the outer third in the extended position of the wing, thus enclosing the costal cell, which is divided into two portions by the humeral transverse vein. The radius 1 (first longitudinal) curves forwards, joining the costa about the junction of the inner two thirds with the outer one-third, thus forming a very narrow subcostal cell. The radius 2 and 3 (second longitudinal) also curves forwards, meeting the costal margin before the tip of the wing is reached, as does the radius 4 and 5 (third longitudinal); hence the marginal and submarginal cells are long and narrow. The media (fourth longitudinal) is highly characteristic. It starts separately from the preceding, and running outwards, after meeting with the anterior basal vein, curves forwards to join with the anterior transverse vein, when it bends at right angles, turning backwards

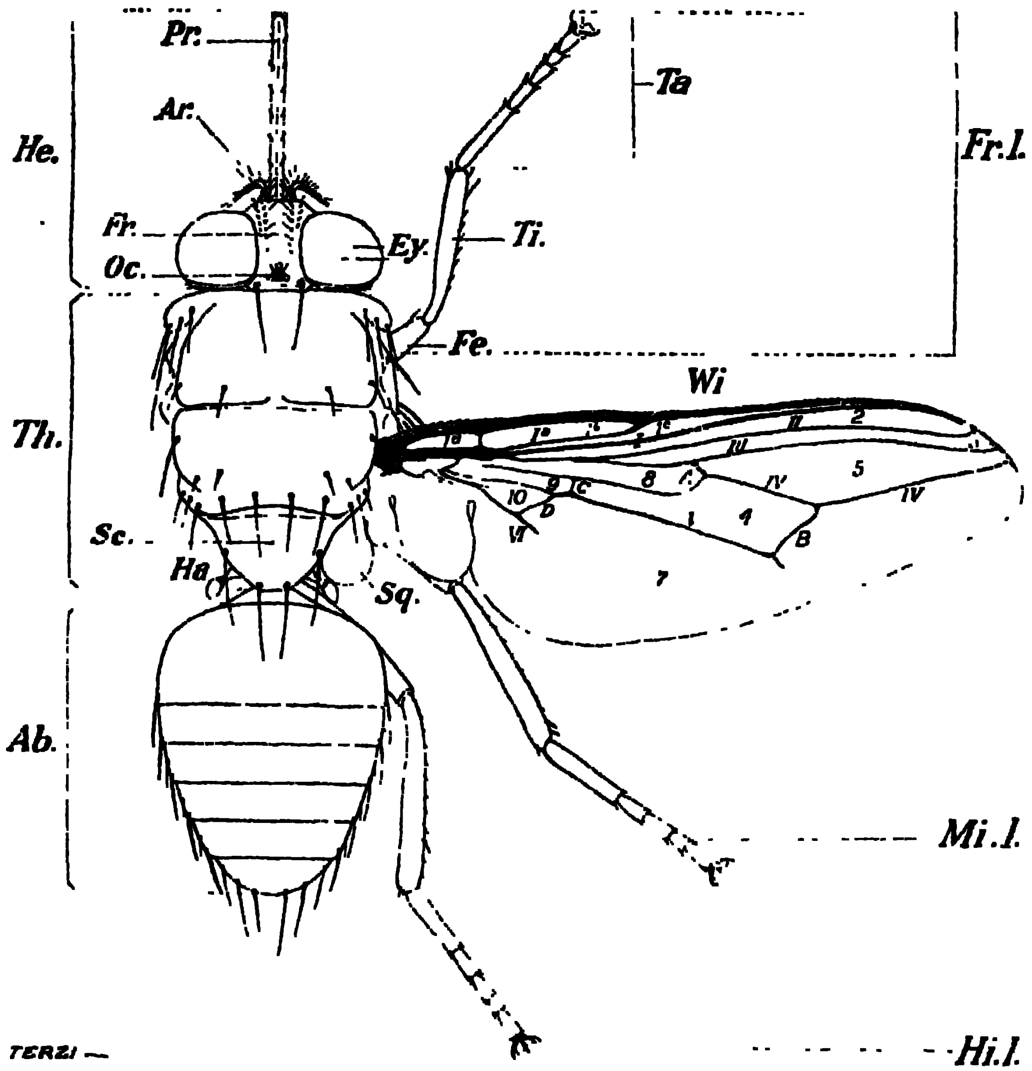


FIG. 432.—DIAGRAM OF A TSETSE-FLY.

(Modified after Austen, from 'Monograph of Tsetse-Flies')

He., head; *Th.*, thorax; *Ab.*, abdomen; *Fr. l.*, front leg; *Mi. l.*, middle leg; *Hi. l.*, hind leg; *Pr.*, proboscis ensheathed by the palpi; *Ar.*, arista; *Fr.*, frons; *Oc.*, occiput; *Ey.*, eye; *Sc.*, scutellum; *Ha.*, haltere; *Sq.*, squama; *Wi.*, wing; *Fe.*, femur, *Ti.*, tibia; *Ta.*, tarsus.

Venation of Wing.—*Ia*, Subcostal or auxiliary vein; 1*a*, 1*b*, two portions of the costal cell divided by the humeral transverse vein; 1*c*, subcostal cell; *I*, radius 1, or first longitudinal; 2, marginal cell; *II*, radius 2 and 3, or second longitudinal; 3, submarginal cell, *III*, radius 4 and 5, or third longitudinal; 8, first basal cell; 5 first posterior cell; *A*, anterior transverse vein; *IV*, media or fourth longitudinal; 9, posterior basal cell; 4, discoidal cell, external to which is the second posterior cell, without a number; *B*, posterior transverse vein; *C*, anterior basal vein; *V*, cubitus 1 and 2, or fifth longitudinal; *D*, posterior basal transverse vein; 10, posterior basal cell; 7, third posterior cell; *VI*, anal or sixth longitudinal.

and outwards to join with the posterior transverse vein, when it again turns and runs obliquely forwards to join the costal vein just in front of the tip of the wing. Between it and the radius 4 and 5 (third longitudinal) lie internally the first (anterior) basal cell, and externally the first posterior cell, separated by the anterior transverse vein, which is very oblique. The cubitus 1 and 2 (fifth longitudinal) joins the anterior basal vein, marking out the posterior basal cell, and then runs forwards to join the posterior transverse vein, marking out the discoidal cell, which is hatchet-shaped, with the handle running up to the anterior basal transverse vein. After this the vein turns backwards to join the margin of the wing, delineating the large second posterior cell. The anal (sixth longitudinal) is very short, being unchitinized after meeting with the posterior transverse basal vein, with which it marks out the posterior basal cell. The third posterior cell is, however, shown by its unchitinized trace. The posterior part of the wing shows an incrassation corresponding to anal 2 and 3.

The legs are simple, rather long, with long claws and pulvilli.

The abdomen is flattened, tapering to the apex, and clothed with short black hairs. The male genitalia are characteristic. The ventral plate of the sixth segment carries a patch of dark hairs on each side of the middle line, behind which is the hypopygium, which is oval, tumid, and marked by a vulviform median groove, the anus, running from its anterior margin backwards to beyond the middle.

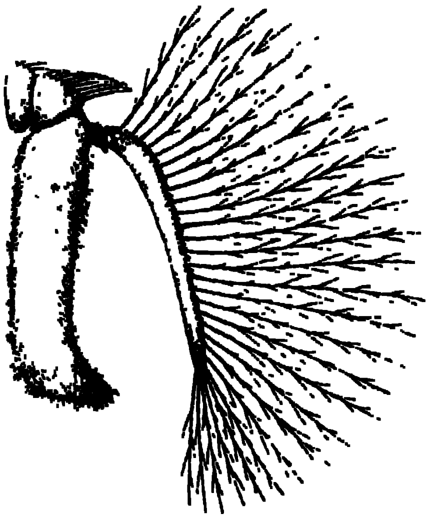


FIG. 433.—ANTENNA OF A GLOSSINA SHOWING THE ARISTA

(After Austen, from 'Tsetse-Flies.')

The proboscis shows the usual rostrum or conical head projection, the haustellum, or proboscis proper, and the labellæ.

The proboscis proper is composed of labrum, hypopharynx, and labium. The labrum arises from the basal bulb of the proboscis in the form of a tube, which is continuous posteriorly with the pharynx, while anteriorly it runs forwards, forming the dorsal wall of the proboscis. In this position it articulates by means of interlocking teeth with the labium, while, opening ventrally, it articulates with the hypopharynx, which closes the potential ventral opening. Farther forwards it separates from the labium, and ends in a point. The tube composed by the hypopharynx and the labrum is the afferent blood or pharyngeal tube. The hypopharynx starts below the pharynx surrounding the salivary efferent duct, and pierces the bulb of the proboscis, appearing on its dorsal aspect. Farther forward it lies in a groove on the labium, articulating laterally with the labrum. Finally it ends as a delicate chitinous tube just posterior to the labellæ. Its canal is the salivary tube or hypopharyngeal canal.

The labium, or second maxilla, starts from the ventral area of the head, and is first swollen to form the bulb. Anteriorly it is grooved dorsally to hold the hypopharynx and the labrum, while farther anteriorly it ends in the labellæ. These structures (labellæ) are joined together in the ventral line, except anteriorly, where there is a V-shaped notch, while dorsally they possess teeth which interlock.

In the ventral line the chitinous floor of the labium is prolonged forwards in the form of a fork, in front of which is a membranous area anteriorly to which the inner wall of each labellum becomes divided into dorsal, median, and ventral segments. Each segment is armed with a series of about ten rasps, composed of some thirty minute bars, in front of which are two pairs of teeth. Between the bases of the anterior pairs of teeth there projects a fan-shaped mass of spine-like scales. The segments are capable of eversion, when the muscles pull backwards the external walls of the labellæ. In this way the teeth would be brought in contact with the skin, and the wound necessary for blood-sucking made, probably by rotatory movements.

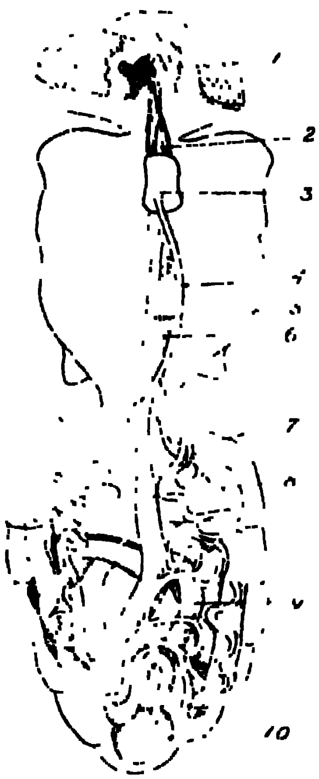


FIG. 431.—ANATOMY OF A TSETSE-FLY.

(After Minchin from Reports of the Royal Society.)

1, Pharynx; 2, œsophagus; 3, proventriculus; 4, thoracic intestine; 5, duct of sucking stomach; 6, salivary duct; 7, salivary gland; 8, sucking-stomach; 9, abdominal intestine; 10, rectum.

Internal Anatomy. The internal anatomy has been carefully studied by Minchin, and does not materially differ from that of *Stomoxys*.

The pharyngeal tube opens into the pharynx, which is situated mainly in the rostrum. Its walls are strongly chitinized, forming the fulcrum. The œsophagus runs upwards and then backwards to open into the proventriculus, and to be continuous via a long ventral duct with the crop, which lies in the first two segments of the abdomen. The chylific ventricle is narrow at first in the thorax, but becomes wider in the abdomen, where it coils several times. There are the usual ileum, colon, rectum, and Malpighian tubules.

The salivary glands are two long coiled tubes lying first in the abdomen, and then passing into the thorax, and probably opening finally on the hypopharynx, though this has not yet been worked out.

Life-History.—The species of *Glossina* live in jungles or bush, along the banks of streams or lakes. They appear to live principally upon the blood derived from big game, but Koch believed that *G. palpalis* lives on that of crocodiles, and Hodges, on that of hippopotami. According to Kinghorn, copulation in *G. morsitans* lasts for several hours. The female in due course produces a single larva, and may produce a second after fourteen to fifteen days. At the completion of intra-uterine life the larva almost completely fills the abdomen of the mother. Its extrusion takes place very rapidly, and it commences to crawl at once. The larvæ, which are yellow-coloured, are to be found as a rule near the roots of banana-trees. These larvæ are composed of twelve segments, the anterior of which carries the two minute mouth-hooks, and the posterior a dark hood or anal segment. The larvæ retire to some hole, and in a few hours become jet black pupæ from which the fully developed insects issue in about six weeks.

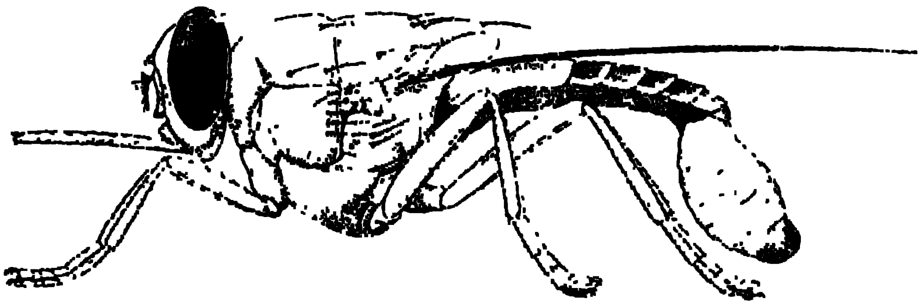


FIG. 135.—A GLOSSINA IN THE ACT OF GIVING BIRTH TO A LARVA. (Modified after Newstead.)

The pupa is 5·53 (5 to 6) millimetres long, and 3·2 (3 to 3·75) broad, according to an average of twenty measurements by Kinghorn, with twelve segments. The anterior four show the longitudinal seam, which bifurcates at the fourth segment, forming an opening through which the imago escapes. The first segment carries the mouth, and the twelfth two lateral tumid, tuberculated lips, connected by dorsal and ventral ridges enclosing a pit, in which the posterior stigmata can be seen.

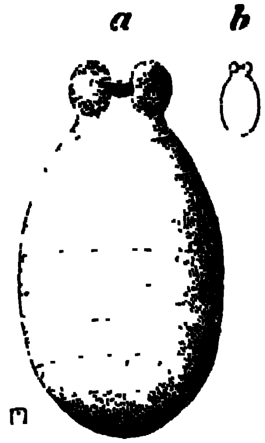


FIG. 136.—PUPA OF A TSETSE FLY. (After Austen, from 'Tsetse Flies.') *a*, Magnified; *b*, natural size.

The larvæ of *G. palpalis* measure 4·5 by 1·75 millimetres, and the pupæ 5 to 5·75 by 3 millimetres.

According to Kinghorn, forty-seven to fifty-three days elapse from the birth of the larva to the escape of the imago in *G. morsitans*.

Bionomics.—As *G. palpalis* is most probably the sole means of propagation of human trypanosomiasis, it is important to have some idea of what is known as to its bionomics, which have been carefully studied by Hodges and Bagshawe.

The main resort of the fly is to be found in bush near water, especially in the undergrowth composed of shrubs, bushes, vines, creepers, tall grass, cane-break tangle, and herbaceous plants. Tall trees alone will not afford the protection necessary for the fly unless they overhang the water, or their foliage reaches so low as to mix with the undergrowth.

The fly is, however, not met with behind a wide strip of papyrus, though it may be found on its water edge. This is explained by Bagshawe on the grounds that papyrus grows best in shallow water, which means that the ground is swampy, a condition which prevents the fly from depositing its larvæ. From a resort such as this a fly can travel for feeding purposes, or be carried by attraction or artificial means. It appears probable from Bagshawe's experiments that a single flight will not reach 70 to 80 yards, but flies can be carried to almost any distance by the agency of boats and floating islands of papyrus. Human traffic also increases the dissemination of the fly, as it is apt to pursue human beings for considerable distances.

Female flies appear to travel farther in search of food than males, probably because they more urgently require it. Bagshawe suggests that this can be made use of in finding the breeding-grounds, where he says plenty of males as well as females are to be found, while females alone may be met with at some distance therefrom. The feeding range, therefore, varies considerably.

Flies bite mostly during the middle part of the day, and not so much at dawn or in the late afternoon.

According to Hodges, the chief conditions required for a breeding-ground are loose, dry, friable earth, situate not more than 20 yards away from the high-water mark of a stream, and protected from sun and rain by the shade of trees and undergrowth.

Such conditions are found on steep banks along lakes, rivers, watercourses, etc., and the larvæ are to be looked for at the bases of shrubs and trees, in the undergrowth, and in earth-filled hollows in tree-trunks and branches at no great distance from the ground.

Bagshawe found the larvæ principally at the roots of bananas with scrub and water in the immediate neighbourhood; at the roots of a shrub called *Allophyllus*, belonging to the Sapindaceæ, especially in the dry season; at the roots of large figs and of the wild date-palm (*Phœnix reclinata*): while he also found a few pupæ in dry earth sheltered by overhanging rocks on wooded banks.

The breeding season appears to be at the commencement of the rains, as Bagshawe generally found empty pupal cases in the dry season.

The pupæ apparently have their enemies which eat them. These are minute winged insects probably belonging to the Chalcididæ, though this is not definitely known.

Pathogenicity.—*Glossina palpalis* is the carrier of *Trypanosoma castellanii*, and *G. morsitans* of *T. rhodesiense*, both of which are the causes of sleeping sickness in Africa.

Classification.—Newstead in 1911 revised the genus *Glossina*, and published a classification based on the male genital armature. This is a very excellent

classification, but requires the addition of female characters to complete it. We have, therefore, kept Austen's revised classification in 1911, which slightly modified, is as follows:—

A. Hind tarsi entirely dark (female of *Glossina tachinoides*), basal half of first and extreme bases of succeeding joints pale. **Glossina palpalis group.**

I. Ground colour of abdomen ochraceous buff, with interrupted dark brown deep transverse bands and sharply defined pale hind borders to segments. A very conspicuous square or oblong pale area in the centre of the second segment. Small species: Body length 7 millimetres—*G. tachinoides* Westwood, 1850.

II. Abdomen not so marked.

1. Third joint of the antenna dusky brown to cinereous black

(*a*) Dorsum of abdomen dark sepia brown, median paler area on second segment, broad, more or less quadrate or irregular, hypopygium of male buff or ochraceous buff—*G. caliginea* Austen, 1911

(*b*) Dorsum of abdomen blackish brown, median paler area triangular, hypopygium of male grey *G. palpalis* Robineau-Desvoidy, 1830.

2. Third joint of antenna pale *G. pallicera* Bigot, 1891.

B. Hind tarsi not entirely dark (except in *G. austeni*).

I Upper surface of abdomen with pale ground colour, drab grey, buff, or ochraceous buff, marked with very conspicuous dark brown or clove brown transverse bands interrupted in the middle line **Glossina morsitans group.**

(*a*) Last two joints of front and middle tarsi with sharply defined dark brown or black tips

(1) Large species: Wide head, darker anteriorly, abdominal bands deep *G. longipalpis* Wiedemann, 1830

(2) Smaller species: Narrower head *G. morsitans* Westwood 1850

(*b*) Last two joints of fore and middle tarsi very narrowly darker, and sometimes the colour is absent in the former *G. austeni* Newstead 1912

(*c*) Last two joints of fore and middle tarsi pale Body length 8 to 10 millimetres—*G. pallidipes* Austen 1895

II Upper surface of abdomen not so banded.

(*a*) Wings dull sepia coloured, palpi (except in *G. tabaniformis*) long and slender **Glossina fusca group.**

1. Third joint of antenna fringed anteriorly and posteriorly with hairs conspicuous when magnified 15 diameters.

(A) Longest hairs in front of third joint equal in length from one quarter to one-third of width of third joint; palpi moderately long—*G. tabaniformis* Westwood, 1850.

(B) Longest hairs in front of third joint equal in length from one-half to one-third of width of third joint; palpi noticeably long and slender *G. nigrofusca* Newstead, 1910.

2. Third joint antennae fringed anteriorly with five short hairs, scarcely noticeable when magnified 15 diameters

(A) Pleura drab grey, hind coxæ buff or greyish buff—*G. fusca* Walker, 1849.

(B) Pleura dark grey, hind coxæ mouse grey—*G. fusci-pleuris* Austen, 1911.

(*b*) **Wings pale, palpi short—Glossina brevipalpis group.**

(1) Dorsum of thorax with four sharply defined dark brown oval or elongate spots, arranged in a parallelogram, two in front and two behind the transverse suture proboscis bulb, with brown or dark brown tip *G. longipennis* Corti, 1895.

(2) Dorsum of thorax without such spots, and proboscis bulb not brown or dark brown at the tip.

- (i.) Wings with upper thickened portion of anterior transverse vein dark and distinct—*G. brevipalpis* Newstead 1910.
- (ii.) Wings with anterior transverse vein *G. medicorum* Austen, 1911

Recently Grunberg has described a new species, *G. ziemanni* Grunberg, 1912 but its position at present is not quite certain

Hæmatobosca Bezzi, 1911.

Stomoxydinæ resembling *Hæmatobia*, but with no bristles on the first and third longitudinal veins, and with fourth longitudinal vein almost as strongly bent as in *Musca*; therefore first posterior cell only very narrowly opens Distribution Southern Europe and China.

Type. *Hæmatobosca atripalpis* Bezzi, 1895.

European Species. -*H. atripalpis* Bezzi 1895.
Asiatic Species. *H perturbans* Bezzi, 1907, found at Tang-San, China.

Hæmatobia Robineau Desvoidy, 1830.

Synonym. *Siphona* Meigen, 1824.

Stomoxydinæ resembling *Stomoxys*, but with spatulate maxillary palps nearly as long as the proboscis: arista feathered dorsally and ventrally, and third longitudinal vein bristly proximally. Body robust, head broad and squat Distribution Europe, India, etc.

Type. *Hæmatobia stimulans* Meigen, 1824.

European Species.—*H. stimulans* Meigen
Asiatic Species. -*H. sanguisugens* Austen, 1909; *H rufipes* Brunetti, 1910, in India.

Bdellolarynx Austen, 1909.

Flies like *Hæmatobia*, but without sexual colour dimorphism. Arista with long hairs above and with six fairly long hairs below. No bristles on first and third longitudinal veins.

B. sanguinolentus Austen, 1909, is a blood-sucker found in India and Ceylon.

MUSCINÆ.

Musca Linnaeus, 1761

Musca putrida is the cause of *Myiase do Seio* in San Paulo

Calliphora Robineau Desvoidy, 1830.

These are the blow-flies or bluebottles, of which *C. erythrocephala* Meigen is the common species. It and the following have been found in the human intestine: *C. azurea*, *C. vomitoria*. *C. limensis* is a common cause of nasal myiasis.

Chrysomyia Robineau-Desvoidy, 1830.

Chrysomyia macellaria Fabricius, 1794.

Synonyms.—*Musca macellaria* Fabricius, 1794; *Lucilia macellaria* Robineau-Desvoidy, 1830; *L. hominivorax* Coquerel, 1858; *Calliphora infesta* Philippi, 1861; *C. macellaria* Jorge, 1878; *C. anthropophaga* Conil, 1878; *Compsomyia rubrifrons* Macquart; *Somomyia montevidensis* Bigot.

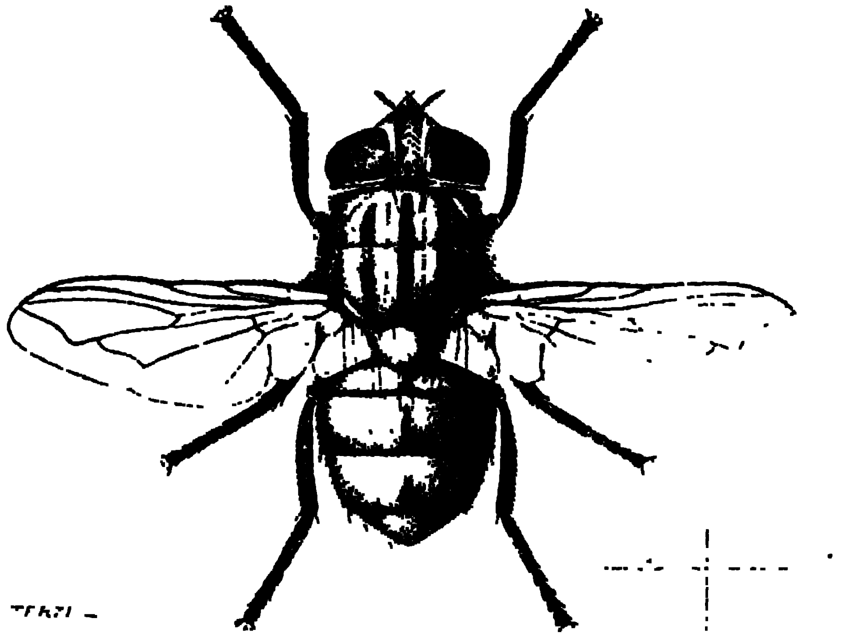


FIG. 437.—*Chrysomyia macellaria*: FEMALE. (× 4.)

In all this fly has twenty-six synonyms, largely due to Walker, Macquart and Robineau-Desvoidy, but these were all carefully consolidated by Arribálzaga.

Muscinæ with blue bodies, red front to the head, and three black lines on the thorax. The body, which is less than 10 millimetres in length, is covered with stiff black hairs.

Life-History.—The female deposits some three or four hundred eggs in a space of a few moments in some wound or decaying matter, but as the same fly may oviposit in different places at different times, the total number of eggs laid by one fly must number some hundreds, or perhaps even thousands. The eggs are white and cylindrical, 1 millimetre in length, and marked by a prominent unilateral ridge. They hatch in from one to nine hours, and produce a whitish footless larva, rather slender,

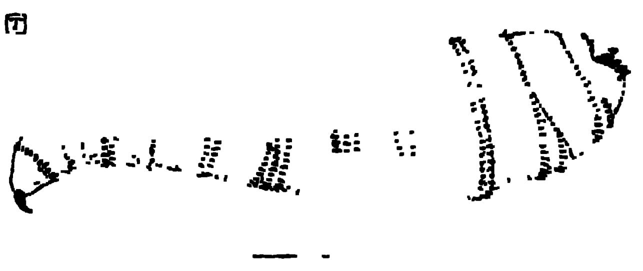


FIG. 438.—*Chrysomyia macellaria*: LARVA. (× 4.)
(After Blanchard.)

with twelve segments, armed with minute spines. It is most active, and burrows into the tissues of the affected animals or into the mass of putrid flesh or decaying matter. It grows rapidly and matures in from five to seven days, when it endeavours to escape from the wound or cavity on to the ground, when it wriggles off and buries itself in the ground at a suitable place, and becomes the brown cylindrical pupa with rounded ends. The pupa is about $\frac{3}{8}$ inch in length, and matures in some nine to fourteen days.

Habits.—It is a pest to man and animals.

Distribution.—America, from Canada to Patagonia, but most common in the tropical and subtropical belts. It is killed by cold winds. In the Southern United States it occurs from July to October. It is also found in the West Indies.

Pathogenicity.—It attacks cattle after castration, spaying, branching, dehorning, and when wounded by ticks or barbed wire. It will enter the uterus if there is placental retention, and will attack the navels and mouths of young calves. Horses and mules may be attacked in the sheaths and vaginæ, and in the navel in colts. Hogs are especially liable to be attacked, but sheep rarely, unless after being worried by dogs. Man is attacked when sleeping in the open air, and more rarely when driving. The symptoms produced in man will be detailed later under Nasal Myiasis in Chapter LXVII.

Treatment.—Injections of chloroform water are the best means of getting rid of the larvæ, but the frontal and other sinuses may have to be opened to remove them if in large numbers.

Prophylaxis.—The use of mosquito curtains and protection to the nose by handkerchiefs are important in man. Wounds of animals should be washed with weak carbolic lotion and dressed with pine tar or oakum and tar.

Chrysomyia viridula.

Causes nasal myiasis in Central America, and will attack ulcers.

Pycnosoma Brauer and Bergenstamm, 1893.

The larvæ of *Pycnosoma putorium* Wiedemann, 1830, are said to be parasitic in man and the domestic animals in Abyssinia, the Belgian Congo, and Lorenzo Marques.

This fly resembles *Chrysomyia,* but the three dark stripes on the dorsum of the thorax are wanting.

Pathogenicity.—It causes nasal myiasis in man, while other species—*e.g., P. megacephala* and *P. marginale,* etc.—are found in cattle.

Lucilia Robineau-Desvoidy, 1830.

Flies of this genus—*e.g., L. cæsar* Linnæus and *L. sericata*—deposit their eggs on ulcers. *L. nobilis* Meigen has been found in the auditory meatus. According to Peiper, *L. cæsar* Linnæus and *L. regina* Macy have been recognized as causes of intestinal myiasis.

Cordylobia Grünberg, 1903.

Cordylobia anthropophaga E. Blanchard.

Synonyms.—*Ochromyia anthropophaga* E. Blanchard, *Glossina grünbergi* Donitz.

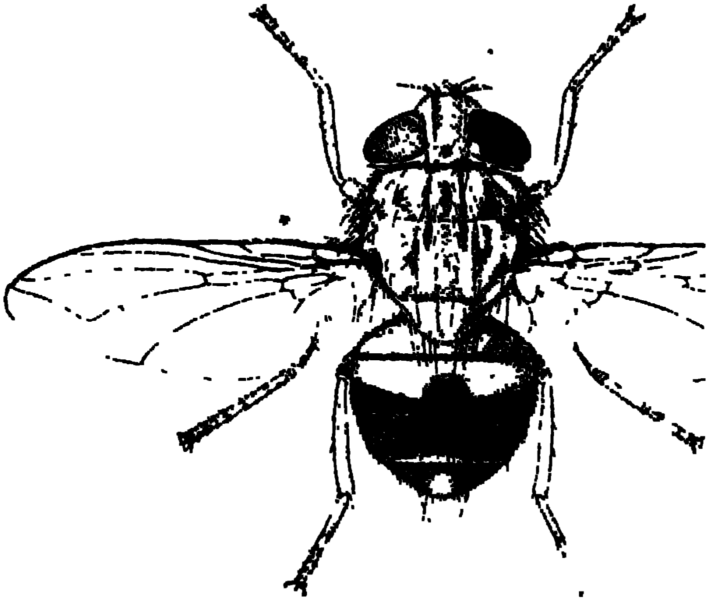


FIG. 439.—*Cordylobia anthropophaga* BLANCHARD: FEMALE. (× 4.)

The larva of this fly, which is called 'ver du Cayor,' because it was first noticed in Cayor, in Senegambia, burrows into the skin and causes a painful swelling. It extends from Senegal to Natal.

Life-History and Morphology.—It is not certain whether the fly lays its eggs upon the ground or upon the clothing of people and the skin of animals. Hence it is not known whether the larva creeps from the ground on to the human being or animal, or hatches in the clothing and simply enters the skin.

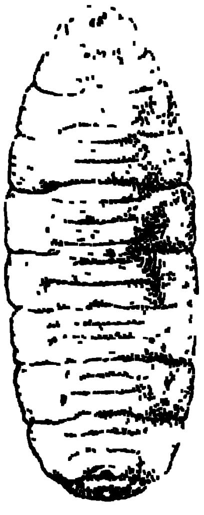


FIG. 440.—LARVA OF *Cordylobia anthropophaga*. (× 4.) (After Austen.)

The larva, which measures about 12 millimetres, is composed of twelve segments, of which the anterior or cephalic is bluntly pointed in front and truncated behind, and carries two black mouth hooklets on its ventral surface. External to these hooklets lie the antennal protuberances. On the third to the eleventh segments there are minute, rather characteristic, brownish, chitinous, recurved spines. The greatest breadth is at the level of the sixth to seventh segments, while the last segment has a flattened posterior surface which carries the posterior stigmata. It is parasitic in men, monkeys, and dogs. The pupa measures 10·3 by 4·6 millimetres, and looks like an ordinary muscid pupa.

The fly measures 9·5 millimetres, and has a yellowish-coloured head, body, and wing. The thorax is marked dorsally by longitudinal dark stripes, while the abdomen has also blackish markings, and the wings are of a brownish tinge. The female is distinguished from the male by the eyes being separated by a broad frontal stripe; in the black colour of the third and fourth abdominal (except the margin) segments: and in the blackish quadrangular median patch on the second abdominal segment. In the male the eyes join.

Cordylobia rodhaini Gedoelst, 1905.

Synonym.—Lund's larva.

Under this term a larva is described as occurring in the Congo Free State which possesses habits similar to those of *Cordylobia anthropophaga*.

The larva of this species also occurs at times under the skin of man in the Belgian Congo.

Auchmeromyia Schiner and Brauer Bergenstanum, 1819.

Auchmeromyia luteola Fabricius, 1805.

Synonym.—*Musca luteola* Fabricius, 1805, Ver de Case.

The larva of this fly is called the 'Congo floor maggot.' It was found by Dutton, Todd, and Christy, living in the floor of native huts to the depth of 3 inches. At night these larvae came out, and sucked the blood of persons sleeping on the ground, or on beds but little raised therefrom, but not on high beds.

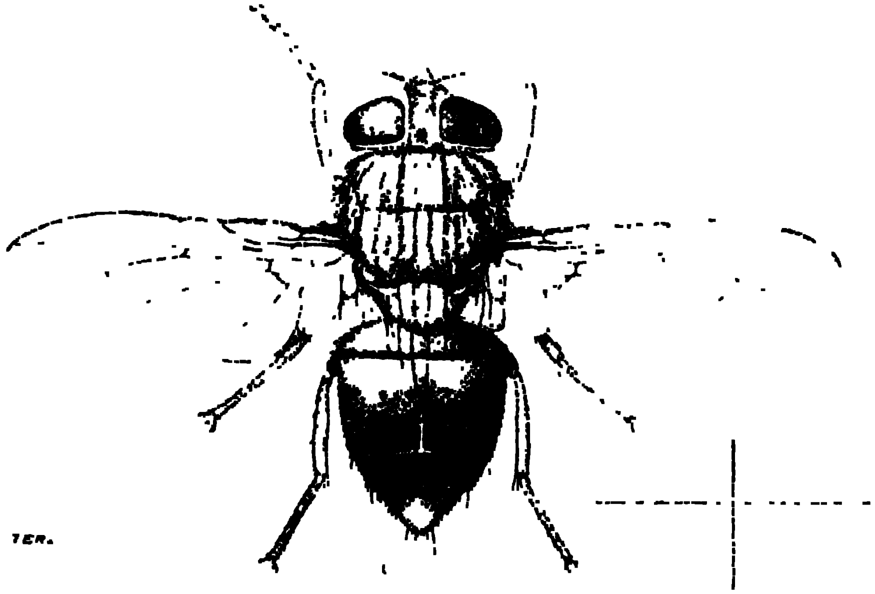


FIG. 441.—*Auchmeromyia luteola* FABRICIUS: FEMALE. (×3.)

The native names for the larvae are, 'Mabunzu,' 'Nchichi,' 'Ntunga,' 'Mvidi,' and 'Kiso.'

Morphology.—The fly is widely distributed in tropical and subtropical Africa. It is 10 to 12 millimetres in length, tawny in colour, with small black hairs giving it a smoky appearance. The head is large, as broad as the thorax. The eyes are separated by a considerable space. The proboscis is folded beneath the head into a deep groove. The palpi are club-shaped, with a long, yellow, flattened third joint, which carries an arista with black hairs on its upper and lower borders.

The dorsum of the thorax is marked by longitudinal black and brown stripes, and shows a well marked transverse suture. The squamæ are large, yellow in colour, and cover the halteres. The first abdominal segment has a narrow dark line posteriorly, the second a central median dark line, which joins with a posterior dark line. The third segment is dark brown, except for a narrow yellow anterior streak. The fourth segment is dark-coloured, with a posterior light brown band. The fifth segment is small, and contains the genital apparatus.

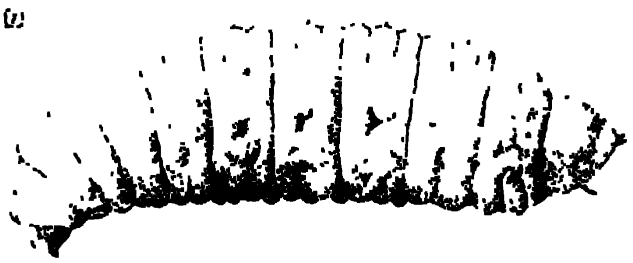


FIG. 412. *Auchmeromyia luteola*: LARVA (× 3.)

The legs are buff-coloured, with black hair and bristles. The fifth tarsal joint is jet black, and has a large cream-white pulvillus.

Life-History. The fly deposits its eggs on the ground of the hut, especially on spots on which urine has been voided. The larva is semitranslucent, of dirty white colour, acephalous and amphipneustic, and has eleven distinct segments. The first segment is divisible into two portions, of which the anterior carries the mouth parts. The broadest segments are the ninth and tenth. There are distinct dorsal and ventral surfaces, at the junction of which in each segment there are protuberances, with a spine and a pit. The ventral surface is flattened, and has three footpads transversely arranged at the posterior margin of each segment. The last segment is large, and carries the posterior spiracles and the anus.

The mouth, which is provided with teeth, leads into an œsophagus, which ends in a proventriculus, and has a dorsal diverticulum. The ventriculus is short. Malpighian tubules mark the commencement of the intestine. The hind gut is coiled. The salivary glands are well marked.

The larva becomes a dark brown or black pupa, 9 to 10·5 by 4 to 5 millimetres, with an anterior conical and a posterior rounded end, and marked by annular ridges. The pupal stage lasts two to three weeks.

Habits.—The fly does not bite man. The larva, as described above, attacks man and fills its dorsal œsophageal pouch with blood, and thus acquires a red colour.

Pathogenicity.—As far as is known it is non-pathogenic.

In 1911 Roubaud described a new genus, *Chœromyia* Roubaud 1911, of which the larvæ of two species, *C. boueti* Roubaud, 1911, and *C. chœrophaga* Roubaud, 1911, were blood-suckers attacking African wart-hogs and African ant-eaters.

Auchmeromyia prægrandis Austen, 1910.

A saffron-yellow fly. It occurs in South Africa.

Pollenia Robineau-Desvoidy, 1830.

The larvæ of *Pollenia rudis* Robineau-Desvoidy have been found in a case of gastric myiasis in man.

Bengalia depressa Walker.

By an error this fly was said to cause cutaneous myiasis in Natal, Rhodesia, British Central Africa, Uganda, and the Sudan, the true causal agent being *Cordylobia anthropophaga* Grünberg. The life-history of *B. depressa* is unknown.

FAMILY ANTHOMYIDÆ Latreille.

Diptera with arista naked or pectinate. Thorax with complete transverse suture. First posterior cell completely open. Abdominal bristles often absent.

This family includes a number of genera known to be troublesome to man—*Fannia* Robineau-Desvoidy, *Hylemyia* Macquart, *Hydrotæa* Robineau-Desvoidy—which may be recognized by the following characters: (*a*) Arista bare—*Fannia*; (*b*) arista plumose—*Hylemyia*; (*c*) arista pubescent—*Hydrotæa*.

Fannia Robineau-Desvoidy, 1830

Fannia canicularis Linnæus, 1761.

Synonyms.—*Homalomyia canicularis* Linnæus, *Anthomyia canicularis* Linnæus.

This species has frequently been reported as being passed in human fæces.

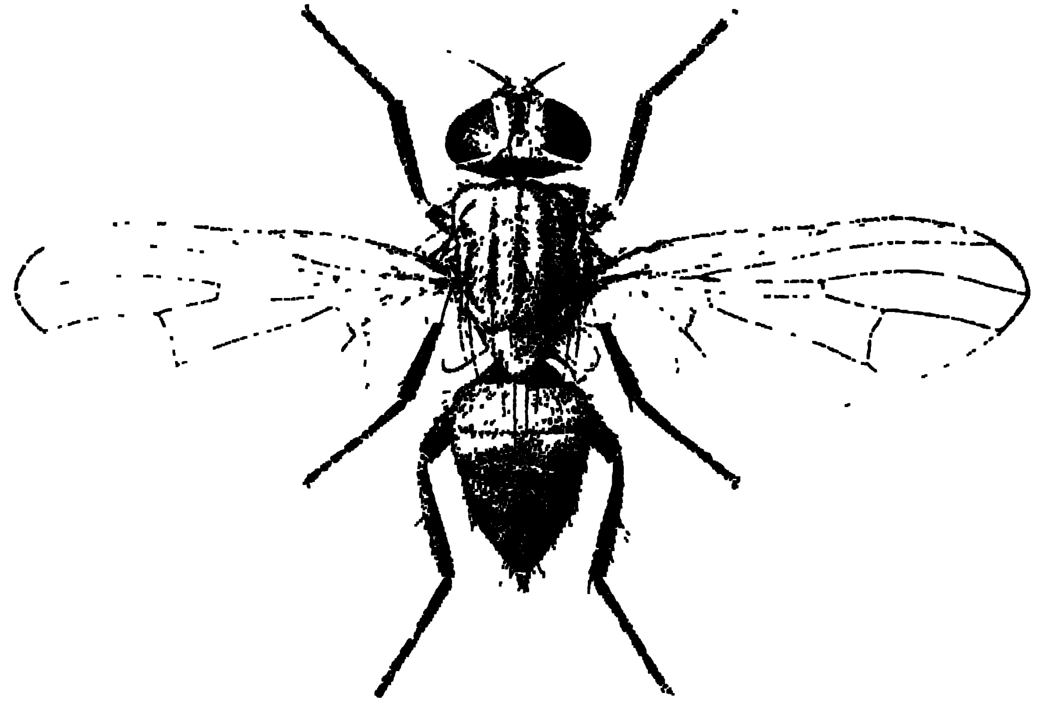


FIG. 443.—*Fannia canicularis* LINNÆUS: FEMALE. (×8.)

The fly is commonly found in houses in Europe and North America. The larvæ normally live in vegetables, by means of which they enter the human digestive tract. They are provided with branched processes on the segments.

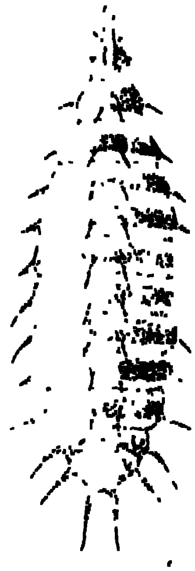


FIG. 444.—LARVA OF *Fannia canicularis*.

Pathogenicity.—Blankmeyer gives an account of a case of this infection which is said to have lasted some twelve years, being associated at first with abdominal pain, bloody diarrhœa, severe pains in the region of the liver. After the initial attack the pains continued, but instead of diarrhœa, constipation resulted, with severe headaches. The abdomen was distended.

The patient was treated with raw pumpkin seeds and then given a saline purge, and passed 1,000 to 1,500 *Fannia* larvæ. After this he still passed a few larvæ for some days, but eventually recovered. This is a curious case, in that the larvæ lived for years inside the man and because it is not clear how such an enormous infection was possible. Chevrel has collected and described seven authentic cases of myiasis of the urinary passages caused by the larva of this fly.

Fannia desjardensii Macquart

Synonyms. *Homalomyia desjardensii* Macquart; *Anthomyia desjardensii* Macquart.

Wellman describes cases of this myiasis in the alimentary canal of human beings in Angola who showed dysenteric symptoms, and which he successfully treated with castor-oil, then santonin, and then castor-oil again.

The disease is locally known as 'ovenvo,' a term which signifies maggots. The editors of the *Journal of Tropical Medicine* in 1907 asked for information

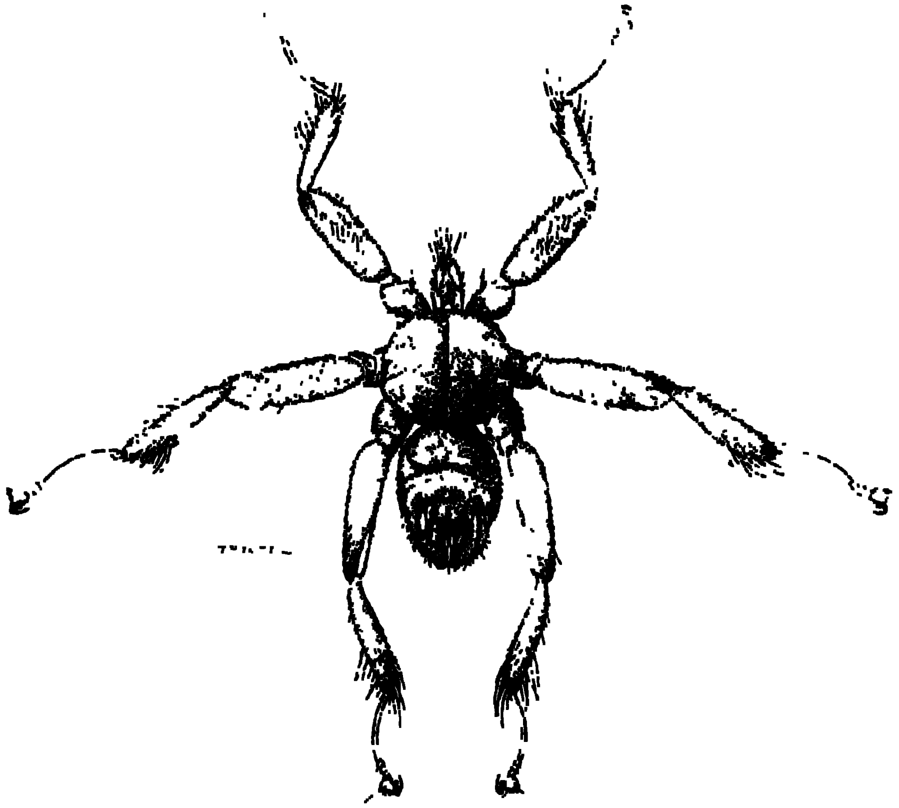


FIG. 445.—*Penicillidia dufouri* WESTWOOD FROM A BAT: FEMALE. (× 8.)

with regard to an African myiasis called 'muculo,' but as far as we know this disease has not been traced. Wellman says that the term is not used in Angola. In *F. desmidensii* the larvæ become pupæ in seven to nine days, and the pupæ insects in another thirteen to fifteen days.

Other Species.- Peiper also lists *F. scalaris*, *F. incisurata*, *F. manicata*, *F. saltatrix* as being causes of intestinal myiasis.

Hydrotæa Robineau Desvoidy, 1830.

Hydrotæa meteorica Linnaeus, which usually attacks animals' eyes and nostrils, is said to attack man also.

SUBORDER III. PUPIPARA.

FIG. 146. NYCTERIBIA SP. (?).

Synonym. *Eproboscidæ.*

The Pupipara are flies which appear to have become altered owing to their parasitic life. They possess a well defined proboscis, which is said by Austen to resemble that of the *Glossinæ* by being armed at its tip with teeth. Wings have been lost in several species, either entirely or after the imago has become parasitic though they may exist throughout life in other species. Their feet are provided with extra ungues to enable them to cling to the hairs, etc., of the host. They do not lay eggs but produce a larva, which soon becomes a pupa.

The suborder is divided into four families: (1) Hippoboscidæ, (2) Nycteribidæ, (3) Braulidæ, (4) Streblidæ.

The Nycteribidæ are parasitic on birds and bats. In this family comes *Penicillidia dufouri* Westwood, which is the carrier of *Ichromaticus vesperuginis* Dionisi, 1898. The Braulidæ are parasitic on bees, and the Streblidæ on bats, and therefore will not be considered further.

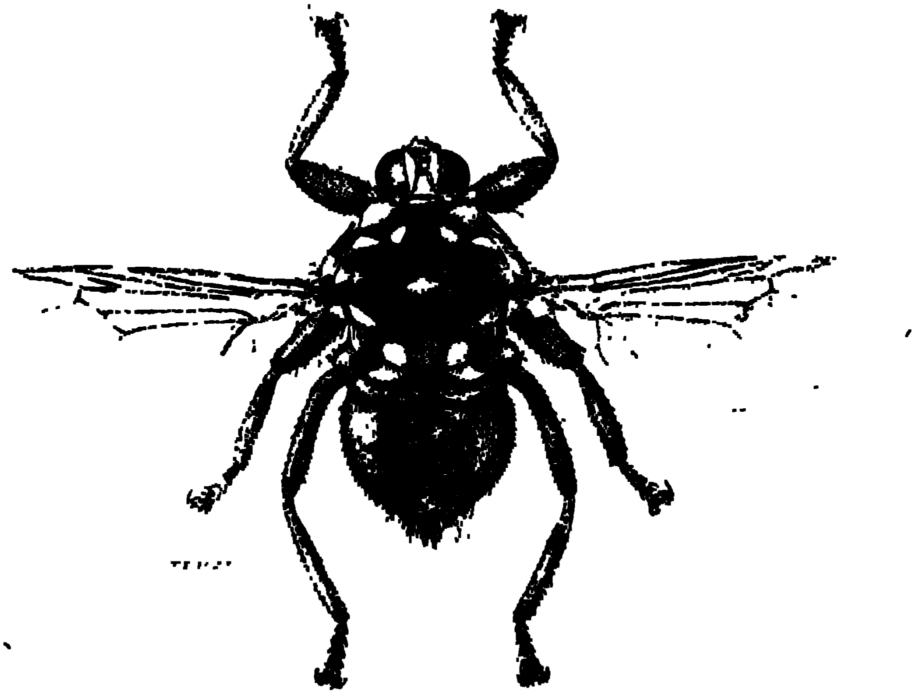


FIG. 147.—*Hippobosca rufipes* VON OLFERS: FEMALE (X 4.)

FAMILY HIPPOBOSCIDÆ.

Pupipara with horny flattened heads and bodies, and with one pointed antenna furnished with a terminal arista. The first joint of the tarsus is usually abbreviated in all, but certainly in the first two legs.

Wings may be well developed, or rudimentary, or entirely absent.

This family is composed of forms parasitic on mammals, and includes the following genera: *Hippobosca* Linnæus, 1761; *Allobosca* Speiser 1902; *Olfersia* Wiedemann, 1830; *Ortholfersia*, *Pseudolfersia* Coquillett, *Lipoptena* Nitzsch, 1818; *Melophagus* Latreille, 1802; *Ornithoctona* Speiser, 1902; *Lynchia* Weyenberg, 1881; and *Ornithomyia* Latreille, 1802.

Hippobosca is parasitic on cattle, horses, dogs, etc., all over the world; *Allobosca* is parasitic on lemurs in Madagascar, *Ortholfersia* on kangaroos in Australia; *Lipoptena* on deer all over the world; and *Melophagus* on sheep.

Hippobosca rufipes von Olfers is thought to be capable of transmitting *Trypanosoma theileri*.

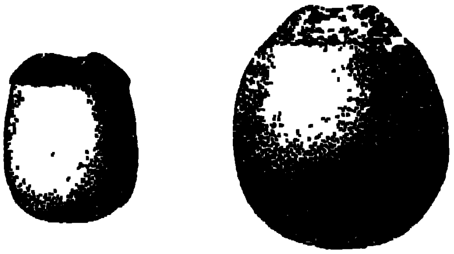


FIG. 448. LARVA AND PUPA OF *Hippobosca rufipes* VON OLFERS. (×4.)

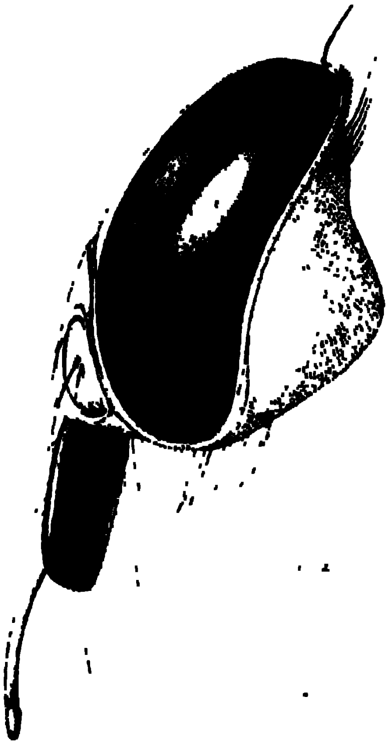


FIG. 449.—HEAD OF *Hippobosca rufipes*: FEMALE.

Hippobosca equina Linnæus is known on horses in the New Forest, England; *Hippobosca capensis* Leach on dogs in Africa, India, Persia, and South Europe; *H. camelina* Leach and *H. maculata* Leach are found in the Sudan and Egypt; and in addition to these *Melophagus ovinus* Linnæus is found all over the world.

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CHAPTER XXXIV

SIPHONAPTERA AND COLEOPTERA

Siphonaptera—Sarcopsyllidæ—*Dermatophilus penetrans*—Pulicidæ—Pulicinæ—*Pulex irritans*—*Xenopsylla cheopis*—Coleoptera—Orthoptera—References.

SIPHONAPTERA Latreille, 1825.

Synonyms.—*Rophoteira* Schellenberg, 1798; *Aptera* Lamarck, 1801; *Aphaniptera* Kirby and Spence, 1826; *Pulicidæ* Stephens, 1829.

Definition.—Hexapoda with laterally compressed bodies and distinctly separated thoracic rings. Wings absent, except for two lateral plate-like appendages on the meso- and meta thorax.

The antennæ are three-jointed, and embedded in grooves. The third joint has nine more or less separated pseudo-joints.

Remarks.—Fleas have come into considerable prominence, owing to the work of the Indian Plague Commission and that of Dr. Verjbitski, of St. Petersburg, who have shown that they are to be looked upon as the main agents by which plague is spread from rat to rat, and from rat to man.

Fleas may also carry blood-parasites—as, for example, *Trypanosoma lewisi*—and, again, they may serve as intermediary hosts for the cysticercus of tapeworms, as in the case of *Dipylidium caninum*.

History.—The knowledge concerning fleas is of recent date. In 1758 Linnæus started with one genus and species, *Pulex irritans*; the second genus was that of the *Chigoe* in 1815, under the term *Rhynchoprion penetrans*; and the third genus was created by Curtis in 1832 under the heading *Ceratophyllus*. The first general systematic treatise was by Kolenati in 1863, the second by Taschenberg in 1880, and the third by Baker in 1904.

Recently much work has been done on these parasites by Rothschild and Jordan.

Morphology.—The head is small, and may or may not possess eyes, which, when present, are only simple pigment masses. Directly behind the head is the antennal groove, in which the antennæ, which are important organs to the flea, lie protected from harm. This groove is continued upwards to the mid-line of the vertex by an incrassation which divides the frons from the occiput. The groove may be open or closed by a process of the gena.

The antennæ are composed of three joints, of which the third, often called the club, may be unsegmented, segmented on the posterior border only, or completely segmented into nine more or less separate pseudo-segments.

The frons may carry a tubercle or notch, situate rather nearer the mouth than the centre of the head, while laterally the eyes, when present, are to be seen. The area of the head below the eyes and extending from the perioral ring to the antennal groove is the gena. A process of this area may be prolonged backwards, so as to meet the hind edge of the post-antennal part of the head, and so to close the antennal groove below in those species which possess a closed antennal groove.

The occipital area carries usually three rows of bristles, the first near the base of the antennae, the second in the middle, and the third near the hinder edge of the head, which are continued forwards on to the frons, and probably delineate the four segments of which the head is composed.

Anterior and ventral to the frons and gena lies the perioral ring, which carries the mouth appendages, which consist of a labrum (epipharynx), mandibles, maxillæ, and palps, hypopharynx, and labium with palps. There does not appear to be a separate clypeus.

The labrum (variously known as epipharynx, hypopharynx, and by other names) is a hollow prolongation of the dorsal wall of head and pharynx. In front it is closed, while behind it opens into the cœlom. Ventrally it shows a groove, converted into a canal when it is articulated with the mandibles laterally. The mandibles consist of basal segments attached to the sides of the mouth, and an anterior portion which projects freely forwards, and shows fine serrations anteriorly. The inner aspect of the mandibles pos groove, converted into a trilobed channel by articulation with the fellow of the opposite side and the hypopharynx.

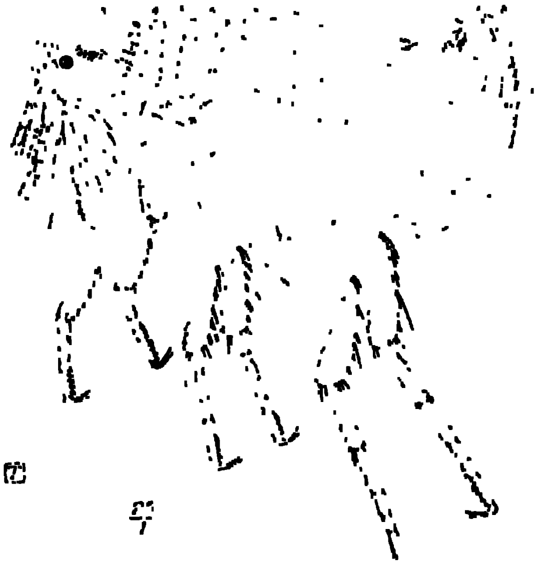

FIG. 450.—*Xenopsylla cheopis*: MALE. (After Jordan and Rothschild, *Journal of Parasitology*.)

1, Labrum, mandibles, and labial palps (at the junction of the last named with the head is seen the triangular maxilla); 2, maxillary palpi; 3, antenna; 4, pronotum; 5, mesonotum; 6, metanotum; 7-12, ordinary abdominal tergites; 13, seventh tergite with bristle (behind this is seen the small eighth tergite); 14, ninth tergite, with sensory plate; 15, tenth tergite; 16-24, sternites of abdominal segments; 25-27, metasternite, 8 mesosternite, 29, prosternite.

The maxillæ are triangular chitinous plates, each possessing a four-jointed maxillary palp. The labium (which, of course, represents the nd maxillæ with their palps) is gle posteriorly, where it is attached the perioral ring, while in front it divided into two one-to-thirteen jointed palps (labial palps), which form a sheath or um for th other mouth parts.

The hypopharynx consists of a basal portion, which is a chitinous plate concave ventrally, extending forwards in the head from the infra-œsophageal ganglion to the mandibulo-basal articulation and an anterior portion, which projects from the basal portion forwards, and contains the canal from the salivary pump.

This anterior portion of the hypopharynx articulates laterally with the mandibles, and its canal opening ventrally, forms the triradiate canal mentioned above, which is continuous with the salivary groove on the mandibles.

The thorax is composed of the usual three divisions, but there are no signs of scutellum or post-scutellum. There is generally one, but there may be two or three rows of bristles on each segment. The pronotum may have a comb. The metanotum may be dentate or serrate apically. Laterally the metathorax is typical, showing a sternite, episternite, and epimerite, while the mesothorax shows a sclerite, divided into two by an internal incrassation running from the coxa upwards. These two divisions represent the episternite and the epimerite. The episternite has the anterior and ventral portion separated off by an oblique incrassation to form a sternite. The posternite or sternite of the prothorax, is not divided. Generally these various sclerites show bristles.

With regard to the abdomen, the first to seventh segments are more or less normal, but the eighth to tenth are modified sexually. The tergites of the second to the seventh segments are normal, carrying bristles and combs in different species. The seventh tergite has a subapical bristle. The first segment has no sternal sclerite, hence the first visible sternite belongs to the second segment. The third to the sixth sternites carry a ventral row of bristles. The seventh has a considerable number of bristles. The sexually different segments must be considered according to sex. In the female the eighth tergite is very broad ventrally, but the sternite is reduced to an elongated plate lying between the ventral edges of the tergite

The ninth tergite carries the sensory plate, with usually fourteen (there may be more) setiferous grooves The ninth sternite is membranaceous laterally, and extends far ventrally where it is strongly chitinized, and lies

FIG. 151. ANATOMY OF A FLEA.

(From the *Journal of Hygiene*, 1906.)

1, Mouth; 2, pharynx, 3, salivary glands, 4, stomach, 5 Malpighian tubes, 6 intestine; 7 rectum

inside the seventh or eighth segment It forms the ventral wall of the vagina, which is joined just anterior to it by the duct of the receptaculum seminis.

The tenth tergite carries a short conical stylet, while the sternite which is triangular, carries a long bristle ventrally before the apex and shorter bristles at the apex.

The eighth tergite of the male is small, while its sternite is large, and from its cavity the copulatory organs project The accessory genital organs belong to the ninth segment the sides of whose tergite form the clasping organ laterally The internal ventral angle of the clasper is prolonged into a manubrium above which is a tubercle like projection The outer side of the clasper has three processes, which are different in *Pulex* and *Læmopsylla*. The ninth sternite has an internal vertical arm and a ventral horizontal arm The latter appears beyond the eighth sternite The penis can be seen between the ninth sternite and the claspers.

Internal Anatomy. - The mouth, which is situate below the base of the labrum, opens into the aspiratory pharynx, which communicates via a long œsophagus, with the stomach. Just before this organ the œsophagus is swollen into a bulb, which represents the proventriculus

At the junction of the stomach with the intestine are the openings of the four Malpighian tubes. The intestine is divided into small intestine, colon, and rectum, the last mentioned opening at the anus.

The salivary apparatus is, as usual, separate from the alimentary canal. It consists of two glands, on each side of the body, lying in the fat-body in front of the stomach. The duct from each gland joins, forming a common duct on each side, which runs forward to open into the salivary pump. This is a hollow, chitinous organ, supplied with powerful muscles, situated at the anterior end of the ventral surface of the hypopharynx.

The duct of this pump, running forwards through the hypopharynx, opens via the triradiate canal already mentioned as formed by the junction of the hypopharynx with the mandibles, into the groove of these organs.

The Act of Biting.—The flea apparently carefully selects the spot at which it is to bite, and then pierces a hole by means of the labrum. This hole is then enlarged by the mandibles, through whose grooves salivary secretion is pumped into the skin. This secretion irritates the vessels, causing a local rush of blood to the part, and this blood is drawn by the suction of the pharynx up a tube formed by articulation of the labium with the mandibles. This tube, of course, is embedded in the skin, which is pierced by its two component parts.

There are therefore two tubes in the mouth-parts of a flea—an efferent, carrying the salivary secretion, and an afferent, carrying the blood, which is taken to the stomach, and hæmolyzed and digested. It appears that the black residual mass is capable of further digestion by the rectal glands. Further bionomics will be given under *Xenopsylla cheopis*. In some people flea-bites may cause a local papular eruption—*e.g.*, ceratophyllus fasciatus.

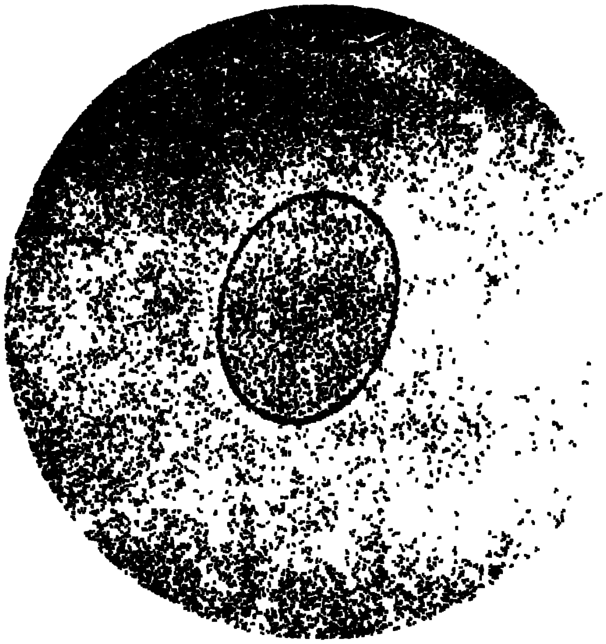
FIG. 452.—EGG OF THE DOG FLEA (× 50 DIAMETERS.)
(From a photograph by J. J. Bell.)

Life-History. The egg is oval, waxy white or opaque porcelain in appearance, smooth, and with a length of about 0·5 millimetre. It is generally deposited between the hairs of the host, and falls off on to the ground. In two to four days the larva is hatched. This larva is an elongated worm-like little creature with fourteen segments. The head is well developed, and has strong mandibles suitable for biting. It lives on dead organic matter, and moults three times as a rule—*i.e.*, three to four days, and again six days, and again seven to fourteen days after hatching. It then spins a cocoon, inside which the pupa becomes the imago in about five days, the whole time required for development being fourteen to thirty-three days.

Dispersal.—Fleas are dispersed mainly by their host travelling about. Such a host as a rat may, of course, be carried by merchandise, and, again, merchandise itself can spread fleas.

Capture of Fleas.—If it is desired to capture fleas, allow a suitable animal to remain in the place, when the fleas will gather on it. Then chloroform the animal, and comb the stupefied or dead fleas on to white paper.

Remedies.—The remedies for fleas are, first and best, a clean house—*i.e.*, plenty of soap and water applied to the floors, etc. Otherwise naphthalene, pyrethrum powders, tobacco leaves and infusions, and benzene may be used.

A flea cannot jump more than 4 inches—an important fact to be noted.

Flea larvæ are delicate little things, and cannot stand disturbance; hence fleas will not be found in houses kept well swept and dusted, but will abound in infected empty houses.

Classification.—The Siphonaptera are classified by Rothschild into three families: (1) Sarcopsyllidæ, (2) Pulicidæ, (3) Ceratopsyllidæ. Only the first two are of importance, the last named being found on bats.

FAMILY SARCOPSYLLIDÆ Taschenberg, 1880.

Synonym.—*Rhynchoprionidæ et Hectopsyllidæ* Baker, 1905.

Siphonaptera without ctenidia. Labial palps rather long, but very weak and fragile; pale, slightly chitinized, formed of one or two segments. Small maxillæ little prominent. Piercing apparatus very developed; mandibles large and strong. Genal extremity always prolonged below and in front into a process, placed behind the insertion of the mandibles. Nota of thoracic segments shorter than that of the first abdominal.

Genera.—*Echidnophaga* Olliff, 1886; *Hectopsylla* Frauenfeld, 1860; *Dermatophilus* Guérin, 1838 or 1839, which, according to Jordan and Rothschild, may be recognized in the following manner:—

I. Hind coxa with patch of spines on inner side—*Echidnophaga*.
II. Hind coxa without such a patch of spines:—
    (*a*) Hind femur with large basal tooth-like projection—*Hectopsylla*.
    (*b*) Hind femur simple—*Dermatophilus*.

We need only consider *Dermatophilus*.

Dermatophilus Guérin, 1838

Synonyms.—*Rhynchoprion* Oken, 1815, *nec* Hermann, 1804; *Sarcopsylla* Westwood, 1836.

This genus contains the species *Dermatophilus penetrans* Guérin, distinguished by having a distinct eye, and *D. cæcata* Enderlein, 1901, with a rudimentary eye. The latter species was found behind the ear of *Epimys rattus* in Brazil.

Dermatophilus penetrans Guérin, 1838.

Synonyms. -*Pulex minimus cutem penetrans* Catesby, 1743; *Pulex minutissimus nigricans* Barrère, 1743; *Acarus fuscus sub cutem nidulans proboscide acutiore* P. Brown 1756; *Pulex penetrans* Linnaeus, 1767; *Rhynchoprion penetrans* Oken, 1815.

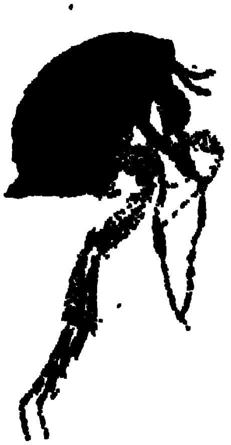

FIG. 453. *Dermatophilus penetrans*: MALE. (MICROPHOTOGRAPH.)

This is the insect variously known as the *Chigoe*, or jigger, and believed to have been discovered by Oviedo in 1551. The home of this little insect appears to be South America, especially Brazil, from which it was conveyed to West Africa about the middle of last century, arriving on the West Coast at Loanda from Rio Janeiro by a ship, the *Thomas Mitchell*, in 1872, whose crew was suffering from jiggers. It was probably noted on the Gold Coast for the first time in the early seventies. It appears to have spread across Africa by Stanley's Expedition and by trade routes, arriving in East Africa in 1895, and from East Africa it spread to India in 1899 by the 4th Bombay Infantry, but luckily the infection did not spread beyond Bombay. In 1900 it reached Madagascar. It affects not merely man, but domestic and wild animals. Perhaps the most noted feature is the way in which it attacks pigs. On the Gold Coast it appeared to be largely kept in existence by these animals. It is very easily captured in the free state by taking a little pig with a pale abdomen, and placing it on its back on the ground on which infected pigs are living. After watching a few moments, a black speck will appear

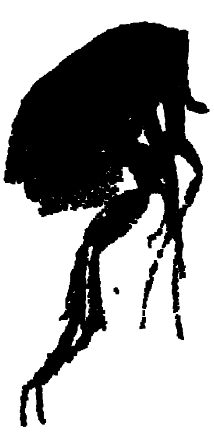

FIG. 454. *Dermatophilus penetrans*: FEMALE. (MICROPHOTOGRAPH.)

on the pig's abdomen, and quickly another and another. These black specks are jiggers, which can easily be transferred to a test-tube. On examination, they will be found to be males and females in about equal numbers. It appears likely that a number of different species, if not genera, are included under the term *D. penetrans*, and there is without doubt room for investigation into jiggers taken from wild and domestic animals and man.

If the reader will look at the list of synonyms, it will be clear that, by the law of priority, the name of this little insect should be *Rhynchoprion penetrans*, and not *D. penetrans*, as the name *Rhynchoprion* Oken is dated 1815; but Rothschild has recently pointed out that *Rhynchoprion* was applied in 1804 by Hermann to a tick, and also by Oken to other ticks in 1815.

Geographical Distribution.—It occurs in Mexico, West Indies, Central and South America, through the whole of tropical Africa, and as far south as Mashona—*i.e.*, 30° N. to 30° S. In Asia it does not appear to flourish; it has only infected Bombay, and will probably not become naturalized, as the monsoon conditions do not appear good for it, for it flourishes in a warm, dry, sandy soil.

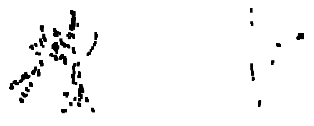

FIG. 455. *Dermatophilus penetrans*. PREGNANT FEMALE.

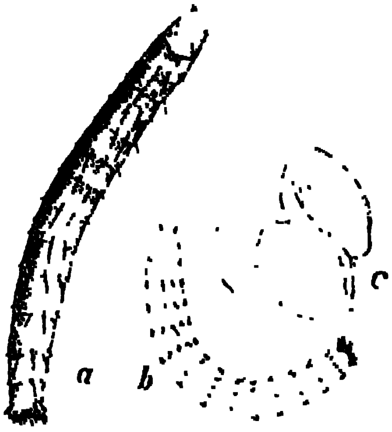

FIG. 456. *Dermatophilus penetrans*. (After Newstead, *Annals of Tropical Medicine and Parasitology*.)

a, Larva; *b*, younger larva; *c*, empty cuticles of eggs.

The female only becomes endoparasitic, and when it first arrives in a place, and is unknown, may cripple people, and cause loss of one or more toes.

Morphology.—The general account already given of the morphology of fleas and the special characters indicate the morphology sufficiently for the purposes of this book.

Life-History.—The males and females live in dry, sandy soil as reddish-brown little insects about 1 millimetre in length, and are very active. They live by sucking the blood of warm-blooded animals. When impregnated, the female burrows into the skin of a warm-blooded animal, whether bird or mammal. The abdomen now swells enormously into the size and appearance of a small pea. If one of these small peas is examined, it will be seen to show the head and thorax anteriorly, and the two last abdominal segments posteriorly. The head is in the bottom of the burrow in the skin, and the posterior abdominal segments block the opening.

The eggs are expelled through the opening in the skin, after which the female jigger is expelled by ulceration. The egg develops into a larva with thirteen segments. This larva spins a cocoon, inside which is the pupa, which gives rise to the imago in about eight to ten days.

Pathogenicity. -This will be described later (Chapter XCVI.), but it may be mentioned that it includes irritation, pus formation, ulceration, and formation of a sore, which may become infected with bacteria, and cause loss of a toe or a leg, or even tetanus may develop.

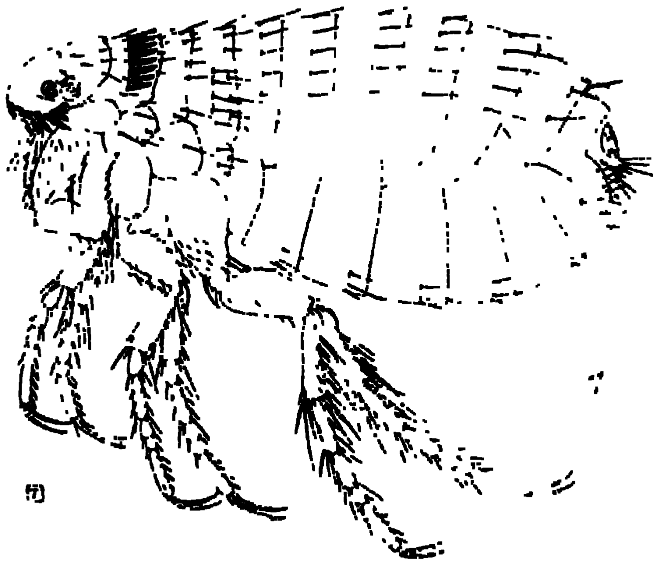

FIG. 457. *Ctenocephalus felis* BOUCHÉ.
This drawing shows the combs on the head and prothorax.

FAMILY PULICIDÆ
Stephens, 1829.

Siphonaptera with body compressed or elongated, always larger than in the preceding family. Head, in comparison to the rest of the body, small; top round; venter protected with hairs; often no eyes. The antennal groove is at times covered by a chitinous plate. The end segment of the antenna is either segmented or unsegmented. Thorax wide; pronotum often with ctenidia. Abdomen never so swollen that the original form is lost. Female never endoparasitic.

There are three subfamilies: *Pulicinæ* Tiraboschi, *Typlopsyllinæ* Tiraboschi, *Hystrichopsyllinæ* Tiraboschi.

SUBFAMILY PULICINÆ.

Pulicidæ with eyes.

The more important genera of the Pulicinæ may be arranged as follows (modified after Jordan and Rothschild):-

A. Ctenidia on prothorax and head -*Ctenocephalus*.
B. Ctenidia on prothorax and only two teeth on cheek at genal angle—*Chiastopsylla*.
C. Ctenidia on prothorax only.
  I. Pygidium freely projecting behind—*Pygiopsylla*.
  II. Pygidium not freely projecting behind
    (1) Club of antenna completely segmented—*Ceratophyllus*.
    (2) Club of antenna incompletely segmented—*Hoplopsyllus*.

D. Ctenidia absent on prothorax and head.

- I. Terminal segment of antennæ short, only distinctly segmented posteriorly. Hind coxa with a comb, fifth tarsal segment with four lateral and one subapical bristle.
  - (1) Forms with small mesial tubercle—*Moeopsylla*.
  - (2) Forms without small mesial tubercle:
    - (A) Mesosternite with internal rod-like incrassation from insertion of the coxa upward.
      - (*a*) Anterior angle of genal edge prolonged backwards into a triangular lobe; pronotum stronger than metanotum—*Pariodontis*.
      - (*b*) Anterior angle of genal edge not produced into triangular lobe—*Xenopsylla*.
    - (B) Mesosternite without internal rod-like incrassation from insertion of the coxa upward—*Pulex*.
- II. Terminal segment of antennæ segmented all round; hind coxa without a comb, fifth tarsal segment with four lateral bristles and one subapical hair.
  - (1) Terminal segment of antennæ symmetrical, genal process with a number of bristles—*Parapsyllus*.
  - (2) Terminal segment of antennæ asymmetrical, proximal segments sloping backwards. Genal process with only one to two bristles—*Rhopalopsylla*.
- III. Terminal segment of antennæ segmented all round, symmetrical. Hind coxa without comb. Fifth tarsal segment with five lateral bristles at least and subapical hair.
  - (1) Antennal groove open behind.
    - (*a*) Abdominal tergites with one row of bristles, except first, which bears two. First hind tarsal segment shorter than second—*Coptopsylla*.
    - (*b*) Abdominal sternites with very numerous short bristles. First mid tarsal segment longer than second—*Goniopsyllus*.
  - (2) Antennal groove closed behind.
    Abdominal tergites with one row of bristles—*Lycopsylla*.

SUBFAMILY TYPHLOPSYLLINÆ.

Pulicidæ with eyes absent or very rudimentary. Head rounded in front. Body thin.

Genera.—*Ctenopsylla* Kolenati; *Ctenophthalmus* Kolenati, 1857; *Typhlopsylla* Wagner; *Neopsylla* Wagner; *Typhloceras* Wagner. Ctenophthalmus can be recognized by having movable ctenidia in front of the ocelli, and the rest can be differentiated as follows:—

- I. Third tarsal with five lateral bristles on each side—*Typhloceras*.
- II. Third tarsal with four lateral and two accessory bristles—*Ctenopsylla*.
- III. Third tarsal with four lateral and no accessory bristles—*Neopsylla*.
- IV. Third tarsal with three lateral and two accessory bristles—*Typhlopsylla*.

SUBFAMILY HYSTRICHOPSYLLINÆ.

Abdominal tergites with one or more ctenidia; posterior tibial spines in numerous short, close-set, transverse rows on posterior border, with about four spines in each row; female with four antepygidial bristles on each side.

Genera. *Hystrichopsylla* Taschenberg, *Macropsylla*.

THE FLEAS OF RATS AND MICE.

The following table gives the fleas observed on rats, mice, and field-mice, by Tiraboschi and Rothschild.

Pulicidæ	Pulicinæ	Pulex	P. irritans L.
		Xenopsylla	X. cheopis Roth. X. brasiliensis Baker.
		Hoplopsyllus	H. anomalus Baker.
		Ctenocephalus	Ct. felis Bouché. Ct. canis Dugès.
		Ceratophyllus	Cer. fasciatus Bosc. Cer. londiniensis Roth. Cer. anisus Roth. Cer. niger Fox. Cer. penicilliger Grube. Cer. walkeri Roth. Cer. pinnatus Wag. Cer. gallinæ Sch. Cer. abantis Roth. Cer. lucifer Roth. Cer. pollionis Roth. Cer. agilis Roth. Cer. californicus Baker.
		Odontopsyllus	Od. charlottensis Baker. Od. telegoni Roth.
		Pygiopsylla	P. colossus Roth. P. hilli Roth. P. rainbowi Roth.
	Typhlopsyllinæ	Ctenopsylla	Ct. musculi Dugès. Ct. spectabilis Roth. Ct. taschenbergi Wag. Ct. aganippes Roth. Ct. ellobius Roth. Ct. pectiniceps Wag. Ct. selenis Roth.
		Stephanocircus	St. thomasi Roth. St. dasyuri Skuse. St. simpsoni Roth.
		Ctenophthalmus	Ct. agyrtes Heller. Ct. assimilis Tasch.
		Typhlopsylla	Typhl. pseudogyrtes Baker. Typhl. prosuma Wag.
		Chiastopsylla	Ch. rossii Waterst.
		Neopsylla	N. bidentatiformis Wag. N. pentacanthus Roth. N. isacanthus Roth.
		Typhloceras	Typhl. poppei Wag.
	Hystrichopsyllinæ	Hystrichopsylla	Hystr. tripectinata Tirab. Hystr. talpæ Curtis. Hystr. narbeli Galli-V.
		Macropsylla	Macr. hercules Roth.
	Sarcopsyllinæ	Dermatophilus	D. penetrans L. D. cæcata Enderlein.
		Echidnophaga	Ech. murina Tirab. Ech. gallinacea Westw. Ech. myrmecobis Roth. Ech. liopus Roth.

Epimys norvegicus Erxleben, 1777.

Pulex irritans Linnæus, *Xenopsylla cheopis* Rothschild, *Ctenocephalus felis* Bouché, *C. canis* Curtis, *Ceratophyllus fasciatus* Bosc, *C. londiniensis* Rothschild, *C. penicilliger* Grube, *Ctenocephalus musculi* Dugès, *Neopsylla bidentaliformis* Wagner.

Epimys norvegicus is the true host of *Ceratophyllus fasciatus*.

Mus musculus Linnæus, 1758.

Ceratophyllus fasciatus Bosc, *C. londiniensis* Rothschild, *C. walkeri* Rothschild, *Odontopsyllus charlottensis* Baker (?), *Ctenocephalus serraticeps* Taschenberg, *C. musculi* Dugès, *Typhlopsylla assimilis* Taschenberg, *C. agyrtes* Heller, *Hystrichopsylla tripectinata* Tiraboschi

Epimys rattus Linnæus, 1758.

Pulex irritans Linnæus, *Xenopsylla cheopis* Rothschild, *Ctenocephalus felis* Bouché, *C. canis* Curtis, *Ceratophyllus fasciatus* Bosc, *C. londiniensis* Rothschild, *Ctenopsylla musculi* Dugès *Dermatophilus caecata* Enderlein, *Echidnophaga rhynchopsylla* Tiraboschi, *E. gallinacea* Westwood.

Of all these fleas, the most important with regard to plague are:

A. Spreading the disease from rat to rat—*Xenopsylla cheopis* Rothschild and its allies; *Ceratophyllus fasciatus* Bosc and its allies; *Ctenopsylla musculi* Dugès; *Ctenocephalus felis* Bouché; *C. canis* Curtis.

B. Spreading the disease from rat to man *Pulex irritans* Linnæus, *Xenopsylla cheopis* Rothschild, *Ctenocephalus felis* Bouché, *C. canis* Curtis *Ceratophyllus fasciatus* Bosc.

Of all these, the most important is *Xenopsylla cheopis* Rothschild and it is believed that its true host is *Epimys rattus*.

Citellus beecheyi Richardson.

This is the ground squirrel of California, which has been proved to play an important part in the plague infection of that country, and its fleas have been recently studied, and it has been found that *Hoplopsyllus anomalus* Baker is capable of carrying the bacillus, and according to McCoy *Ceratophyllus acutus* Baker can also convey the disease from squirrel to squirrel.

Arctomys bobæ Schreb.

This is the tarbagan, and its common flea is *Ceratophyllus silantieri* Wagner, 1898.

Pulex Linnæus, 1758.

Pulicinæ with head without notch on the frons; antennal groove closed behind by a genal process. Strong incrassation separating occiput and frons. Eye large, a little pointed below, with two bristles beneath it, and one on the oral edge. Anterior angle of genal process projecting somewhat downwards, and usually bearing a small tooth (remains of a comb). Anal coxa is pear-shaped, carrying a number of hairs on the inner posterior portion, as well as in front, and carrying a row or patch of short spines near apex. Greatly reduced thorax, the tergites being short, each with a row of bristles, but without subapical spines on the mesonotum. Mesosternite characteristic, very narrow, with ventral edge close before apex, stigmata not being entirely covered. No internal rod-like or cariniform incrassation from the insertion of the coxa to the dorsal edge.

Male with eighth tergite with small manubrium; clasper with very large flap on inside of which are two processes, forming a kind of claw. Manubrium of clasper large, curved. Ninth sternite boomerang-shaped, with its upper end pointed. Internal wire-like spring of ninth sternite and penis making several coils.

Female No hairs above stigma of eighth stergite. Stylet with long apical bristle and short bristle near apex. Anal sternite truncate, bristles confined to the apical edge.

Species *P. irritans* Linnæus.

Pulex irritans Linnaeus, 1758.

Synonyms *Pulex vulgaris* Raius, 1710; *P.* [illegible] Linnaeus, 1746; *P. hominis* Dugès, 1832; *P. simulans* Baker, 1895; *P. dugesi* Baker, 1904.

This, in a much restricted sense, is the *P. irritans* of Linnaeus, which included all fleas, but now the term is restricted to the parasite of man. It is essentially an Old World flea, those of America being but distantly connected, but has become now

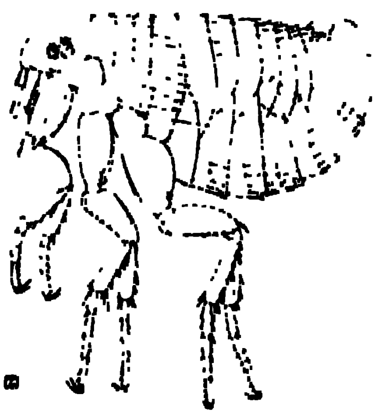

FIG. 458.—*Pulex irritans*: MALE.

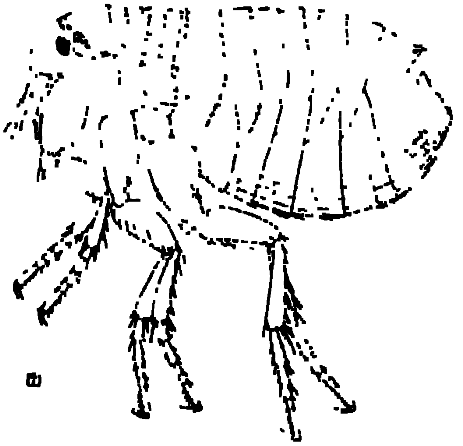

FIG. 459.—*Pulex irritans*: FEMALE.

cosmopolitan through trade. It appears to have been introduced into the eastern tropics by European trade. It is absent from the Sahara and the Haussa countries south of it, but it abounds all through Africa where there are European settlements.

The question whether there are different varieties on the different races of mankind is not settled. Baker described a *Pulex dugesi* or *P. irritans dugesi* from West Mexico on *Citellus macrourus* and man, but is the only person who indicates this.

P. irritans is also found on animals, particularly the badger (*Meles taxus*) in England: on dogs, cats, rats, and other animals in various parts of the world.

Xenopsylla Glinkiewicz, 1907.

Synonym.—*Laemopsylla* Jordan and Rothschild, 1908.

Pulicinæ with third segment of antennæ distinctly segmented only on posterior side. Eye round; one bristle below, one in front of eye, third at oral edge. Frons without tubercle, four-segmented labial palpus; closed antennal groove. Pleura of the mesosternite divided by a suture into an episternite and an epimerite, with the dorsal apical bristle of the seventh abdominal tergite remote from the edge of the segment, with short spines on the inner surface of the coxa of the third leg, with a rod-like incrassation on the inside of the coxa of the second leg; fifth tarsal segment with four lateral bristles besides the subapical hair.

Male with clasper provided with two or three small processes, manubrium narrow: upper internal portion of the ninth sternite not very sharply defined.

Female with the stylet bearing, besides the long apical bristle, a short bristle situated in a notch before apex.

Type.—*Xenopsylla cheopis* Rothschild. This genus is found in Africa and Central Asia in particular.

At the time of writing there are some twenty four species known

Xenopsylla cheopis Rothschild, 1903.

Synonyms. *Laemopsylla cheopis* Rothschild, 1903; *Pulex cheopis* Rothschild 1903; *P. brasiliensis* Baker, 1904; *P. murinus* Tiraboschi, 1904; *P. philippinensis* Herzog, 1904.

This is the rat-flea in all parts of the tropics, and is believed to be the principal transmitter of bubonic plague from the rat to man. Its home is believed to be the Nile Valley, where it lives on various hosts, but it has spread from there by the agency of the rats.

It is often referred to in literature by the name *P. pallidus* Taschenberg, which is really a different species.

Jordan and Rothschild report it on man or animals from the Egyptian Sudan, Pretoria, Beira in East Africa, Entebbe, Uganda, Benguella, Angola, Réunion, Marseilles, Plymouth, Aden, Bombay, Agra, Arabia, Japan, West Australia, New South Wales, Colombia, Paraguay.

They have found it on man, *Epimys norvegicus, E. rattus, Mus chrysophilus*, and several other animals.

Morphology.—Episternum of metathorax separated from sternum. The latter carries a bristle as long as that on the former. Hind femur angulate ventrally at the widest part. Fifth segment of fore- and mid tarsi, with three spine-like bristles ventrally at apex: lateral ones very stout in male. Clasper with two distinct free processes; manubrium long. Penis without a brush near apex.

Life-History.—The eggs are round, waxy-white or pearly in colour, and number one to five at each oviposition. They hatch in Bombay in two days, and produce the little larvæ, which at once hide themselves away from the light. In about a week's time these larvae, which at first are very active, become sluggish, and, ceasing to eat, spin cocoons composed of fine white silk-like fibres. The cocoon becomes covered with rubbish, and is hard to see. In about seven to fourteen days the imago escapes from the cocoon. The total development, therefore, requires about twenty-one to twenty-two days.

Bionomics. The young flea is capable of living without a feed of blood for some seven to fourteen days, but if not fed then it dies. The length of life of a flea is difficult to ascertain, but *Xenopsylla cheopis* will live forty-one days on a rat and twenty-seven days on a man. Therefore, the whole life of a rat-flea from birth to death is about sixty-three days. A rat flea is more readily attracted by a rat than by a man. It breeds at all temperatures, but has one optimum temperature above and below which it does not thrive so well. Dampness is injurious to the flea, killing the larva and hindering development.

X. cheopis is the commonest rat-flea, being probably the flea of *Epimys norvegicus* in India, while in Western Europe *Ceratophyllus fasciatus* is the flea of the same rodent. It is found on *E. norvegicus*, *E. rattus*, and *Nesokia bengalensis*, also on musk-rats, guinea-pigs, cats, rabbits, antelopes, kangaroos, and men.

The infection with plague bacilli does not appear to affect the flea's health, for it has an immunity dependent, apparently, on phagocytosis.

Hoplopsyllus Baker.

Closely related to *Pulex*, but distinguished at once by the ctenidia on the prothorax. *Hoplopsyllus anomalus* Baker is the plague carrier of the Californian ground squirrel

FAMILY CERATOPSYLLIDÆ Baker, 1905.

Siphonaptera with ctenidia present on the metathorax and abdomen; eyes rudimentary or absent.

Genus.—*Ceratopsylla* Kolenati

The species of this genus are found on bats

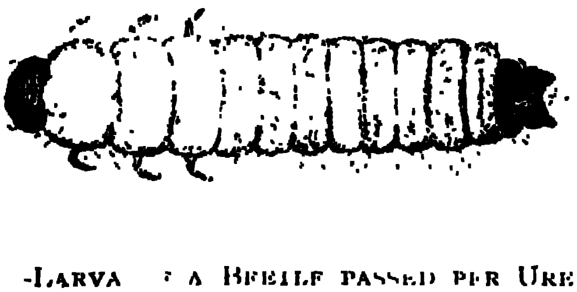

FIG. 460.—LARVA OF A BEETLE PASSED PER URETHRAM.
(After King.)

COLEOPTERA.

Hexapoda with biting mouth-parts. Anterior wings altered to form cases for the thin posterior wings.

Remarks.—The larvæ of beetles have rarely been recorded as parasites of the alimentary canal, or found in abscesses in man in the temperate and tropical regions. *Silvanus surinamensis* Linnæus bites people at night.

ORTHOPTERA.

The bite of *Enyaliopsis durandi* Lucet causes a nasty eruption (according to Wiggins, 1910, in man in Uganda), with high fever and general illness, and finally sloughing at the site of the bite.

E. petersi Schaum, the nantundua of Nyassaland, according to Stannius, can cause ulceration by the action of a yellow fluid which it emits.

The *Phasmidæ*, or stick insects, are said to eject a fluid which may cause blindness if it gets on to the conjunctiva.

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CHAPTER XXXV

THE ANIMAL CARRIERS OF DISEASES

Preliminary—Historical—Protozoal diseases—Helminthiasis—Myiasis—Bacterial diseases—Diseases of unknown causation—Chance transmission—Imperfect carriage of parasites—Terms—References.

PRELIMINARY.

THE present chapter is an attempt to put in concrete form the rôle of the 'animal carrier' of disease.

Animals can produce traumatisms by their bites, and can cause disease by injecting chemical substances manufactured in their bodies—e.g., American and Australian tick paralysis—but these questions do not now concern us. The problems which we are about to consider are those associated with the spread of diseases known or suspected to be parasitic. Such diseases are divisible into those caused by animal and those caused by vegetal parasites. The latter are the simpler, as their carriage does not involve any great morphological changes in the parasite, such as often accompanies the carriage of an animal parasite, which, as it is the more complex, we will consider first.

A given animal parasite apparently has some form of *sexual generation* in some stage of its life-history, and it is probably merely our lack of knowledge which prevents us from acknowledging this as a proven fact.

The host in which the sexual generation takes place is called the *definitive host*, and is probably the original host, in which, as a rule, the parasite does not produce severe forms of disease and may produce no ill effects at all. This shows that it and its host have become so adjusted that it does not overproduce itself in the host, which on its part does not poison or otherwise attack the parasite.

It is certainly not the object of the parasite to kill its definitive host, but to leave it by some route which causes no great disturbance of its tissues or functions. Hence intestinal parasites leave by means of the fæces, but in so doing they are flung into new dangers, and therefore require protection by encystment. These cysts may be eaten by another individual of the same species as the original definitive host, and the cycle may begin again; but the dangers of the outer world may be guarded against by entering some animal's body in which no development occurs. Such an animal would be a protective ***intermediary host***, and such a cycle can be exemplified by the amœba of dysentery and house-flies.

This extremely simple carriage is also shown by animals which convey bacteria, but some of these undergo multiplication in the gut of the intermediary host—as, for example, the plague bacillus—and may even have their virulence raised—as, for example, Eberth's bacillus. Returning again to the animal parasite, this may grow and multiply in this second host, and may invade its tissues and dwell therein for a length of time. This is quite different from the short passage of an amœbic cyst in the flies' intestines. The second host now becomes a true *intermediate host*, but it is something relatively new interposed in the life cycle of the parasite, which has not yet adjusted itself to its new host, nor has this host adjusted itself to the parasite; and the result is that the parasite almost invariably causes disease in the intermediate host, which may be a vertebrate or an invertebrate, *e.g.*:

The Definitive Host.

Parasite.	*Definitive Host.*	*Intermediate Host.*	*Nature of Parasitism.*
Filaria bancrofti.	Man but little affected pathologically.	Culex and Stegomyia mosquitoes severely affected by infection.	True parasitism of the vertebrate.
Plasmodium malariæ.	Anopheline mosquitoes unaffected pathologically.	Man suffers from malarial fever.	True parasitism of the mosquito.

It is therefore obvious that these two diseases, from the point of view of evolution, have two quite different origins. The first is originally a parasite of man, and, as Hindle has pointed out, Manson's original idea of water infection may be the true method, and that *ab initio* the 'Larvofilaria' lived in water and pierced the human skin, as it does to-day on leaving the mosquito, and requires, as Bahr has shown, dampness in order to live while it pierces the skin. The mosquito carrier is therefore a relatively new acquisition, and the mosquito, not having adjusted itself to these conditions, often dies, as Bahr has shown. On the other hand, *Filaria bancrofti*, barring accidents, causes no symptoms in man, but if there are accidents the disease ensues.

It is quite otherwise with the malarial parasites, in which the anopheline mosquito is the definitive host and man the intermediate host. Here the mosquito is not affected pathologically, but man suffers from malarial fever. Here the malarial parasite must have been originally a sort of coccidioform parasite of the mid-gut of the mosquito, and may have spread from mosquito to mosquito by hereditary infection, as Schaudinn suggested, the sporozoites—*i.e.*, the infective agent—going all over the body, and so entering the salivary glands, and subsequently, when the evolution of warm-blood animals took place, becoming blood parasites, at first accidentally.

The passage from the *intermediate host* to the *definitive host* we call *transmission*.

It is never directly inoculative, like infection, but it may be—

1. Ingestive, via the alimentary canal.
2. Penetrative, via the unbroken skin and mucous membranes.

In the first it is the arthropod which ingests the parasite; in the second the parasites come in contact with the unbroken skin or mucosæ, through which they force their own way, and so enter the body of the intermediate host, which is usually the vertebrate in this case.

Following our life cycle, we come to the passage from the definitive to the intermediate host, and this may be called 'infection,' because it is so often followed by disease in the intermediate host This generally takes place by the agency of the product of the sexual generation—*i.e.*, some descendant of the *zygote*, using this term in the widest sense to mean the product of the fusion of male and female elements.

Infection of the vertebrate is usually *inoculative*, and may be performed in two ways:

(*a*) *The Direct.* In this the blood-sucker simply transmits the parasite unchanged after holding it for a short time.

(*b*) *The Indirect.*—In this the parasite undergoes development in the blood-sucker.

INFECTION AND TRANSMISSION.

Parasite	*Definitive Host.*	*Infection*	*Intermediate Host.*	*Transmission.*
Plasmodium malariæ	Anopheline mosquitoes	Sporozoites from zygote. — Inoculative	Man.	Micro- and macro-gametocytes. — Ingestive.
Filaria bancrofti.	Man.	Microfilaria from egg. — Ingestive.	Culicine mosquitoes.	Larvofilariæ. — Penetrative.

The direct is unusual, as a blood-sucker as a rule takes a full meal from one individual, and does not feed again for a day or so, but it may take place—as Edmond and Étienne Sergent have shown to be the case of the tabanid flies, which bite camels in North Africa, and which spread the trypanosome disease, 'el debab'—by this method, because they acquire a full meal from several individuals, and because the camels resent their attentions.

Infection may also be *contaminative*. In this method the parasite, escaping with the carrier's fæces, enters the new host via wounds, either pre-existing or caused by the carrier itself.

In the case of the Arthropoda infection is generally *ingestive*, as it sucks the blood of the vertebrate and so obtains the blood parasite.

Finally, just as the fly is an *intermediary or temporary host* for the amœba of dysentery, so blood-sucking flies may take up some blood-containing parasites and immediately pass them on to a healthy animal in a second feed: but while biting through the skin they inject this second animal with the parasite, and infection results.

We will now assume that the definitive and intermediate hosts have been living together for long periods undisturbed, and that they have adjusted themselves to the parasite and the parasites to them. Under circumstances such as these there will be little or no sign of disease in the intermediate host, which has now become a 'reservoir' for the parasite.

Assuming that the definitive host is a blood sucking arthropod, and that man enters such an area as a new comer, and is bitten by the blood-sucker, then several things may happen to the parasite.

A. It may be killed off and no infection follow.
B. It may find in man a suitable intermediate host, and cause—
  (1) Acute epidemic disease.
  (2) Chronic endemic disease.
  (3) No disease, only infection.

The second is obviously better for the parasite than the first, and the third than the second.

Therefore, in studying the carriage of an animal parasite of man by some other animal, we must know

1. The parasite.
2. The definitive hosts:
   (*a*) Reservoirs.
   (*b*) Non-reservoirs.
3. The method of infection.
4. The intermediate hosts.—
   (*a*) Reservoirs.
   (*b*) Non-reservoirs.
5. The method of transmission.

But there is another question which it is necessary to consider when man is the definitive host. This question is whether the intermediate host is new, and if so, whether any trace of the old original life-cycle still persists. It should be remembered that man evolved later than blood-sucking insects, as evidenced by tsetse flies found in geological formations in America— so Sambon informs the writers.

Therefore, in order that man may be the definitive host and the blood-sucker a pathologically affected intermediate host means a comparatively recent evolutionary change. Therefore an old original life cycle may still be discoverable, if sought for, and may be of value in prophylaxis, which is the end and aim of the study of the animal carrier.

With these preliminary remarks we may now turn to the history of the subject.

Historical. The history of the animal carrier of disease may be divided into three periods by the dates 1878 and 1898, *i.e.*, by Manson's and by Ross's discoveries, and these periods will be:

I. Early views.
II. Manson's period.
III. Ross's period.

I. *Early Views.*—This period is characterized by gropings in search of truth, mainly by suggestions and by theories, but also by the first experiments with bacteria.

In 1577 Mercurialis suggested that *plague* might be spread by house flies, and in 1666 Sydenham opined that the autumnal diseases of England were due to the flies of summer. In 1769 Bancroft advanced the theory that *Frambœsia tropica* was a fly-borne disease, and in 1808 Crawford believed insects to be carriers of infection. In 1848 Nott of Alabama brought forward reasons to support the insect origin of *yellow fever*. In 1853 Moore referred to flies as possible carriers of *cholera, typhoid, tuberculosis, anthrax*, and *leprosy*, to the last named of which Linnæus had already invited attention, while Raimbert in 1869 performed the first actual experiments to try to prove that flies carried anthrax.

In 1853 Beauperthuy argued that mosquitoes spread *yellow fever*.

II. *Manson's Period.*—This opens with the publication of Manson's epoch-making discoveries of the carriage of *Filaria bancrofti* by mosquitoes, and it must never be forgotten that he grasped at once that this was a new infection of the mosquito, and that water was the original method; and thus he discovered two great truths, of which so far only one has been properly appreciated, because the insect carriage laid the foundation of Ross's great work.

In 1881 Findlay definitely accused mosquitoes as being the transmitters of yellow fever, and conducted experiments in which he is considered to have been successful in transmitting the disease experimentally by their bites.

In 1883 King formulated the theory that malaria was spread by mosquitoes, and in the same year Thomas demonstrated the carriage of *Fasciola hepatica* by snails, while Grassi and Stiles showed that parasitic worms were carried [illegible]

In 1895 Bruce discovered that *Trypanosoma brucei* was spread by a tsetse-fly, a fact which led eventually to clearing up of the carriers of trypanosome diseases.

During the closing years of this period Ross in India was hard at work dissecting mosquitoes in the face of much difficulty, thus opening the way for the last period of our history.

III. *Ross's Period.*—Just twenty years ago (1898) the new stage of research into the animal carrier in disease was opened by Ross's most important, careful, and laborious work into the causation of malaria, and the carriage of its parasites by the anopheline mosquitoes.

This discovery was followed in 1899 by the classical paper by Nuttall, on 'Insects as Carriers of Disease,' while in 1900 Reed, Carroll, and Agramonte showed that *Stegomyia (ædes) calopus* was the carrier of yellow fever.

The rest of this period has been referred to in the opening chapter of this book, and need not be recapitulated, and we will now pass on to study the results of this work, by considering the parasites in the zoological order followed in the preceding chapters.

A. PROTOZOAL DISEASES.

Amœbic Dysentery.—We have already seen that amœbiasis in man is principally caused by *Loeschia histolytica*, which, escaping as *cysts* in the fæces, is taken up by house flies—that is to say, flies belonging to the genera *Musca*, *Fannia*, *Calliphora*, etc.

The cysts do not undergo development in the fly, which serves merely as a carrier and protector for them, which, escaping with the flies' fæces on to human food, afford a means of infection.

This carriage is interesting, indicating that the environment of the alimentary canal of the fly is not suitable for the development of this amœba, though it is known that there are amœbæ passing their whole life-cycle in insects—*e.g.*, *Endamœba blattæ*.

With regard to *L. histolytica*, it is believed that the sexual life-cycle occurs in man, but it is not definitely known whether gametes are formed in the human intestine, or whether autogamy takes place in the cyst, which is improbable, but in either case the life-cycle does not require more than one host, and infection can take place by direct contamination of the food, without passing through the fly.

Animals can be infected with amœbic dysentery, but there is no evidence at present of any animal, other than man, acting as a reservoir, but this does occur in human carriers.

To demonstrate what we mean we give the following table:—

AMŒBIC DYSENTERY.

Parasite.	*Definitive Host.*	*Reservoir.*	*Transmission.*	*Intermediary Host.*	*Infection.*	*Incidental Host.*
Loeschia histolytica.	Man in carrier stage.	Man in carrier stage.	Cyst Ingestive.	Flies.	Cysts ingested from contaminated food or drink.	Man in acute and chronic infections.

Flagellate Diarrhœa and Dysentery.—Whatever may be the views of zoologists, medical men have little doubt that some of the flagellates, such as *Giardia intestinalis*, produce diarrhœa; and Wenyon and O'Connor have shown that their cysts have been found in flies, and that in general the process of infection is much the same as in man, but the reservoir is different. There is little doubt in our minds that man is more or less accidentally infected with many of these parasites, and certainly with *Giardia intestinalis*, which appears to us to be a true parasite of the rat.

If there is a sexual cycle, it takes place either in the cyst or in the vertebrate.

FLAGELLATE DIARRHŒA AND DYSENTERY.

Parasites.	*Definitive Host.*	*Reservoir.*	*Transmission.*	*Intermediary Host.*	*Infection.*	*Intermediate Host.*
Giardia intestinalis and others.	Man in chronic cases and as carriers, and rat	Rats	Cysts ingested.	Flies.	Cysts ingested with contaminated food or drink	Man in acute cases.

Sleeping Sickness. We have already indicated that we think that there are several forms of this disease—viz., that caused by—

1. *Trypanosoma gambiense.* Synonym: *T. nigeriense.*
2. *Trypanosoma castellanii.* Synonyms: *T. ugandense, T. gambiense pro parte.*
3. *Trypanosoma rhodesiense.*
4. *Other Forms of Trypanosomes.* (*a*) Some type of *T. brucei* in the laboratory infection of Professor Lanfranchi; (*b*) some type of *T. vivax* found by Macfie

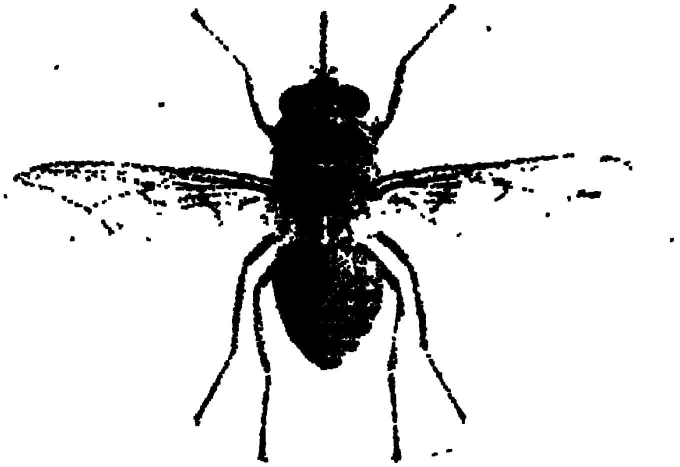

FIG. 401.—*Glossina palpalis* ROBINEAU-DESVOIDY, 1830: THE CARRIER OF THE TRYPANOSOME OF THE CASTELLANI TYPE OF SLEEPING SICKNESS.

(From a photograph by J. J. Bell.)

The carrier of the first (*T. gambiense*) has never been properly studied. Possibly it is not *Glossina palpalis*, and as nothing can be said definitely, we will not pursue this subject further, except to say that Yorke and Blacklock consider man to be the principal reservoir, with domestic cattle as a secondary reservoir.

With regard to *T. castellanii*, we have noted that Miss Robertson's researches have shown that it never multiplied in the vertebrate in cells of the liver, spleen, or lungs, and that there was no schizogony, and that division was simple and longitudinal, taking place always in the circulating blood and producing ***transmission forms***, which are her ***short blood forms***.

These forms can be ingested by *Glossina palpalis* (but one has to be sure that it is really *palpalis*, as flies apparently of this species have been found by King, using Newstead's more accurate methods of classification, not to be this species), first establishing themselves in the posterior part of the mid-gut and then multiplying and forming many types therein, but moving on the tenth to twelfth day to the proventriculus in the form of *long, slender, non-infective trypanosomes*, from which they find their way via the hypopharynx to the salivary glands after the sixteenth day. In these glands they assume a crithidial form, from which after multiplication ***small infective trypanosomes*** appear after the eighteenth to twenty-first day—*i.e.*, some two to five days after infection of the salivary glands.

Miss Robertson never saw any signs of conjugation or of sexual forms, as described by Minchin, Gray, and Tulloch, but considers the cycle in the fly has this significance, and if so the fly is the *definitive host*, and susceptible animals can be infected by its bite.

Is there hereditary infection of the fly via the ova, as shown by O'Farrell to take place with a crithidia in a tick? This question is so far answered in the negative

Is there an animal reservoir for *T. castellanii*? Perhaps there is, but notwithstanding Duke's experiment with an antelope, we believe that no such reservoir has been proven, and this is supported by the very small numbers of wild glossinæ which have been found to contain *T. castellanii*. One suspects that if there is a reservoir, it must be in man himself when he becomes more or less immune to the disease

The possibility of direct infection during sexual intercourse must be remembered, in addition to insect carriage.

There appears to be no doubt that the fly at present labelled *Glossina palpalis* is the carrier of the disease, as all experiments tend to show.

CASTELLANI TYPE OF SLEEPING SICKNESS.

Parasite.	*Definitive Host.*	*Definitive Reservoir.*	*Infection.*	*Intermediate Host.*	*Intermediate Reservoir.*	*Transmission.*
Trypanosoma castellanii.	*Glossina palpalis.*	Hereditary infection of tsetse flies (?)	Short salivary trypanosomes.	Man.	Game animals (?).	Short blood trypanosomes.
			Inoculative.			Ingestive.

Rhodesiense Type of Sleeping Sickness.—Kinghorn and Yorke have described short blood trypanosomes in man, and, judging by Miss Robertson's Castellanii experiments, these must be the transmission agents which infect *Glossina morsitans*, in the salivary glands of which short trypanosomes occur, which infect the vertebrate, which is the intermediate host.

We now come to the very important question of the intermediate reservoir of this trypanosome. Bruce says that *T. brucei* and *T. rhodesiense* are one and the same parasite. Assuming this to be true, the intermediate reservoir would be the African antelopes —*e.g.*, *Catoblepas gnu*, the wildebeest: *Strepsiceros capensis*, the koodoo: *Tragelaphus scriptus* var. *sylvaticus*, the bush-buck. But there are doubts about this, because—

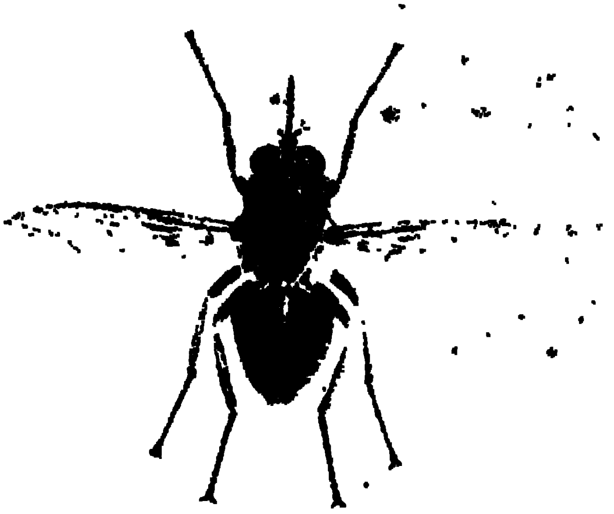

FIG. 462.—*Glossina morsitans* WESTWOOD, 1850: THE CARRIER OF THE TRYPANOSOME OF THE STEPHENS AND FANTHAM TYPE OF SLEEPING SICKNESS.

(From a photograph by J. J. Bell.)

1. Stephens and Blacklock have shown that two distinct trypanosomes have been called *T. brucei*—viz.:—

(*a*) *Monomorphic.*—This is the original strain of *brucei* discovered by Bruce in cattle suffering from nagana in Zululand.

(*b*) *Polymorphic.*—This is a posterior nucleated form from Uganda, where the Rhodesiense form of sleeping sickness is unknown.

2. Chalmers and O'Farrell, working with a posterior nucleated trypanosome, sent to them in dogs inoculated from a case of sleeping sickness in the Bahr-el-Ghazal province of the Anglo-Egyptian Sudan, found it to differ markedly in serological experiments and animal inoculations from the original strain of *T. rhodesiense*. This shows that merely obtaining a posterior nucleated trypanosome in a sleeping sickness area does not prove that it is *T. rhodesiense*, or, indeed, has anything to do with sleeping sickness.

3. Laveran's cross immunity experiments mentioned in Chapter XIX. show that *T. brucei* and *T. rhodesiense* are quite different from an immunity point of view.

4. Taute has injected himself with 2 c.c. of blood from a dog infected with *T. brucei*. He did not become infected, and suffered no bad effects.

5. Taute fed *Glossina morsitans* upon animals infected with *T. brucei*, and after waiting the necessary time these flies were allowed to feed upon two men, with negative results, although control animals became infected and died.

Thus the chain of evidence is strengthening which tends to show that *T. brucei* is not *T. rhodesiense*, and if this is so, then we do not know the intermediate reservoir of this trypanosome, and its chart becomes:—

STEPHENS AND FANTHAM TYPE OF SLEEPING SICKNESS.

Parasite.	*Definitive Host.*	*Definitive Reservoir.*	*Infection.*	*Intermediate Host.*	*Intermediate Reservoir.*	*Transmission.*
Trypanosoma rhodesiense.	*Glossina morsitans.*	Hereditary infection of tsetse flies (?).	Short salivary trypanosomes. — Inoculative.	Man.	Game animals (?)	Short blood trypanosomes. — Ingestive.

With regard to the other forms of sleeping sickness due to trypanosomes allied to *T. vivax*, etc. (*vide* p. 1280), too little is known about them and their carriers, and therefore it is impossible for us to discuss the means of infection and transmission. *G. tachinoides* is suggested as a possible carrier.

Chagas' Disease.—Chagas has shown that *Trypanosoma cruzi* in the vertebrate intermediate host finally enters the lungs, where it loses its flagellum, while its two extremities join, and it becomes a sphere, inside which eight daughter spheres arise, which, elongating and entering red blood cells, become male and female trypanosomes. These are the transmission agents which carry on the life-cycle of the parasite in *Lamus megistus* (*Triatoma megista*) when it sucks infected blood.

In this insect the trypanosome lives and multiplies in the gut of the insect, and gives rise to crithidial forms in the mid-gut. These eventually develop into small trypanosomes, which pass into the salivary glands, and from there are injected into the intermediate host when the insect bites.

He considers that the armadillo, *Dasypus novemcinctus*, may be the intermediate reservoir, and that *Lamus geniculatus*, which lives with this animal, may also be a definitive host, as may *Lamus infestans* and *L. sordida;* while Brumpt has shown that *T. cruzi* can develop in *Clinocoris lectularius* and in *Leptocimex boneti.* (It must be remembered that Triatoma can be infected naturally with a trypanosome.)

There is no evidence of hereditary infection in these insects, but there is some evidence that at times infection may be contaminative from the insect fæces via the bite, but this requires more investigation.

The chart of this disease would be:—

CHAGAS' DISEASE.

Parasite.	*Definitive Host.*	*Infection.*	*Intermediate Host.*	*Intermediate Reservoir.*	*Transmission.*
Trypanosoma cruzi.	*Lamus megistus* (synonym, *Triatoma megista*).	Short salivary trypanosomes. — Inoculative.	Man	*Dasypus novemcinctus.*	Male and female trypanosomes. — Ingestive.

Leishmaniasis. The nature of the carrier and the reservoir is very uncertain at the present moment. Judging by the more marked resistance of the dog to experimental infection in India and the Sudan, we may assume that there are at least two kinds of kala-azar. It is believed by certain authorities that a flea is the transmitter of the Mediterranean type, whereas the Indian and Sudan type are not so transmitted. Patton's incrimination of the bug has not stood the test of time. Archibald has suggested and brought forward evidence that, at least in regard to the Sudan, infection is probably due to the ingestion of cysts from water arthropods.

The development of generalized kala-azar in Archibald's monkeys, after the successful inoculation of Oriental sore, points to a close relationship between the two diseases, as suggested long ago by Manson.

There is no complete evidence at present that the espundia parasite is essentially different from that of kala-azar, but it may prove in the long run to be different, because of its marked different clinical results.

The present state of our knowledge, which is unsatisfactory, may be summarized as follows:—

TROPICAL KALA-AZAR.

Parasite.	*Inter-mediate Host.*	*Intermediate Reservoir.*	*Trans-mission.*	*Definitive Host.*	*Method of Infection.*
Leishmania donovani.	Man.	(?)	Parasites passed in faeces. — Ingestive (?).	Water insect (?) Biting insects (?)	Cysts in drinking-water (?). — Ingestive (?). Inoculative (?).

MEDITERRANEAN KALA-AZAR.

Parasite.	*Inter-mediate Host.*	*Inter-mediate Reservoir.*	*Trans-mission.*	*Host Nature Doubtful.*	*Method of Infection.*
Leishmania infantum.	Man.	Dogs (?).	Blood-sucking insect (?) — Inoculative (?)	Fleas (?).	Blood-sucking insect (?). — Inoculative (?). Contaminative (?).

Coccidiosis.—The discovery of a coccidial oöcyst in a fly's intestine by Wenyon and O'Connor suggests that possibly this is the method of infection of man by these parasites, the fly only acting as an *intermediary host,* as in the case of *Loeschia.* Perhaps this ought to be included with chance infections.

Malaria.—The three well-recognized malarial parasites have as their *definitive host* various species of anopheline mosquitoes. The classification of the Anophelinæ is as follows:—

A. Costa with less than four main dark spots—*Protoanopheles.*
B. Costa with four main dark spots:—
  I. Sixth vein with not more than three dark spots—*Deuteroanopheles.*
  II. Sixth vein with more than three dark spots—*Neoanopheles.*

The Neoanopheles have no malarial carriers.

DIVISION I.: PROTOANOPHELES CHRISTOPHERS, 1911.

The division contains the following genera:—

A. *Costa without pale areas* :—
  I. Female palps with second segment disproportionately long—*Stethomyia.*
  II. Female palps with second segment not disproportionately long—*Anopheles.*

B. *Costa with at least one pale area* :—
- I. Mesothorax without true scales.
    - (*a*) Wing scales mixed dark and light—*Patagiamyia.*
    - (*b*) Wing scales not so mixed:—
        - 1. Wing scales not inflated—*Myzorhynchus.*
        - 2. Wing scales inflated—*Cycloleppteron.*
- II. Mesothorax with true scales—*Arribalzagia.*

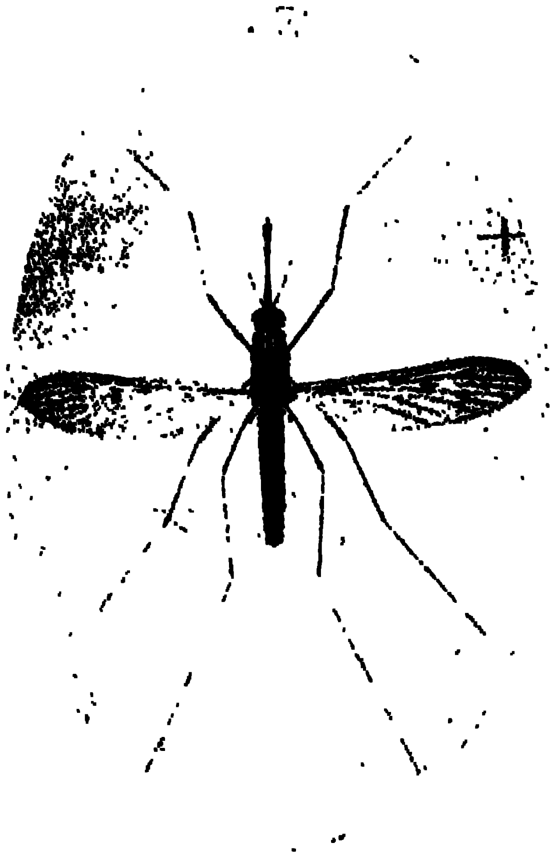

FIG. 403. — *Anopheles maculipennis* MEIGEN, 1818 A CARRIER OF THE MALARIAL GERMS.

(From a photograph by J J Bell.)

James distinguishes between *true scales*, which are broad and have distinct striations, and *false scales*, which are hair-like and have indistinct striations.

The question whether any of these serve as *definitive reservoirs* by infection of the ova, as suggested by Schaudinn, has never been proved, but we doubt whether much research has been attempted in this direction.

The anopheline mosquitoes known definitely to transmit malaria, arranged according to recent methods of classification and following Hindle and our previous lists, are as follows:—

I. Anophelines definitely known to be able to carry the malarial parasites through the complete cycle of quartan, tertian, or subtertian infections, or only as far as zygotes:—

(*a*) ANOPHELES CARRIERS.

Number.	*Mosquito*	*Observer.*	*Observation.*	*Habitat.*
1	*A. algeriensis* Theobald, 1903	The Sergents.	To sporozoites.	North Africa.
2	*A. bifurcatus* Linnæus, 1758.	Grassi.	Tertian.	England.
3	*A. maculipennis* Meigen, 1818.	Many.	Quartan, tertian, malignant tertian.	Europe.

(*b*) PATAGIAMYIA CARRIER.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
4	*P. pseudopunctipennis* Theobald.	Darling.	Malignant tertian.	Panama Canal Zone.

(*c*) CYCLOLEPPTERON CARRIERS.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
5	*C. mediopunctatum* Theobald.	Cruz.	Tertian.	Brazil.
6	*C. nolotrichum*—*A. intermedius* Chagas.	Cruz.	Tertian.	Brazil.

(*d*) ARRIBALZAGIA CARRIER.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
7	*A. pseudomaculipes* Chagas.	Cruz	Tertian.	Brazil.

DIVISION II.: DEUTEROANOPHELES CHRISTOPHERS, 1911.

This division may be classified as follows:—

- A. Terminal segment of female palpi less than half length of penultimate. Tarsi not broadly banded:—
  - I. Mesothorax without true scales—*Myzomyia*.
  - II. Mesothorax with true scales—*Pyretophorus*.
- B. Terminal segment of female palpi at least half length of penultimate. Tarsi broadly banded:—
  - I. Mesothorax not completely covered with true scales *Pseudomyzomyia*.
  - II. Thorax completely covered with true scales:—
    - (*a*) Abdomen without lateral scale tufts:—
      - 1. Palpi moderately shaggy—*Nyssorhynchus*.
      - 2. Palpi markedly shaggy—*Myzorhynchella*.
    - (*b*) Abdomen with lateral scale tufts—*Cellia*.

Most of these genera possess malarial carriers.

(e) Myzomyia Carriers.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
8	*M. albirostris* Theobald.	Staunton	Malignant tertian zygote.	Malaysia.
9	*M. culicifacies* Giles	Stephens and Christophers	All forms.	India and Ceylon.
10	*M. formosaensis* I. and II. Tsuzuki = *M. aconita* Dönitz = *Anopheles kochii* Dönitz.	Tsuzuki	Malignant tertian.	Formosa.
11	*M. funesta* Giles = *M. kumassi* Chalmers.	Many, including Chalmers, in Kumassi.	Malignant tertian, including Kumassi zygote and sporozoites.	Tropical Africa.
12	*M. hispaniola* Theobald.	Sergents.	Tertian	North Africa, South Spain
13	*M. listoni* Liston.	Kinoshita, Stephens, and Christophers	Tertian.	India.
14	*M. turkhudi* Liston	Stephens and Christophers.	Malignant tertian.	India.

(f) Pyretophorus Carriers.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
15	*P. costalis* Loew.	Many	All forms.	Tropical Africa.
16	*P. myzomyfacies* Theobald.	Sergent.	Sporozoites.	Algeria.
17	*P. superpictus* Grassi	Grassi, Bignami, and Bastianelli.	Tertian.	Europe.

(g) Pseudomyzomyia Carrier.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
18	*P. ludlowi* Theobald.	Christophers.	Malignant tertian zygote.	Malaysia, Andamans.

(h) NYSSORHYNCHUS CARRIERS.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
19	*N. annulipes* Walker.	Kinoshita.	Malignant tertian.	Australia.
20	*N. fuliginosus* Giles.	Stephens, Christophers, and Addie.	Quartan, malignant tertian.	India.
21	*N. maculatus* Theobald.	Staunton.	Malignant tertian.	India.
22	*N. maculipalpis* var. *indiensis* Theobald.	Stephens and Christophers.	Malignant tertian.	India.
23	*N. stephensi* Liston = *Neocellia stephensi* Theobald.	Stephens, Christophers, Liston, and Bentley.	Tertian.	India.
24	*N. theobaldi* Giles.	Stephens and Christophers.	Quartan, malignant tertian.	India.
25	*N. willmori* James.	Addie.	Sporozoites.	India.

(i) CELLIA CARRIERS.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
26	*C. albimana* Weidemann.	Darling.	All forms.	Central and Tropical America.
27	*C. argyrotarsis* Desvoidy.	Darling.	Malignant tertian.	West Indies, South America.
28	*C. pharænsis* Theobald.	Newstead, Dutton, and Todd.	Tertian.	Egypt.
29	*C. tarsimaculata* Goeldi.	Darling.	Tertian, malignant tertian.	South. America.

(j) MYZORHYNCHELLA CARRIER.

Number.	*Mosquito.*	*Observer.*	*Observation.*	*Habitat.*
30	*M. arabiensis.*	Patton.	Sporozoites.	Aden Hinterland.

II. Anophelines believed to be malarial carriers for epidemiological reasons:—

Number.	*Mosquito.*	*Observer.*	*Habitat.*
31	***Stethomyia aitkeni*** James.	Daniels, Christophers.	Malaysia, India.
32	***Pyretophorus chaudoyei*** Theobald.	Billet.	Algerian Oases (saline waters).
33	***Mysomyia d'thali*** Patton.	Patton.	Aden.
34	***Myzomyia kochi*** Dönitz =***M. aconita***= ***M. formosænsis***.	Daniels.	Malaysia.
35	***Myzomyia lutzi*** Theobald.	Lutz.	Brazil.
36	***Nyssorhynchus karwari*** James and Liston.	Staunton.	Malaysia, India.
37	***Anopheles*** (?) ***martini*** Laveran.	Laveran.	Cambodia.
38	***Myzorhynchus mauritianus*** Grandpré (?=***M. paludis***= ***M. aconita***).	Ross.	Mauritius, Madagascar.
39	***Anopheles*** (?) ***pursati*** Laveran.	Laveran	Cambodia.

III. Malarial carriers in Lists I. and II. under synonym names. (The nomenclature is in such confusion that it is quite impossible to be certain whether these synonyms are correct):—

(*a*) ***Myzomia funesta*** (Giles, 1900); ***Anopheles kumassii*** Chalmers, 1900.

(*b*) ***Myzomia formosænsis*** :—

1. ***Anopheles constance*** Laveran, Madagascar.
2. ***Anopheles jamesi*** Theobald, India.
3. ***Anopheles jeporensis*** James, India.
4. ***Anopheles kochii*** Dönitz, Malaysia.
5. ***Anopheles mauritianus*** Grandpré, Mauritius.
6. ***Anopheles paludis*** Theobald, West Africa.

(*c*) ***Stethomyia atkeni*** :—
Anopheles vincenti Laveran, Tonkin.

(*d*) ***Myzomia listoni*** :—
Anopheles cohæsus, Doune Japan.

IV. Probably not carriers:—

(*a*) ***Myzorhynchus barbirostris*** Van der Walp, India, Ceylon, Malaysia, China.

(*b*) ***Myzomia rossi*** Giles, India, Ceylon, China.

(*c*) ***Pyretophorus sergenti*** Theobald, Algeria.

(*d*) ***Myzomia sinensis*** Wiedemann, India, Malaysia, China.

V. Said to be a carrier, but reason unknown to us:—
Cycloleppteron grabbami Theobald, West Indies, South America.

An infective mosquito, when biting a man, injects the salivary sporozoites into his blood and gives him the infection.

When a mosquito bites a suitable human carrier it receives the macrogametocytes and microgametocytes, which enable the parasites to undergo sexual development in its body.

The scheme is:—

MALARIA.

Parasites.	*Definitive Hosts.*	*Definitive Reservoir.*	*Infection.*	*Intermediate Host.*	*Intermediate Reservoir.*	*Transmission.*
Plasmodium malariæ, ***Plasmodium vivax,*** ***Laverania malariæ.***	Anopheline mosquitoes.	Unknown.	Salivary sporozoites. — Inoculative.	Man.	Human carriers.	Macrogametocytes and microgametocytes from blood. — Ingestive.

B. HELMINTHIASIS.

Trematode Infections.—The trematode infections of man have as their intermediate host a mollusc. The definitive host is a vertebrate, from whom the eggs escape in the urine, the fæces, or the respiratory secretions. These eggs hatch in water, producing a ciliated, actively swimming miracidium, which will enter and develop in some definite genus of mollusc. Chalmers and Pekkola, watching the miracidia of schistosoma, noted that they rapidly entered the known susceptible molluscs, rejecting other genera.

It would appear that the mollusc is liable to disease and death if too heavily infected.

It is therefore necessary to note the classification and method of recognition of the known carriers.

PHYLUM MOLLUSCA Cuvier.

Synonyms.—*Palliata* Latreille; *Malacozoa* de Blainville.

Definition.—Metazoa with no sign of primitive segmentation, with well-developed distinct cœlom (gonad and pericardial), enteron, and hæmocœl, with (or has lost) a radular sac, with periœsophageal ring; dorsal moiety is the cerebral commissure, and the ventral the labial commissure; and with a dorsal and a ventral nerve trunk. Body wall differentiated into an antero-dorsal, ***cephalic*** portion, with the sense organs, a postero-dorsal, the ***pallium or mantle***, which secretes externally a calcified cuticle, ***the shell***, and develops the ***ctenidia***, or respiratory organs, on its lower surface, and a ventral portion, ***the foot***, or organ of locomotion. A ***veliger***, or free trochosphere larva, is nearly always present.

Classification.—The phylum so defined is divided into three grades as follows:—

A. Gonadial and reno-pericardial cavities communicate—*Isopleura, Siphonopoda*.

B. Gonadial and reno-pericardial cavities separate—*Prorhipidoglossamorpha*.

The Isopleura contains the 'Chitons', and the Siphonopoda the 'Cephalopods, with which we are not concerned.

Grade Prorhipidoglossomorpha Grobben.

Definition.—Mollusca in which the gonadial and reno-pericardial cavities are separate, the foot is wholly posterior to the head, and a visceral commissure is present.

Classification.—The Prorhipidoglossomorpha are divided into three classes as follows:—

A. *Body bilaterally symmetrical* :—
  I. Mantle united ventrally to form a tube. No ctenidia—Class I., *Scaphopoda* Bronn.
  II. Mantle not so united; ctenidia present—Class II., *Lamellibranchia* de Blainville
B. *Body asymmetrical*—Class III., *Gastropoda* Cuvier.

We are only concerned with the third class.

Class Gastropoda Cuvier.

Definition.—Prorhipidoglossomorpha with asymmetrical organization, with well-developed head, with shell formed in one piece and spirally coiled, at least in the larva.

Classification.—The class may be divided into two subclasses:—

A. Visceral commissure twisted into a figure of eight, mostly diœcious—*Streptoneura*.

B. Visceral commissure not so twisted, with shortened visceral commissure monœcious—*Euthyneura*.

Subclass I.: Streptoneura Spengel.

Definition.—Gastropoda, diœcious, with a few aberrant genera; maximum torsion of visceral mass and commissure. Head with only one pair of tentacles.

Classification.—The Streptoneura are divided into two orders:—

A. Nervous system not concentrated. Infraœsophageal commissure present. Ctenidia bipectinate and free at their distal ends—*Aspidobranchia*.

B. Nervous system somewhat concentrated. Intraœsophageal commissure present. Ctenidium monopectinate and attached to mantle along its whole length—*Pectinibranchia*.

Only the last concerns us.

Order Pectinibranchia.

Definition. Streptoneura as defined above.

Classification. The Pectinibranchia are divided into two suborders:—

A. Without proboscis, pallial siphon, or Leiblein's unpaired œsophageal poison gland—*Tænioglossa*.

B. With proboscis, pallial siphon, and Leiblein's poison gland—*Stenoglossa*.

Only the Tænioglossa are of importance to us.

Suborder Tænioglossa.

Definition.—Pectinibranchia with the characters given above, with three teeth, one lateral and two marginals, on each side of the median tooth of the radula.

Classification.—There are two tribes:—

A. Creeping forms, with foot flattened ventrally—*Platypoda.*

B. Free-swimming forms, with foot flattened laterally -*Heteropoda.*

We are concerned with the Platypoda.

Tribe Platypoda.

Definition.—Tænioglossa with the characters given above.

Classification.- There are some fifty-five families, of which we are interested in the Melaniidæ only.

Family Melaniidæ Gray.

Definition.—Platypoda with spiral shell and elongated spire. Operculum horny. Foot short. Mantle border fringed. Viviparous. Fluviatile.

Classification.—Several genera.

A. Shell long:- -

I. Shell turriculated, aperture enlarged anteriorly—*Melania.*

II. Spiral very long, aperture notched anteriorly—*Faunus.*

B. Shell short, thick, and aperture rounded - *Other genera.*

Melania Lamarck.

Synonyms. *Thiara* Mergele: *Pyrgula* Crist.

Definition. -Melaniidæ with turreted shell, acute apex, whorls ornamented with striæ or spires; aperture oval, pointed above; outer lip sharp, sinuous. Operculum subspiral.

Type Species.- -*Melania hastula* Leach.

Remarks.- Some 400 or more species distributed throughout Southern Europe, India, the Philippines, Japan, and the Pacific Islands. Distinct groups in the Southern United States.

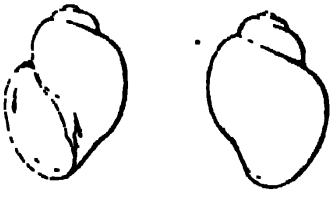

Fig. 464.- *Bulinus contortus* (p. 893).

According to Nakagawa, *Melania obliquegranosa* Smith and *M. libertina* Gould are intermediate hosts of *Paragonimus ringeri* Cobbold, but Kobayashi believes that the cercariæ seen by Nakagawa in these molluscs are not those of *P. ringeri.*

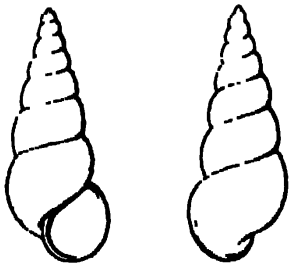

Fig. 465.- -*Blandfordia japonica* Adams, 1861. The Carrier of *Schistosoma Japonicum.*

Blandfordia Adams, 1863.

Definition. -Melaniidæ with ovate conical shell, apex truncated. Aperture elliptical, peristome continuous, operculum subspiral. Rostrum elongated. Tentacles very short, eyes sessile. Foot large; divided into two parts by a transverse sulcus.

Type.—*Blandfordia striatula* Menke.

Other Species.- *B. bensoni* Adams: *B. japonica* Adams; *B. pyrrhostoma* Cox: *B. viridescens* Carpenter.

We are only concerned with *B. japonica,* which is the carrier of *Schistosomum japonicum.*

Subclass II.: Euthyneura Spengel.

Synonym. *Platymalakia* von Jhering.

Definition. Gastropoda monœcius with radula possessing uniform teeth on each side of the median tooth. Head usually with two pairs of tentacles. Detorsion of organization when adult.

Classification.—

A. Marine forms with aquatic respiration—*Opisthobranchiata*.
B. Aerial or fresh-water (exceptionally marine) forms, with pallial cavity, but no ctenidium. No free larval form—*Pulmonata*.

Order Pulmonata Cuvier.

This order is divided into two suborders:—

A. Aquatic forms, with a single pair of tentacles—*Basommatophora*.
B. Terrestrial forms, with two pairs of tentacles—*Stylommatophora*.

Suborder Basommatophora.

Definition.—Pulmonata with an external shell and a single pair of well-developed contractile but not invaginable tentacles, at the bases of which lie the eyes.

Classification.—There are some eleven families, but only the following concern us:—

A. Shell thin, dextral; no inferior pallial lobe—*Limnæidæ*.
B. Shell sinistral, inferior pallial lobe prominent—*Planorbidæ*.

Family Limnæidæ Broderip.

Definition.—Basommatophora with shell thin, horn coloured, and capable of retaining the whole animal when retracted. Aperture single; lip sharp, No inferior pallial lobes. Tentacles angular and flat.

Remarks.—These molluscs are found in fresh water all over the world.

Type Genus—*Limnæa* Lamarck.

Genus Limnæa Lamarck.

Definition.—Limnæidæ with spiral shell, more or less elongated, thin pointed spire translucent; body whorl large; aperture rounded; columella obliquely twisted.

Type Species.—*Limnæa stagnalis* Linnæus.

Other Species.—The hosts of *Fasciola hepatica* are:—*L. truncatula* Müller, Europe, Asia, Africa; *L. oahuensis*, Eyd, Sandwich Isles; *L. viator*, D'Orbigny, South America; *L. humilis*, Say, North America.

Family Planorbidæ Adams.

Definition.—Basommatophora with sinistrally coiled shell. Inferior pallial lobe very prominent, transformed into a branchia; tentacles tapering.

Classification.—

A. Shell discoid, branchia not folded—*Planorbis*.
B. Shell ovoid, with prominent spire. Branchia not folded—*Bulinus*.

Genus Planorbis Guettard.

Definition.—As above. Shell discoidal, dextral, many whorled; aperture crescentic. Peristome thin, incomplete; upper margin projects.

Type.—*Planorbis corneus* Linnæus.

Planorbis boissyi Potiez and Michaud, 1838.

Synonym.—*P. laurenti* Bourguignat.

Remarks.—This is the intermediate host of *Schistosoma mansoni* in Egypt and the Sudan, as discovered by Leiper.

Planorbis olivaceus Spix.

This is the carrier of *S. mansoni* in Brazil.

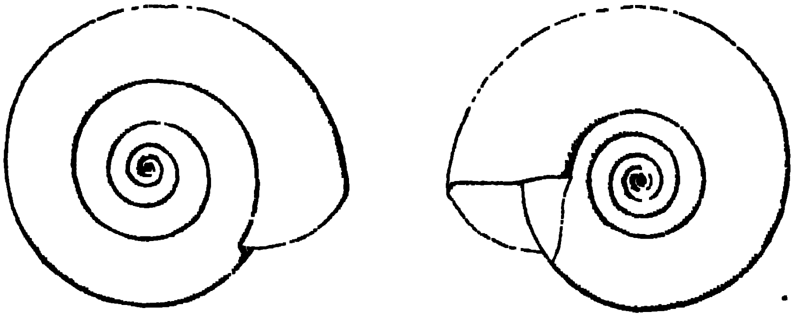

FIG. 466.—*Planorbis olivaceus.* THE CARRIER OF *Schistosoma mansoni* IN BRAZIL.

Genus Bulinus Adamson.

Synonyms.— *Nauta* Leach; *Aplexa* Fleming. Often spelt *Bullinus.*

Definition.—Planorbidæ with ovoid shell, prominent spire, branchia folded.

Type.—*Bulinus hypnorum* Linnæus.

Classification.—The species of importance to us are:—*Bulinus contortus* Michaud, 1829; *Bulinus dybowski* Fischer, 1891; *Bulinus alexandrina* Innes; *Bulinus innesi* Bourguignat.

The above are the hosts of *Schistosoma hæmatobium* in Egypt.

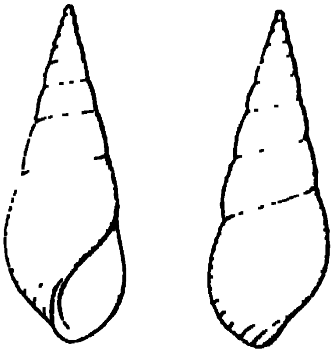

FIG. 467.—*Physa* (*Physopsis*) *africanus* KRAUSS. A CARRIER OF *Schistosoma Hæmatobium.*

Family Physidæ Dall.

Definition.—Basommatophora with visceral mass and shell sinistrally coiled. Shell thin, with a narrow aperture; tentacles cylindrical. No inferior pallial lobe.

Type Genus.—*Physa* Draparnaud.

Remarks.—*Physopsis* is distinguished from *Physa* by the spire not being at all exserted, and having the columella truncated at the end.

Phya or *Physopsis africanus* is the carrier of *S. hæmatobium* in Brazil.

TREMATODE INFECTIONS.

Trematode.	*Definitive Host.*	*Definitive Reservoir.*	*Transmission.*	*Intermediate Host.*	*Infection.*
Fasciola hepatica.	Man.	Sheep.	Miracidium in water. - Penetrative.	Species of Limnæa.	Cercaria encysted on weeds. — Ingestive.
Fasciolopsis buski.	Man.	Pig.	Miracidia in water.	Shrimps (?).	(?) - Ingestive (?).
Metagonimus yokogawai.	Man.	Unknown.	Ditto.	*Melania libertina.*	Cercaria under scales of fish. -- Ingestive.
Paragonimus ringeri.	Man.	Carnivora.	Ditto	Ditto.	Cercaria in water. -- Penetrative, or in crabs ingestive.
Clonorchis sinensis.	Man.	Cats, dogs, pigs	Ditto.	Ditto.	Cercaria encysted in muscles of fish. — Ingestive.
Schistosoma hæmatobium.	Man.	Man.	Ditto.	Subgenera and species of *Bulinus.*	Cercaria in water. — Penetrative.
Schistosoma mansoni.	Man.	Man.	Ditto.	Species of *Planorbis.*	Cercaria in water. — Penetrative.
Schistosoma japonicum.	Man.	Cats.	Ditto.	*Blandfordia nosophora vel japonica.*	Cercaria in water — Penetrative.

CESTODE INFECTIONS.

(These are on the same lines as the trematode infections.)

Cestode.	*Definitive Host.*	*Definitive Reservoir.*	*Infection.*	*Intermediate Hosts.*	*Transmission.*
Dibothriocephalus latus.	Man.	Dogs, cats.	Eggs in water.	Cyclops, fish.	Plerocercoid in muscles. — Ingestive.
Dipylidium caninum.	Man.	Dogs, cats	Eggs on fur.	Dog and cat, louse or flea.	Dog licking cysticerci. Cat milk cysticerci. — Ingestive.
Hymenolepis diminuta.	Man.	Rats, mice.	Eggs on fur.	Meal broth beetles, rat flea.	Food cysticerci. — Ingestive.
Tænia solium.	Man.	Man.	Eggs in fæces.	Pigs.	Cysticerci in muscles. — Ingestive.
Tænia saginata.	Man.	Man.	Eggs in fæces.	Cattle.	Cysticerci in muscles. — Ingestive.
Echinococcus.	Dog, jackal.	Dog, jackal.	Eggs on fur.	Man, sheep.	Cysticerci in muscles. — Ingestive.

C. MYIASIS.

Myiasis comprises the infestation of the vertebrate body with the *larvæ of diptera*, and the disorders which arise in the body of the host therefrom.

The vertebrate is an *intermediate host*, because not merely is it protective to the fly larva, but in it the larva grows and develops until it is about to pupate.

There is no doubt that this is an advantage to the fly, and that this method of protection is in process of evolution. In Chapter XXXIII. we have written upon the change in habits of flies, and will merely remind the reader that there is ample evidence that within quite recent years a scatophilous fly has so changed its habits that

NEMATODE INFECTIONS.

(These are on the same lines as trematode and cestode as a rule.)

Nematode.	*Definitive Host.*	*Definitive Reservoir.*	*Infection.*	*Intermediate Host.*	*Transmission.*
Filaria bancrofti.	Man.	Man.	Microfilaria in blood. — Ingestive.	Culex and Stegomyia.	Larvofilaria. — Penetrative.
Loa loa.	Man.	Goat (?) sheep (?)	Microfilaria. — Ingestive.	Species of chrysops.	(?)
Dracunculus medinensis.	Man.	Man.	Larvæ in water. — Ingestive.	Species of cyclops.	Water. — Ingestive.
Ascaris lumbricoides.	Man	Pig.	Eggs. — Ingestive	Rats.	Larvæ on food. — Ingestive.

it has deposited its larvæ on the skin of sheep and become a producer of myiasis thereon.

Myiasis will form the subject-matter of Chapter LXVII. (p. 1619), and here it is only necessary to say that the larvæ may be deposited in the natural cavities of the body, placed in neglected wounds, live in the subcutaneous tissue, or pass through the alimentary canal.

In this chapter we are merely concerned with the method by which the larva reaches man, and it would appear that it is always, or nearly always, due to the direct action of the mother fly; but there is a curious observation, which is that an ***intermediary animal carrier*** exists, at all events, in the case of *Dermatobia cyaniventris*, which has been studied by Blanchard, Surcouf, Rincones, Tovar, Zepeda, and Sambon.

According to the last-named observer, *D. cyaniventris* lives in Trinidad and Central and South America, and its young produce cutaneous myiasis in man, monkeys (the brown howler and the capuchin), pumas, agoutis, cattle, goats, pigs, and birds (the toucan and the turkey).

Man is most liable to be infected while working in the mahogany forests of Honduras and Columbia, as many as a hundred maggots being found in a single patient. These maggots are called by the natives 'mosquito worms,' because they are deposited by a culicine mosquito, *Janthinosoma lutzi*.

The history is as follows:—

The female *J. lutzi* lays its eggs in water; these hatch and produce the imago, which is then seized by the *D. cyaniventris* (according to Kudi), and some eight to eighteen long, pale, yellow eggs are glued one after the other to the velvet surface of the gnat's first second to third abdominal segments.

The eggs are quite ready to hatch, and Sambon says that some of them quickly become uncapped, and that the anterior part of the larva is protruding. The mosquito now goes off to get a meal of warm vertebrate blood, and while it is so doing the larvæ drop out of their shells and enter the skin via the hole made by the mosquito. This much is known, but we may well ask whether this happens with any other insects. Sambon says that the common house-fly spreads the book-scorpion, *Chermes nodosus*, in this way, and says that he has seen *Pediculus capitis* do the same thing. If this be so, then the study of entomology, applied to man and animals, has still much work in front of it.

Restricting our attention to *Dermatobia cyaniventris*, the chart of its carriage is as follows:—

DERMATOBIA MYIASIS.

Parasite.	*Intermediary Hosts.*	*Infection.*	*Intermediate Host.*	*Intermediate Reservoir.*	*Transmission.*	*Definitive Stage.*
Larva of *D. cyaniventris.*	*Janthinsoma lutzi.* Carries eggs. Only female.	Mosquito sucks blood; larva enters wound. — Penetrative.	Man.	Warm-blooded vertebrates.	Larva escapes from skin.	Free living.

D. BACTERIAL DISEASES.

The spores of bacteria enable them to spread from host to host with a degree of protection during the passage, but non-sporing forms will be benefited by the aid of a carrier, which not merely affords protection, but also a means of dissemination. We will divide the discussion into flies, fleas, and lice.

1. FLIES.

This 'intermediary host' is often a non-blood-sucking fly of the nature of the 'common house-fly,' which is a potential carrier of disease, because it and its kind frequent decaying matter and excreta for the purpose of laying the eggs, while both it and its larvæ are filth feeders.

If it and its allies only fed upon filth, there would be but little harm, but, unfortunately, they are attracted to many articles of human food, cooked and raw, such as milk, meat, butter, sweets, etc.; and the distances within reason to which flies travel is limited by the necessities of food and shelter, but they go to the nearest place, and if both exist at hand they do not travel.

Nicholls, working in St. Lucia, has shown that the fly *Limosina punctipennis* Wiedemann lives and breeds almost exclusively upon human excrement, and that it is a carrier of *Bacillus coli communis*. In Africa flies belonging to the genus *Pycnosoma*—*e.g.*, *P. marginale*—do the same as do other species in India and China.

These flies one and all are great feeders, and are accustomed to vomit frequently, while they pass a considerable amount of excrement. Graham Smith records 1,102 vomit marks and nine fæcal deposits on an area of a cupboard window 6 inches square. Bearing this in mind, it can readily be appreciated how well they contaminate food and what efficient disseminators of germs they may be.

Graham Smith describes fæcal deposits as round, opaque, often raised, spots of a yellowish, brownish, or whitish colour, while vomit spots have an opaque centre and a clear periphery bounded by a darker zone.

But the body of the fly is thickly clothed with hairs or setæ, and as it walks over filth, particles containing bacteria are apt to cling to these hairs.

We therefore have to consider:-

A. The external carriage of germs.
B. The internal carriage of germs.

With regard to the former, Graham Smith's experiments with *B. prodigiosus* show that this bacillus can be cultivated from the legs and wings of infected flies for eighteen hours after infection. It must be remembered that flies are everlastingly cleaning themselves, and it is a matter of common knowledge how the proboscis is rubbed by the anterior pair of legs, which become contaminated therefrom.

Therefore the external carriage of germs from filth to food is possible, provided that it takes place within a relatively short time.

With regard to the internal carriage, the same observer has shown that, though there is no evidence that *B. prodigiosus* multiplies therein, it can live in the alimentary canal of flies for four to five days.

The investigation of the presence of *B. typhosus* in a fly is most difficult, because there are non-lactose fermenters present as normal denizens of the fly. Faichnie has shown that it tends to be present in the intestine, and not on the legs, but Cochrane's experiments show that it may be recovered from the external washings of flies. The bacilli so obtained were tested with typhoid serum, and gave positive reactions, and even by immunizing animals therewith and testing the serum so obtained against stock *B. typhosus*, positive results were obtained.

With regard to the spread of *B. typhosus* and *B. paratyphosus A* and *B* via the larva to the fly, the only experiments of real moment are those of Faichnie, who worked with uncultivated germs, the flies being bred in infected fæces. He showed that this was highly probable, though other workers have failed with cultivated material. Faichnie, however, did not say that he separated the larvæ which had fed upon the excrement therefrom, and therefore did not say that he had excluded the possibility of the newly hatched flies feeding upon the excrement. Hence the subject of the carriage from the larva to the imago is *sub judice* at present.

Finally, as far as is known, flies do not suffer in health from the carriage of germs pathogenic to man.

Is the fly, with its non-lactose fermenters, the original home of the enteric fevers of man? We have not sufficient knowledge at present to discuss this subject, but we have said enough to demonstrate its importance.

For epidemiological reasons, supported by bacteriology, it appears probable that 'epidemic or summer diarrhœa' is due to Morgan's bacillus spread by flies.

For epidemiological reasons it seems possible that flies may infect food with the germs of the choleras.

There is no doubt that flies can obtain the tubercle bacillus from sputum, keep it alive in the crop for three days, and in the intestine for twelve or more days, and thus can contaminate food by the fæces up to the fifth day, and sometimes up to the sixth to fourteenth day.

Anthrax spores remain infective in flies for twenty days, being found in the fæces, while in dead flies the period is indefinite; moreover, they can pass via the larva to the imago.

At this stage we may point out that the infection of wounds produced by biting flies may be carried out by the agency of non-biting flies. Patton was the first to point out that non-biting flies—*e.g.*, *Musca pattoni*—suck the blood which exudes from the bites made by tabanids, stomoxys, etc. As *M. pattoni* breeds in bovine excrement, the possibility of bacterial infection of the wound is to be remembered.

The possibility of the Klebs-Loeffler bacillus and allied organisms being spread by flies must not be forgotten, though there is no evidence that this is the usual form of infection; still, judging from a case of conjunctival diphtheria seen in Khartoum by Chalmers, it is possible that it may occur as the means of infection of unusual sites, as Graham Smith has shown that the germ can live in the crop and intestine for twenty-four hours and longer, and, further, that the vitality may be *under-estimated*.

Ophthalmia, for epidemiological reasons, especially the Egyptian ophthalmia, is believed to be spread by flies, and Perry and Castellani have shown that *Microneurum funicolum* de Meijere, 1905—the eye-fly of Ceylon and Java—is a possible carrier of the Koch-

Weeks bacillus and a spreader of the severe forms of ophthalmia found therein.

Flies can also carry the plague bacillus in living virulent form in their alimentary canal for forty-eight hours, but they do not play any great part in the dissemination of the disease.

They also may be regarded with suspicion as spreaders of coccal infections, as these germs have been found in their alimentary tracts, as well as externally.

Flies are therefore of great importance as intermediary hosts of bacteria, and as such are worthy of study.

We require to know the house-flies of the tropics, but these are little investigated, though Nicholls at St Lucia has found the following breeding in human fæces:—

Drosophila melanogaster Meigen.
Limosina punctipennis Wiedemann.
Sepsis species.
Sarcophaga aurifinis Walker.
Sarcophaga species.
Sarcophagula species.

In Africa and the East generally:—

Pycnosoma marginale Wiedemann.
Pycnosoma chloropyga Wiedemann.

In India by Patton:—

Musca domestica Linnæus.
Musca domestica var. *determinata* Walker.
Musca nebulo Fabricius.
Musca pattoni Austen.

In England the investigation is much more complete—*e.g.*:—

Musca domestica Linnæus
Musca corvina Fabricius.
Calliphora erythrocephala Meigen
Calliphora vomitoria Linnæus.
Lucilia cæsar Linnæus.
Pollenia rudis Fabricius.
Fannia canicularis Linnæus.
Fannia scalaris Fabricius.
Anthomyia radicum.
Sarcophaga carnaria Linnæus.
Sepsis punctum Meigen.
Piophila casei Linnæus.
Scatophaga stercoria Linnæus.
Drosophila fenestrarum.

Also *Scenopinus fenestralis* and species of Stomoxys and of Psychoda; but these two last have already been described, and now it behoves us to look at the classification and structure of the non-biting flies.

We have already given the classification of the Diptera in Chapter XXXIII., and need only consider that of the families.

Family Phoridæ.

Phora femorata occurs occasionally in houses. *Aphiochæta ferruginea* Brunner causes intestinal myiasis.

Family Scenopinidæ.

Scenopinus fenestralis Linnæus is the so-called window fly, which is probably the only household fly which is not injurious to health.

FAMILY EMPIDÆ.

Orthorrhapha brachycera with medium or small bodies and small heads. Antennæ with the first two joints very small and hardly distinct, the third joint annulated, often with terminal bristle. Wings with three large complete basal cells, of which the third is shorter than the second. The posterior basal transverse vein is parallel to the border of the wing. Empodium membranaceous.

It is doubtful whether these insects attack man. As a rule they live on the juices of other insects and plants.

SUBORDER II. CYCLORRHAPHA.

Section 1: Aschiza.—This group includes the family Syrphidæ, of which no species is known to bite man.

Section 2: Schizophora.—This group includes the true flies characterized by a distinct frontal lunula and a frontal suture; antennæ with three simple segments, and an arista which is generally dorsal. They may be classified into—

Muscoidea.

Synonym.—*Eumyidea.*

This superfamily is divided into:—

TRIBE 1: *Muscoidea acalyptratæ*, without squamæ covering the halteres.

TRIBE 2: *Muscoidea calyptratæ*, with squamæ covering the halteres.

MUSCOIDEA ACALYPTRATÆ.

A large number of families are grouped together under this division, of which the most important for our purposes are—

1. Sepsidæ.
2. Oscinidæ.
3. Drosophilidæ.
4. Borboridæ.

These families can be recognized as follows:—

A. Subcostal (auxiliary) vein present. Radial 1 (first longitudinal) terminates near or beyond the middle of the wing.

  I. With a distinct bristle on each side of the face near the oral margin.

   Front never bristly near antennæ; abdomen somewhat elongate, cylindrical, usually narrowed near base. Small black flies found about decaying matter—*Sepsidæ*.

B. Subcostal vein absent, vestigial, or incomplete. Radial 1 usually ends in the costa before the middle of the wing. Head not produced into lateral processes.

  I. Hind metatarsi incrassate and usually shorter than the second joint—*Borboridæ*.

II. Hind metatarsi not incrassate and always longer than the following joint.
   (a) Discal and basal cells united: anal cell absent: front bare, or at most bristly above; small, usually light-coloured flies—*Oscinidæ*.
   (b) Discal and second basal cells separated: anal cell complete, though small. Scutellum not elongate and triangular, and without spines on margin. Oral vibrissæ present. Arista long plumose—*Drosophilidæ*.

FAMILY SEPSIDÆ.

The Sepsidae include the genus *Piophila*, of which the species *Piophila casei* Linnæus may cause intestinal myiasis. *Sepsis violacea* is a dung-fly often found in houses.

FAMILY OSCINIDÆ Latreille, 1804.

Muscoidea acalyptratæ with front without bristles: crown with only a few short bristles, border of mouth without vibrissæ. Middle tibia with small spurs: costa of wings without bristles. Subcostal vein absent. Anterior of two small basal cells united with discal cell: posterior wanting.

The genera with which we are concerned are *Microneurum* Becker, 1903, and *Hippelates* Loew, 1863.

Microneurum Becker, 1903.

Microneurum funicola de Meijere, 1905.

Synonym.—*Siphonella funicola* de Meijere, 1905.

This little fly is the common 'eye-fly' of Ceylon and Java, which causes great annoyance by hovering in front of the eyes, especially when reading or writing indoors.

It is said to suck blood, but our experience is quite opposed to this. It chiefly attacks the eyelids and the ears, and since the experiments performed by Sir Allan Perry and Castellani it has been suspected as a possible carrier of the Koch-Weeks bacillus, which is the cause of severe attacks of conjunctivitis. It objects to the odour of such substances as Odol, which may be used to drive it away.

Hippelates Loew, 1863.

Some authorities consider this genus not well founded, and state that a revision of the genera of the Oscinidæ is urgently required.

The species *Hippelates flavipes* Loew, *H. plebejus* Loew, and *H. pusio* Loew, attack men and domestic animals by darting at the eyes and other parts of the body in search of moisture or perspiration. They also attack wounds, sores, scratches, ulcers. Their life-history is unknown. In habits they are diurnal, frequenting open and sunny places. They are found in the southern United States, in Florida, Alabama, and Texas. Veils can be used as a protection, and eucalyptus oil or a menthol spirit lotion can be sprinkled on the coat collar to drive them away.

FAMILY DROSOPHILIDÆ.

This family includes the species *Drosophila ampelophila* Loew, commonly called the fruit-fly, and found hovering over fruit in houses; and as it is attracted by excrementum it must be regarded as dangerous. There are a large number of species of *Drosophila* known.

FAMILY BORBORIDÆ.

This family includes *Borborus equinus*, a small fly sometimes found in houses.

MUSCOIDEA CALYPTRATÆ.

MUSCINÆ.

Musca Linnæus, 1761.

Musca domestica Linnæus, 1761.

Musca: face in its lower part silky yellow; shot with blackish-brown. Median stripe black; antennæ brown, palpi black.

Thorax dusty grey, with four equally broad longitudinal stripes.

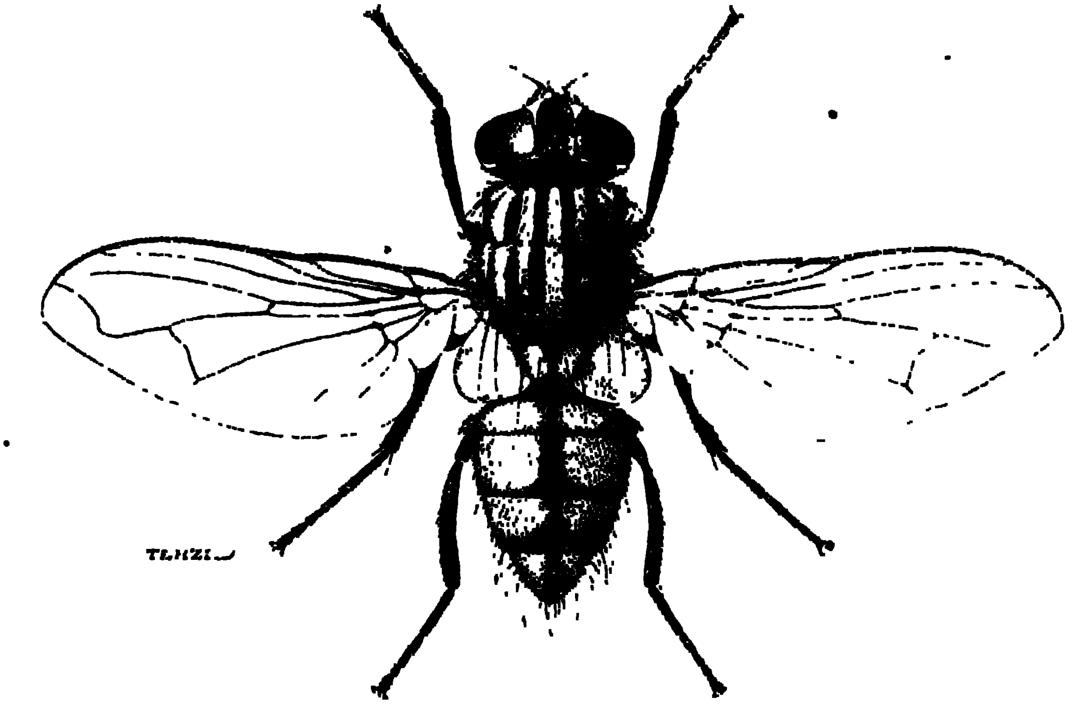

FIG. 468.—*Musca domestica* LINNÆUS. (×6.)

Scutellum grey, with black sides. Wings tinged pale grey with yellowish base. Legs blackish-brown. Abdomen yellowish, with dorsal blackish-brown line, except the last segment, which is entirely blackish-brown. Eyes separated by a wide frontal stripe in the female, and near together in the male. Length, 6 to 7 millimetres; wing breadth, 13 to 15 millimetres.

Remarks.—It has been known for many years that flies can carry micro-organisms on their legs. In 1888 Celli proved that flies, fed upon pure cultures of typhoid bacilli, were able to transmit virulent bacilli with their excrement. Early observations also proved that flies were capable of transmitting cholera. In the Spanish-American War, in the Army Concentration Camps of 1898, flies were found to be spreaders of typhoid. Lime was sprinkled on the fæcal pits, and the flies on the soldiers' mess-table were noticed to have their legs whitened with the lime.

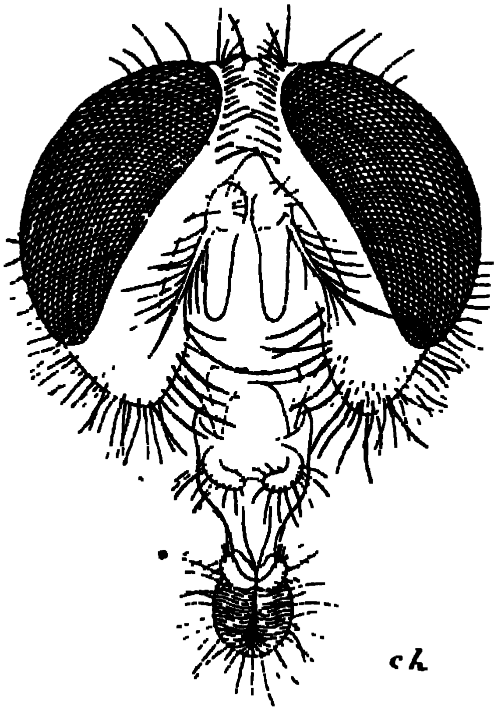

FIG. 469.—HEAD OF *Musca domestica* LINNÆUS: FEMALE. (After C. J. Martin.) *ch.*, Pseudo-tracheæ.

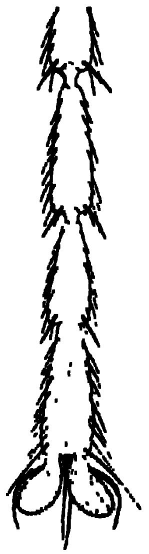

FIG. 470.—LEG OF *Musca domestica*. (After C. J. Martin.)

The flies which breed in human excrement in America are: (1) *Musca domestica*, house-fly; (2) *Drosophila ampelophila*, fruit-fly; (3) *Fannia canicularis*, little house-fly; (4) *F. brevis*, little house-fly; (5) *Stomoxys calcitrans*, stable-fly; (6) *Phora femorata*; (7) *Sarcophaga trivialis*.

Of these the most common are the house and the stable flies. The house-fly is 98 per cent. of all flies infesting houses.

In the Boer War of 1900-02 flies were held to be great spreaders of typhoid. In 1902 a paper, entitled 'An Inquiry into the Influence of Soil, Fabrics, and Flies in the Dissemination of Enteric Infection,' was published by Firth and Horrocks in the *British Medical Journal*, and they showed that the ordinary house-fly (*Musca domestica*) can convey enteric infective matter from excreta or polluted materials, or objects on which they may walk, rest, or feed. Such infective matter appears to be attached to their heads (mandibles), legs, wings, and bodies. Klein has grown the typhoid bacilli from flies caught in an infected area.

Flies have long been accused of being the spreaders of dysentery, and recently this view has been experimentally proved by several authors, including one of us. Other diseases, including intestinal myiasis, are said to be spread by flies.

The flies found by Newstead in houses in Liverpool, or bred from refuse and excreta, were *Musca domestica* in quite 90 per cent. of all flies, while the other species met with were—*Calliphora erythrocephala*, the blow-fly; *Scatophaga stercoraria*, the dung-fly; *Borborus equinus*, a small fly; *Stomoxys calcitrans*, the stable-fly; *Fannia canicularis*; *F. scalaris*; *Anthomyia radicum*, the root-fly; *Psychoda phalænoides*, the owl-midge.

Morphology.—The vertex shows three ocelli, situated on a slightly raised ocellar triangle, which is surrounded by another triangle, the vertical triangle.

Between the upper and lateral edges of the clypeus (face) and the lower edge of the epicranium can be seen the crescentic opening of the ptilinum.

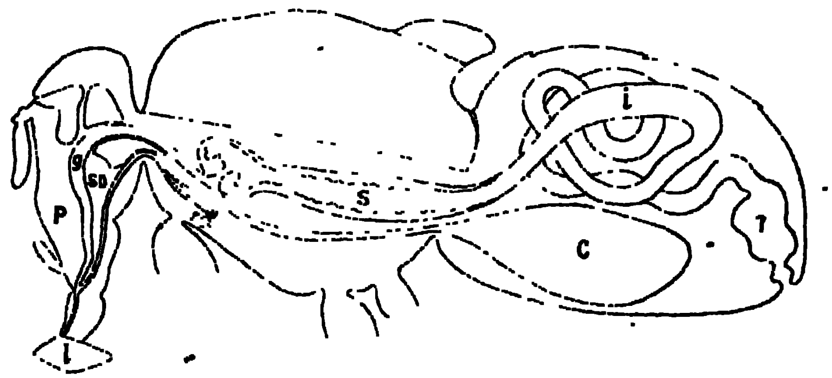

FIG. 471. -ANATOMY OF *Musca domestica*.
(After C. J. Martin.)

l., Labella; *P.*, proboscis; *S.D.*, near salivary duct; *g*, gullet; *S*, mid-gut; *i.*, intestine; *C*, sucking stomach; *T*, rectum.

The proboscis consists of the rostrum, the haustellum (proboscis proper), and the labellæ. The rostrum is a truncated cone containing the pharynx; the haustellum is grooved anteriorly to contain the labrum, epipharynx, and the hypopharynx. Posteriorly it is strengthened by a sclerite called the 'theca,' which distally carries the fork (*furca*).

The labrum and the epipharynx, with the hypopharynx, as is usual, form the pharyngeal tube, while the hypopharynx contains the salivary or hypopharyngeal tube. The labellæ are complicated organs with a number of channels (pseudo-tracheæ) on their distal surface.

Each labella has lobes anterior, middle, and posterior, with respectively twelve, twenty-one, and three channels, which eventually run to the oral aperture, which lies at the base of the oral pit. This pit is kept open by two discal sclerites. In the oral pit the pseudo-tracheæ cease, and the sides of the channels are covered by overlapping teeth.

The pro- and meta-thoraces are much reduced, while the mesothorax is well developed, and shows a typical structure. The venation of the wings may be briefly described by saying that the costa and subcosta are well marked, and the usual costal and first costal cells are present. Radius 1 cuts off the subcostal cell; R. 2 and 3 the first radial, and R. 4 and 6 the third radial; while media 1 and 2 bound the radial and fifth radial cells, which are separated by the radio-median nerve. Median 3 and cubitus 1 cut off the median and second median cells, which are separated by the medio-cubital vein. The anal vein is incomplete, and therefore does not separate the cubital and anal cells.

The abdomen consists of eight segments in the male, and nine in the female. The first segment in both sexes is rudimentary, and fused with the second. The second, third, fourth, and fifth are well developed. The sixth, seventh, and eighth in the male are atrophied, and surround the anal and genital orifices. The sixth, seventh, eighth, and ninth in the female form the long ovipositor, which can be retracted into the abdomen.

The pharyngeal tube mentioned above ends in the pharynx, which has a chitinous wall, the fulcrum. The œsophagus runs into the thorax, where it opens into the proventriculus, and sends a long duct to the trilobed crop which lies in the abdomen. The proventriculus is really a valve which leads to the chylific ventricle. This tube is narrow in front and wide behind, and much coiled. At the junction with the Malpighian tubes it becomes the intestine, which runs to the rectum. There are the four usual rectal glands.

The salivary glands are two long tubes whose ducts unite in the head and open into the salivary duct of the hypopharynx. The labial glands lie in the proboscis at the base of the labellæ, and by their secretion keep the tip moist.

The reproductive organs consist in the female of ovaries, spermathecæ, accessory glands and ducts, and the ovipositor. In the male they consist of testes, vasa deferentia, an ejaculatory duct, and penis.

Life-History. This was first studied by de Geer in 1752-78, next by Bouché in 1834, Packard, junior, in 1873, and more recently by ourselves and a number of other people. The most recent works are those by Newstead in Liverpool and Hewitt in Manchester.

The house-flies lay their eggs by preference in human fæcal matter when somewhat decomposed, in horse-manure, goat-manure, cow-dung, and in fermenting vegetable substance, on which the larvæ can feed when hatched.

But these grubs can eat textile fabrics and paper when in need of nourishment. Usually the fly works its way into the rubbish-heap or loose earth to lay its eggs, but this is not invariable.

FIG. 472.—EGG, LARVA, AND PUPA OF *Musca domestica*.
(After C. J. Martin.)

The time required for the development to be gone through depends upon the temperature of the air, being most rapid from 22° to 35° C.; upon the food, being more rapid when animal food is available; on moisture, which is most necessary; and upon fermentation, which is also necessary. The egg takes from one to three days to hatch into the larva, which lives rather less than a week, and then turns into the pupa, which produces the imago.

The whole time required is usually twelve to twenty days, and never less than eight days.

Aldridge gives the following table for India :—

Stage.		Hot weather.		Cold weather.
Eggs	..	One day	..	Two days.
Larvæ	..	Five days	..	Fourteen days.
Pupæ	..	Three days	..	Five days.

In Colombo, Ceylon, we found the development to be quick, and to resemble the times given in Aldridge's hot-weather table.

Egg.—The imago becomes sexually mature in ten to fourteen days, and eggs are laid as soon as the fourth day after fertilization, usually 120 to 150 eggs laid being in a batch. The egg is cylindrically oval, being broader posteriorly, and has two curved ribs along its dorsal aspect. It hatches by splitting at the dorsal portion of the anterior end.

Larva.—The larval life is divided into periods or instars by the ecdyses.

First Instar.—The larva is 2 millimetres in length, with a slender body, the head being at the narrow end, with a spiny area on the anterior ventral edge of each segment, and posteriorly two stigmatal openings. This stage lasts twenty-four to thirty-six hours.

Second Instar.—The larva develops a pair of anterior spiracles. This stage lasts twenty-four hours.

Third Instar.—The larva eats vigorously for the first two days, and then, ceasing to feed, still increases in size. This stage lasts three to four days, and ends in pupation. The larva has a well-developed alimentary canal.

Pupation.—Pupation takes place in three to four hours, and consists of the larva contracting (especially anteriorly) inside its own skin, from which a puparium with rounded ends is formed. Length about 6·3 millimetres, which is at first creamy-yellow, but later becomes dark brown. This is a typical coarctate pupa, around which the spiral locomotory pads may be seen.

Pupa.—The pupal stage lasts about three to five days, when the imago, dilating its frontal sac, ruptures the anterior end into dorsal and ventral portions, the whole separating by a circular split at the sixth segment.

Fly.—The young fly is at first underground or in the middle of a rubbish-heap, through the interstices of which it makes its way to the surface by the aid of its ptilinum or frontal sac. When first hatched it is rather grey in colour, and has to allow its wings to dry before it is able to fly.

Habits.—After hatching the fly sets about to obtain food, and on this point it is not particular as to the kind, as anything, from typhoid fæces and dysenteric fæces to a pudding, are quite agreeable to its oral lobes. It also has a liking for human sweat, much to the annoyance of a person desiring a rest on a tropical afternoon. It works all day, but rests at night in any place which is dark. It is not known whether it has a particular preference for the spots on which to defæcate, as fly-specks are abundant. It is believed to defæcate about fifty times in twenty-four hours. A number of experiments have been performed to see how far *Musca domestica* can fly, but they are not satisfactory. It is believed that a female fly becomes sexually mature and deposits ova in ten days after leaving the pupal case, that she lays four batches of eggs at intervals of ten to fourteen days, and that then she dies, but these figures must be received with great caution. Jephson believes that the limit of life of an adult fly is three weeks, but a hibernating or æstivating fly must live much longer. Indeed, a fly has been known to live sixteen weeks.

Enemies.—The enemies of the house-fly are numerous, and include fungi (*e.g.*, *Empusa muscæ*), protozoa (?), nematode worms (?), mites (*i.e.*, larvæ of *Trombidium muscarum* Riley, *T. muscæ* Oudemans, the genus *Pigmeophorus*, nymphs of *Tyroglyphus*), spiders, pseudo-scorpions, centipedes, larvæ of beetles, ants, wasps; also members of Cynipidæ, insects which produce galls on plants (*e.g.*, *Figites anthomyiarum* and *F. scutellaris* attack the maggots, while *Spalangia niger* of the Pteromalidæ lays its eggs in the pupæ); and *Stenomalus muscarum* is also a pupal parasite, as is *Nasonia brevicornis*, *Pachycrepoideus dubius*, and *Muscidifurax raptor*. Toads, lizards, and rats are expert fly-catchers.

Pathogenicity. It is a carrier of the bacilli of enteric fever, dysentery, cholera, infantile diarrhœa, framboesia tropica, anthrax, tuberculosis, ophthalmia, oriental sore, and parasitic worms (*e.g.*, *Ascaris lumbricoides*).

Calliphora Robineau-Desvoidy, 1830.

These are the blow-flies or bluebottles, of which *C. erythrocephala* Meigen is the common species.

ENTERIC FEVERS.

Organism	*Infected Host.*	*Infected Reservoir.*	*Transmission.*	*Protective Host.*	*Infection.*
Bacillus typhosus.	Man.	Man. · Typhoid carriers.	Bacilli in urine and fæces. — Ingestive.	Flies.	Bacilli on to human food. — Contaminative.

2. FLEAS.

These insects have been accused of spreading leprosy and tuberculosis, but only one bacterial disease of man has really been proved to be carried by them, and this is the plague.

The Plague.—The ætiology of plague has been placed on a sure footing by the labours of Kitasato, Yersin, Cantlie, Simpson, Thompson, Kolle, Martini, and the Special Committee already mentioned, together with the Second Indian Commission.

It is caused by the *Bacillus pestis* of Kitasato and Yersin, which is found in the fluid of the initial cutaneous vesicle, the buboes, the spleen, the blood, and the sputum in cases of pneumonia. When inoculated into monkeys, cats, rats, guinea-pigs, squirrels, mongooses, bats, jerboas, etc., it causes the typical disease, while in bovines and equines it only causes local reactions. Canines, birds, and reptiles appear to be immune. It causes a natural epizoötic in rats, which apparently is the true disease, from which that of man must be looked upon as an offshoot. In rats it produces either as acute or a chronic attack, the post-mortem appearances of which are different.

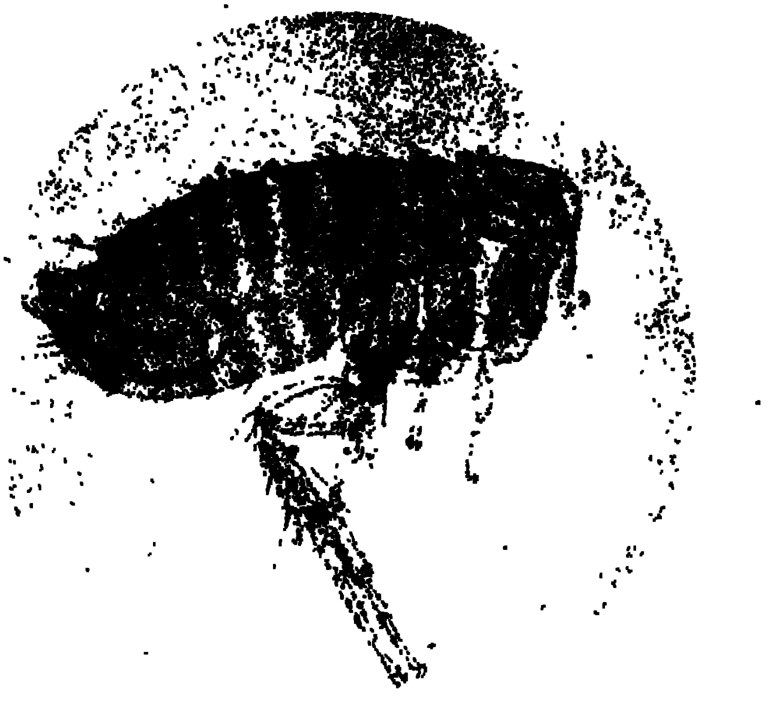

FIG. 473.—RAT FLEA.

In the acute type a bubo is found in 85 per cent. of infected rats, being present usually in the neck or axilla. If the bubo is absent, a plague rat can be recognized by the subcutaneous congestion, the purplish-red appearance of the muscles, the waxy, mottled, or finely granular appearance of the liver, the hæmorrhages, and the pleural effusions. The diagnosis can be confirmed by finding the bacilli in the bubo, the spleen, or the blood.

The chronic type of the disease consists of encapsuled caseous foci, or abscesses containing bacilli, and found in the spleen and other organs. This form plays no part in the spread of the disease.

The epizoötic does not continue with equal virulence all the year round, for it appears to be profoundly altered by the temperature, being diminished in the hot weather of the tropics and the cold weather of the Temperate Zone. Thus in Bombay the Plague Commission found 1,766 plague-infected rats in one week in the season December to May, and only 20 to 30 in the season June to November. The cause of this variation has already been given.

But all rats are not equally infected, for it was found in Bombay that there were two principal species, *Epimys norvegicus* and *E. rattus*, and that during the epizoötic period no less than 1,334 of the 1,766 belonged to the former species, while in the non-epizoötic period it alone carried on the disease. The reason assigned for this difference was that the numbers of the flea population of the two rats were very different, *E. norvegicus* possessing about double the number of *E. rattus*. Further, it was noticed that the curve of *E. norvegicus* infection began to rise about ten days before that of *E. rattus*, which points to the origin of the infection of the latter from the former in the first instance.

E. norvegicus, which is not nearly so numerous in Bombay as *E. rattus*, lives outside houses, for the most part in sewers, drains, and stables, and has a great facility for burrowing, and is a good climber. It, however, has never been found above the third floor of a house. It forms its nest in one of its burrows, and breeds all the year round, but has two special seasons, one in March and one from June to October, the average family being eight.

E. rattus is more common in Bombay than *E. norvegicus*, especially in houses, where it increases, relatively to the other, up to the third floor, but above that level it alone infects the house. It is not so common in gullies, compounds, stables, go-downs, and food and tea shops as *E. norvegicus*. The common meeting-ground of the two species appears to be the lower floors of houses, gullies, and go-downs. Though a domesticated rat, it can climb and burrow. It forms its nest in cupboards, heaps of firewood, etc., and breeds all the year round, but especially from June to October, the average family being five.

The spread of the plague from *E. norvegicus* to *E. rattus*, according to the experiments of the Commission, is neither by direct contact nor by air, soil, or food, but solely by the flea. Contact was excluded by placing healthy rats in the same room with plague-infected animals from which the fleas had been removed, when it was found that none of them developed plague. The experiment was kept up for a long time, replacing dead infected rats with freshly infected rats, and, further, the room was never cleaned out, so that the healthy animals lived in contact with the infected urine and fæces, and even ate food polluted therewith, and yet not one contracted plague, thus excluding transmission by contact, soil, and food.

Again, when healthy animals were suspended in cages 2 feet from the ground, so that the fleas could not get to them, or placed on the ground, and surrounded by 6 inches of tangle-foot, over which a flea cannot pass, as it is said to be incapable of jumping more than 4 inches, or surrounded by a curtain of wire gauze so fine that a flea could not penetrate it, and exposed to infection, they escaped, though others not so protected became infected, thus disproving aerial infection. Further, the transmission by the rat-flea was proved by constructing a glass box, inside which two wire cages were placed at a little distance, but side by side, each standing in a tray filled with sand. Each cage had a lid, through which rats, food, water, etc., could be introduced, and the whole apparatus was covered in with fine muslin to prevent the escape of the fleas. A plague-infected rat and a number of rat-fleas were placed in one cage. When this rat died, a healthy rat was placed in the other cage, and after some time the dead body of the infected rat was removed, when it was found that the new rat became infected with plague, and fleas containing plague bacilli were found upon it. This experiment was repeated many times, 15 per cent. of the exposed rats taking the disease. Further, fleas infected by biting plague rats, when placed upon healthy rats, produced the disease in 55 per cent. of the experiments.

The Commission calculated that the blood of an ordinary plague rat in two-thirds of the cases contains more than 100,000,000 bacilli per cubic centimetre, and that a flea's stomach could hold 0·5 cubic millimetre of blood. Therefore, when the flea gorged itself on the average plague-stricken rat it received at least 5,000 bacilli. These bacilli are found only in the stomach and in the alimentary canal posterior to that viscus, especially the rectum, and escape from the flea solely with the faeces. It was proved, however, that the bacilli multiplied in the body of the flea by allowing infected fleas to feed solely on uninfected rats, a fresh one being supplied each day, when abundant bacilli were found up to the twelfth, and once to the twentieth day, thus proving that multiplication must have taken place, otherwise the original number of bacilli would have become much diluted by the feeds with fresh blood. Further, it was discovered that the proportion of fleas in whose stomach multiplication took place was six times greater in the epidemic than in the non-epidemic season. In the former season the bacilli could be found easily up to the fourth and even to the twelfth day, while in the latter never after the seventh day. Infected fleas were found to transmit the disease for seven to fifteen days.

The method of infection probably is in one of two ways—either faecal pollution of the proboscis, or else faecal pollution of the wound made by the proboscis, which was found quite large enough for the purpose of introducing the bacilli into the skin. Both males and females can transmit the disease, but it was found that one infected flea alone was unlikely to do so. The flea most commonly found on rats, and the one by which the infection in these experiments was usually spread, was *Xenopsylla cheopis*, but others—*e.g.*, *Ceratophyllus fasciatus* and *Pulex irritans*—were found also capable of causing the disease.

Bacot and Martin have proved the inoculative method of infection in *Ceratophyllus fasciatus*, which, when blood-sucking, injects the bacilli, when they are present in its stomach in such numbers as to cause temporary obstruction at the entrance to that organ.

With regard to the spread of the disease to man, the Commission believes that the infection generally comes from *Epimys rattus*, because the habits of that rodent bring it into close relationship with man, and because the curve of its epizoötic begins to rise ten to fourteen days before that of the epidemic. This period is calculated to be made up of three days, during which the flea leaves the dead rat, to which is added another three days, which is the incubation period of plague in man, and five and a half days, which is the average duration of the fatal illness in man.

Xenopsylla cheopis appears to be the flea by which plague is spread from *Epimys rattus* to man. This rat-flea will not merely bite man when it cannot get rat's blood, but is capable of living for three to four weeks on man's blood, and is often found on human beings after inspection of plague-stricken houses.

Further, it is believed that the spread of plague is due, not to migration of rats, but to the carriage of infected rats on ships, and of fleas in merchandise or on human beings. The Commission apparently consider the last to be the most important method.

Pneumonic plague, which occurs only in 2·5 per cent. of cases during bubonic epidemics, spreads from man to man by bacilli carried by the air, for Strong and Teague demonstrated that the sputum in invisible droplets containing viable plague bacilli was frequently to be found in the air near a patient. Teague and Barber have shown that the fine droplets of sputum disappear very quickly unless there is a considerable amount of aqueous vapour in the atmosphere, as is found in very cold climates, and hence the tendency for pneumonic plague to spread in those rather than in warm climates. On the other hand, the bubonic or septicæmic is not spread from man to man, but from rats to man. The epizoötic is the real disease, and the epidemic is only an offshoot.

The above ætiology explains fully the predisposing causes of sex, women staying more in the house than men; of house, of season, of climate, and also the carriage of the disease from one place to another by people, fodder, grain, bales of cotton and clothing, rags, etc.

Verjbitski in 1908 showed that bugs could act as carriers of the bacilli, and this has been confirmed by Jordansky and Kladnitsky, while Walker considers *Clinocoris rotundatus* to be one of the carriers of plague in India, having found 22 per cent. infected with *B. pestis* when collected from infected native huts. Moreover, he successfully transmitted the disease from man to the rat by means of *C. rotundatus*.

In California, Wherry, McCay, and others have shown that the ground-squirrel (*Citellus beecheyi*) is subject to plague, and that its commonest flea, *Ceratophyllus acutus* Baker, is the vector from squirrel to squirrel, and, further, that this flea will bite man Further, they record a subacute case of plague in a boy where the infection was believed to be acquired by contact with ground squirrels. With regard to the outbreak in Manchuria and North China, Gray suggested that it started among men who handled the tarbagan (*Arctomys bobæ* Schreb), which is susceptible to epizoötic plague, and that these men on returning to their homes introduced the disease into three provinces, as pneumonic and septicæmic plague, while it was spread by the agency of the breath and personal contact of clothes and belongings by coolies travelling in parties and sleeping together in overcrowded insanitary inns, especially as the cold of the winter induced an indoor existence. These travelling parties infected adult males who stayed at the inns or were travelling, and so it spread to the ordinary population. No infected rats could be found, in 20,000 examined, while isolation of the patients and their contacts, together with efficient disinfection, were sufficient to diminish the death-rate. Further researches, however, tended to show that, though the tarbagan suffers at times from plague, the epizoötic is not extensive, and its direct relationship to human plague negligible. The pneumonic form of plague may be in epidemics, especially in cold weather, but it is also to be noted that, although it starts from association with an epizoötic, it tends to die out without being succeeded by a bubonic outbreak, but it may infect rats and so cause a bubonic outbreak. The marmot (*Spermophilus citellus*), which is common around Mukden, was susceptible to the infection. There has been an epizootic in Suffolk, and a few cases of bubonic plague in man.

We therefore have to consider the rôle of the flea and the role of the vertebrate in plague, and with regard to the latter there does appear to be some such sequence as this:—The *enzoötic*, the *epizoötic* ; and these become in man:—The *endemic*, the *epidemic*, the *pandemic*.

The fleas we have described in Chapter XXXIV. (p. 857), but it is necessary to say a few words with regard to the rats.

CLASS MAMMALIA.

SUBCLASS EUTHERIA.

ORDER GLIRES Linnæus, 1758.

Definition.—Eutheria with toes armed with claws. Size usually small or medium. Front teeth chisel-shaped and separated from the grinding teeth by a wide space.

Classification.—This classification is taken from Swenk:—

A. Upper front teeth two, both large (suborder *Simplicidentata*).

- I. *Fur not sprinkled with quills.*
  - (*a*) Tail very broad, flat, scaled; hind feet webbed; size large—*Castoridæ*.
  - (*b*) Tail round or compressed; hind feet not webbed; size small to medium.

1. **Fore feet modified for digging, their claws very large; eyes and ears very small; form stout and short; large external cheek pouches**—*Geomyidæ*
2. Fore feet not modified for digging; their claws normal, eyes and ears generally large; form slender.
    - (A) Grinding teeth at least four in each jaw, tail long-haired, generally bushy, not scaled—*Sciuridæ*.
    - (B) Grinding teeth not more than three in each jaw, or if four (Perognathus and Zapus), the tail closely haired, sometimes scaly.
    - (C) With large external cheek pouches—*Heteromyidæ*.
    - (D) Without external cheek pouches:—
        - (1) Hind feet not greatly elongated, little if any longer than front feet, tail not longer than rest of body—*Muridæ*
        - (2) Hind feet greatly elongated, much longer than front feet; tail much longer than rest of body—*Zapodidæ*

II. *Fur thickly sprinkled with sharp, stiff, spine-like quills*—*Erethizontidæ*.

B. Upper front teeth four, the second pair minute and placed directly behind the first pair; hind legs much longer than front legs; ears very large, tail very short (suborder *Duplicidentata*)—*Leporidæ*

FAMILY SCIURIDÆ GRAY, 1821.

Squirrels and Marmots.

The genera of the Sciuridæ, which concern us, may be recognized by the following table taken from Swenk:—

A. Sides without a furred membrane (subfamily *Sciurinæ*, true squirrels and marmots).
- I. Tail long, much over one half of length of body; form slender, coloration usually spotted or streaked.
    - (*a*) Cheek pouches absent, tail bushy, the hairs growing outward, arboreal (squirrels)—*Sciurus*.
    - (*b*) Cheek pouches present, large; tail well haired, but not bushy, mainly terrestrial
        - 1. Nail of thumb well developed; back conspicuously striped lengthwise with five dark and two or four white stripes.
            - (A) Premolars in upper jaw one on each side; back with two white stripes; rump rufous; tail with hairs shorter than rest of body (eastern chipmunks)—*Tamias*
            - (B) Premolars in upper jaw two on each side; back with four white stripes; rump greyish; tail with hairs as long as rest of body (western chipmunks)—*Eutamias*
        - 2. Nail of thumb rudimentary, back striped lengthwise with seven lines alternating with six rows of spots, or irregularly and indistinctly spotted with whitish, or plain without either distinct spots or streaks (ground squirrels)—*Citellus*.
- II. Tail short, less than one-half of length of body; form stout, coloration always plain.
    - (*a*) Skull highly arched, causing the head to appear convex above, tail very short, flattened; thumb-nail well developed, normal, fur short and full (prairie dogs)—*Cynomys*.
    - (*b*) Skull nearly straight, causing the head to appear flat above; tail short, bushy, not flattened; thumb-nail broad and flat; fur long, coarse, and heavy (woodchucks)—*Marmotta*.

B. Sides with a densely furred membrane joining front and hind legs (subfamily Pteromyinæ, flying squirrels)—***Sciuropterus***.

Genus Citellus Oken, 1816.

Synonym. -*Spermophilus* F. Cuvier, 1825; *Citellus* Lichtenstein.
Definition. -As above.
Type Species. - *Citellus citellus* Linnæus, 1766.
We are, however, concerned with *C. beecheyi* and with *M. bobak*.

Citellus beecheyi Richard, 1829.

Definition. Citellus of large size with large prominent ears. Tail more than two-thirds of body-length. Colour above mixed black and pale yellowish brown.
Remarks. This is the ground squirrel of California mentioned above.

Genus Marmotta Blumenbach, 1779.

Synonym. - *Arctomys* Storr, 1780.
Definition. As above
Type Species. -*Marmotta marmota* Linnæus, 1758.

Marmotta bobak Muller, 1776.

Definition. Marmotta of medium size resembling the type, but of uniform colour, being above yellowish brown, overlaid with black.
Remarks. This is the tarbagan of Mongolia and Central Asia.

FAMILY MURIDÆ Gray, 1821.

Rats and Mice.

The genera of the Muridæ, which concern us, may be recognized as follows: —

- A. Crowns of grinding teeth, with tubercles arranged in transverse rows.
  - I. Rows of tubercles in grinding teeth three, very distinct in upper jaw; tail long and scaly. Subfamily *Murinæ* (Old World rats and mice).
  - II. Rows of tubercles in grinding teeth two, tail generally hairy Subfamily *Cricetinæ* (American rats and mice)
- B. Crowns of grinding teeth divided into raised loops or triangles of enamel, not tubercular.
  - I Upper front teeth narrow, compressed each one thicker than wide at base; body not clumsy; tail always long; eyes and ears large and prominent Subfamily *Neotominæ* (wood rats and cave rats) *Neotoma*
  - II. Upper front teeth broad, each one wider than thick at base; body clumsy; tail short; eyes and ears small and inconspicuous. Subfamily *Microtinæ* (voles and lemmings)

Subfamily Murinæ Baird, 1857.

Definition. As above.
Remarks. The Murinæ comprise the genus *Epimys* Trouessart, 1857, to which belong the rats and mice, of which two are of great importance in the spread of plague viz., *Epimys rattus* and *E. norvegicus*.

Genus Epimys Trouessart, 1857.

Definition. Murinæ with first and second upper molars, with two tubercles on inner side. Upper incisors with outer cutting edge entire.

Epimys rattus Linnæus, 1758.

Synonym. -*Mus rattus* Linnæus.
Slender rats with very pointed muzzles and large out-standing ears, large prominent eyes, long tail, and greyish-black fur.

The tail, which is 25 per cent. longer than the length of the head and body together, is brown and regularly annulated. Feet medium-sized, but comparatively long and slender.

Body variable, 14 to 19 centimetres in length. Colour variable: light rufescent, brown on the dorsum, white or grey on the venter, but may be darker or lighter. Mammæ two to three.

There are two varieties of this rat: ***alexandrinus***, which is larger and heavier; and ***rufescens***, which is smaller and redder; but there are any number of intermediate species. It breeds frequently throughout the year.

It is essentially a house rat, living in the tiles or thatch of the roof, or in holes and recesses in the floor, but it will live in the crowns of cocoanut trees.

Its pathogenicity is important, for it is the plague rat of Upper India. It is supposed to have entered Europe with the Asiatic invasion.

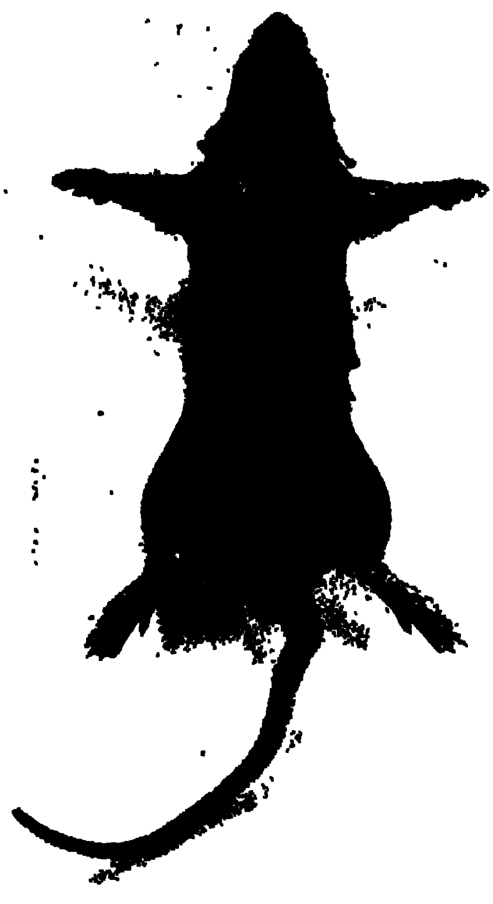

FIG. 474.—RAT. PLAGUE RESERVOIR.

Epimys norvegicus Erxleben, 1777.

Synonym. *Mus decumanus* Pallas, 1778.

Large, heavy rats, with heavy, uniformly tapering tails; dark coloured dorsally, lighter coloured ventrally; only 89 per cent. of the length of the head and body. Heavy, flesh-coloured feet, short round ears, and broad heavy snout.

Colour brown on the dorsum and dirty white on the venter. Footpads large; heart-shaped mammæ ten to twelve in number.

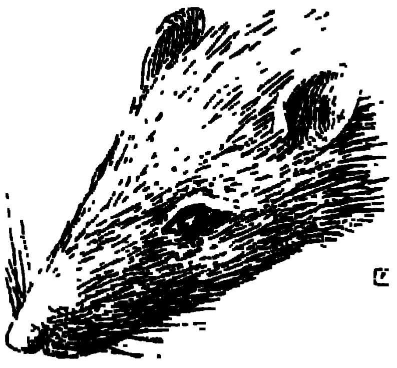

FIG. 475.—HEAD OF *Epimys rattus*.
(After Hossack.)

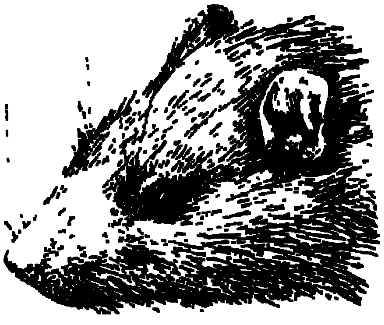

FIG. 476.—HEAD OF *Epimys norvegicus*.
(After Hossack.)

This is the brown sewer or ship rat, which is supposed to have come from China to Europe, and from Europe to India. It is the plague rat of Bombay It is very prolific, producing several litters of eight to ten young per annum.

The chart of plague is as follows:—

PLAGUE.

Organism.	*Infected Host.*	*Infected Reservoir.*	*Transmission.*	*Propagative Host.*	*Infection.*
Bacillus pestis.	Man.	Murinæ.	Bacilli obtained by blood-sucking. — Ingestive.	Fleas.	Bacilli in fæces into wound by bite. — Contaminative. More rarely inoculative.

3. LICE.

Relapsing Fevers.—With the downfall of Schaudinn's views many authorities consider spirochætes to be bacteria—*e.g.*, Dobell considers them to be such because the longitudinal division is said to be based on imperfect observation, and hereditary transmission can occur with *Bacillus cuenoti* in the germ cells of the cockroach.

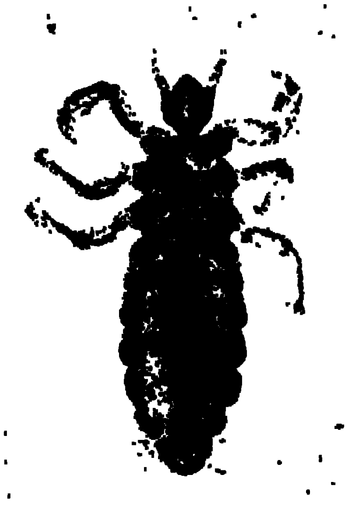

FIG. 477.—*Pediculus corporis* DE GEER, 1778: MALE. CARRIER OF TYPHUS, ETC.

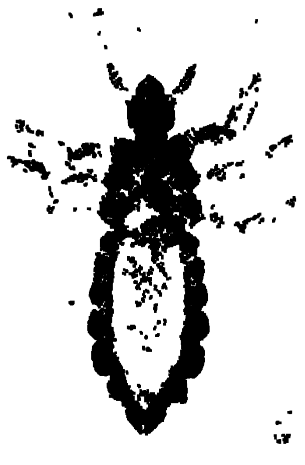

FIG. 478.—*Pediculus corporis* DE GEER, 1778: FEMALE. CARRIER OF TYPHUS, ETC.

(From a photograph by J. J Bell.)

Many of them are said to be flagellate; their nucleus is diffuse, like bacteria, and there is no conjugation, sex formation, or encystment known, and it would appear as though a coccoid-like infective granule was the important method of their infection of the host.

They therefore behave more like the bacteria than like animal parasites in the carrier.

For our present purpose relapsing fevers may be divided into two groups as follows:

I. The *Louse Group*, which is characterized by being carried by the louse. These are the European, the North African, the Indian, and the American types.

From the infective blood the spirochætes pass into the alimentary canal of the louse, and from thence into its cœlom, where they remain, and from there they find their way into the eggs, which are infective, as are their larvæ.

Infection of man is brought about by contaminative means— *i.e.*, the louse in biting causes irritation, the man scratches his skin, causing abrasions, and at the same time kills a louse, crushes it, and rubs it into the abrasions, which become infected. Nicolle and Blaizot believe that the organisms which are infective are granules just before they reappear as spirochætes. Sergent and Foley have stated that there were very small virulent forms in man during apyrexia.

In this life-cycle there is no definitive host, merely two hosts of equal value. Only the insect is the *preservative host* and the vertebrate the *intermediary host*.

I. THE LOUSE GROUP OF RELAPSING FEVERS.

Parasites.	*Preservative Host.*	*Preservative Reservoir.*	*Infection.*	*Intermediate Host.*	*Transmission.*
S. recurrentis, *S. berbera*, *S. carteri*, *S. novyi*.	Pediculus corporis	Lice by hereditary transmission	Small forms in body cavity. Contaminative	Man.	Small blood forms. — Ingestive.

Spirochætal Epidemic Jaundice. This is caused by *Spiroschaudinnia icterohæmorrhagiæ*, which may have its reservoir in rats, from which it probably escapes in the urine, and after living in water enters via the alimentary canal or the skin. It is believed to have been caused, but very rarely, as the result of a rat-bite. It is introduced here as a convenient place, though not known to be due to lice.

Parasite.	*Host.*	*Reservoir.*	*Method of Infection.*
Spiroschaudinnia icterohæmorrhagiæ.	Man.	Rats (?).	Contaminated water (?).

II. The *Tick Group*, which is characterized by being spread by the genus *Ornithodorus*. The known forms are the African (perhaps a separate East African), the Persian, the Colombian, with the Panamanian.

This group differs from the louse group in the pre-eminence of the *infective granule*, which, according to many authorities, is in itself doubtful.

Spirochætes enter the tick with the infective feed, bore their way into the cells of various organs, and break up into coccoid bodies, the infective granules. These granules pass into the second generation, and so the tick is a *preservative reservoir*. They also pass into the Malpighian tubules, from which they escape when the thick white Malpighian excrement is passed, which only takes place towards the end of a feed. The spirochætes now enter the new host via the hole made in the skin by the tick for its meal of blood.

II. THE TICK GROUP OF RELAPSING FEVERS.

Parasite	*Preservative Host.*	*Preservative Reservoir.*	*Infection.*	*Intermediate Host.*	*Transmission.*
Forms allied to *S. duttoni* and found in Africa, East Africa, Colombia, Panama, and perhaps in Persia	Species of *Ornithodorus*— e.g., *O. moubata*, *O. turicata*, *O. talaje*, and perhaps *O. savignyi*.	The ticks by hereditary transmission	The infective granules(?) — Contaminative.	Man	Blood spirochætes. — Ingestive

We have followed Balfour's suggestion that the Persian relapsing fever is not caused by *Argas persicus*, but by a species of Ornithodorus, probably *O. savignyi*. It must be admitted that many authorities disbelieve in the infective granule.

4. PHLEBOTOMUS FLIES.

Verruga Peruviana. It has been suggested that the carrier of this disease may be *Phlebotomus verrucarum* Townsend, 1913, but this appears to be very doubtful.

E. DISEASES OF UNKNOWN CAUSATION.

The evidence in favour of pellagra being an insect-borne disease has not increased, and many authorities believe it to be a deficiency disorder. The insects which were accused were species of Simulium and some Chironomid biting flies. There are suggestions that Rocky Mountain fever and tsutsugamushi disease are bacterial infections, and Noguchi has found a spirochæte in yellow fever.

Disease.	*Host.*	*Reservoir*	*Transmission.*	*Carrier.*	*Infection.*
Pappataci fever.	Man		Blood sucking. -- Ingestive.	Species of phlebotomus.	Bites. -- Inoculative.
Dengue fever	Man		Blood-sucking. - - Ingestive.	*Stegomyia culex* (?)	Bites. — Inoculative.
Yellow fever.	Man.	Man in mild attacks. — Monkeys (?).	Blood-sucking. — Ingestive	*Stegomyia calopus*	Bites — Inoculative.
Rocky Mountain fever.	Man		Blood sucking - - Ingestive.	*Dermacentor venustus* - *D. andersoni.*	Bites. - (?)
Tsutsugamushi disease.	Man	*Arvicola hatanezumi* (?)	Blood-sucking. — Ingestive	*Microtrombidium akamushi.*	Bites. -- (?)
Trench fever spirochæte (?).	Man.	—	Blood-sucking. - - Ingestive.	Lice.	Bites. - - Contaminative.
Typhus	Man	--	Blood-sucking. - Ingestive.	Lice.	Bites. - (?)
Acute anterior poliomyelitis	Man.	-	Blood-sucking. — Ingestive.	*Stomoxys calcitrans*	Bites. - Inoculative.

F. CHANCE TRANSMISSION.

Numerous blood-sucking and non-blood-sucking insects may by chance obtain an organism and carry it in their proboscis, and directly infect an open sore—*e.g.*, flies and yaws, which, according to Castellani's observations and experiments, is far from a rare occurrence.

G. IMPERFECT CARRIAGE OF PARASITES.

Parasites may develop up to a certain point in the alimentary canal of insects in which they are unable to complete their life-cycle—*e.g.*, the malarial germ in many anophelines only proceeds as far as the zygote.

H. TERMS.

TERMS FOR ANIMAL PARASITES.

Definitive host	Host with sexual life of parasites.
Intermediate host	Host with asexual life of parasites.
Intermediary host	No development of parasite. Merely carriage.
Definitive reservoir	Natural supply of infection of intermediate host.
Intermediate reservoir	Natural supply of infection for definitive host.
Transmission	Passage from intermediate to definitive host.
Infection	Passage from definitive to intermediate host.
Contaminative	Abrasions or bites contaminated by fæces, etc.
Inoculative	Parasites injected by insect during biting.
Ingestive	Parasites taken into alimentary canal *per os*.

TERMS FOR BACTERIA.

Infected host	Vertebrate infected by bacterium.
Infected reservoir	Vertebrate carrier.
Protective host	Arthropod carrier without germ increasing in number.
Propagative host	Arthropod carrier with germ increasing in number.
Transmission *Infection*	As in animal parasites.

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SECTION II

VEGETAL PARASITES

CHAPTER XXXVI

SCHIZOMYCETES

Preliminary—Thallophyta—Schizomycetaceæ—Eubacteriales—Coccaceæ—Bacillaceæ—Spirillaceæ—Mycobacteriaceæ—References.

PRELIMINARY.

In our previous editions we drew attention to the numerous text-books and easily available works on bacteriology, which we decided not to consider, and we hold to that view still; but we notice that the works on this subject, as supplied to the student of medicine, are perhaps somewhat lacking in systematic classification.

To meet this need we have written the present chapter, which merely considers those bacteria which are of importance from the point of view of tropical medicine; and instead of giving descriptions of their characters, these are merely indicated by tables. Hence it should be used in conjunction with a good textbook on bacteriology, in which the details with reference to the species can be found.

It is well known that the nomenclature of the bacteria is in hopeless confusion, but an International Botanical Congress was to have been held in London in 1915, at which the medically important nomenclature of the schizomycetes would have been considered, and probably some such congress will take place after the war.

In the meanwhile the reader can find the existing rules in 'Règles Internationales de la Nomenclature Botanique,' published in Jena in 1912, and we may perhaps be permitted to remind him that names of orders should end in *-ales*, or suborders in *-ineæ*, and of families in *-aceæ*, while names of genera must be in the singular number and *written with a capital letter*, and those of subgenera and sections should resemble that of the genus.

With regard to species, it is designated by a *binomial name*, the first portion of which is the *generic name*, while the second portion is the *specific name*, and is usually begun with a small and not a capital letter, and is, further, of the nature of an adjective as a rule.

It is difficult to say what should be taken as the standard for bacterial nomenclature and classification, but it appears to us that it is useless to go further back than Migula; in any case the reader will realize that in no instance can a species be designated by more than two words—viz., the generic and the specific.

With regard to the value of bacterial species based upon biological and not upon morphological differences, the remarks which we wrote on this subject in regard to the Protozoa hold good here, and need not be repeated, while we would refer the reader again to the section on evolution in Chapter V., p. 112.

The *Regnum Vegetabile*, or vegetal kingdom, is usually divided into four great phyla or groups—viz., the Thallophyta, the Briophyta, the Pteridophyta, and the Phanerogamæ, but of all these only the first need concern us.

The Thallophyta include a great variety of plants whose vegetative body may consist of one or many cells, forming a more or less branched structure.

These plants may be defined and classified as follows:—

PHYLUM THALLOPHYTA.

Definition.—Vegetabiles with a cellular structure, which is generally little differentiated, and reproducing asexually by division and by spore formation or sexually, after conjugation, by oöspores.

Classification.—The Thallophyta may be divided into:—

- A. Thallophyta with chromatophores and often with chlorophyll—Class I., *Algæ* Roth, 1707.
- B. Thallophyta without chromatophores or chlorophyll—Class II., *Fungaceæ* Linnæus, 1737.

There can be no doubt that the Fungaceæ are descendants of the Algæ, which, because of a saprophytic or parasitic environment, have altered their food habits and have adapted themselves to new methods of nutrition, and hence no longer require chromatophores or chlorophyll, as they no longer manufacture their food with the aid of sunlight, but subsist on decaying animal or vegetal material rich in organic substances.

They may be parasitic or saprophytic, or a form which is usually parasitic may at times become a saprophyte, or *vice versa*.

With regard to their origin, the three great divisions probably differed in their evolution; thus the Schizomycetes are probably derived from the Cyanophyceæ, or Blue Green Algæ, while the Phycomycetes and the Eumycetes stand in closer relationship with the Chlorophyceæ, or Green Algæ; and it is because of this great difference in origin that the Schizomycetes are kept apart from the Fungaceæ, and are classified with the Algæ, although they are often included in the loosely used term *Fungi* (auctores).

Another less usual classification is to divide the Thallophyta into two great groups, of which the first includes the Cyanophyceæ and the Schizomycetes, while the second embraces the Myxomycetes, the Peridineæ, the Conjugatæ, the Diatomenæ, the Heterocontæ, the Chlorophyceæ, the Characeæ, the Phycomycetes, the Phæophyceæ, the Rhodophyceæ, the Eumycetes.

We will now turn to consider the Schizomycetes.

SCHIZOMYCETACEA Naegeli, 1857.

Definition.—Thallophyta without chlorophyll and as a rule without chromatophores, with the vegetative body consisting of a single cell, in which the nucleus is not present in the form typical for other thallophytes. Reproduction by fission or spore formation.

Classification.—The Schizomycetes may be divided into orders as follows:—

A. **Cells without sulphur or bacterio-purpurein—Order I., *Eubacteriales.***
B. **Cells containing sulphur—Order II., *Thiobacteriales.***
C. **Motile rods in pseudoplasmodial masses embedded in a gelatinous matrix and forming highly developed cysts—Order III., *Myxobacteriales.***

Only the first order contains forms of importance in tropical medicine.

ORDER I. EUBACTERIALES.

Definition.—Schizomycetes which contain neither sulphur nor bacterio-purpurein.

Classification.—The Eubacteriales may be divided into families as follows:—

A. Cells, in free condition, usually globular, in division somewhat elliptical—Family 1, *Coccaceæ* Zopf, 1885, *emendavit* Migula, 1900.
B. Cells, long or short, cylindrical, straight; division one direction—Family 2, *Bacillaceæ* Fischer, 1894.
C. Cells, spirally curved or representing part of a spiral; division in one direction—Family 3, *Spirillaceæ* Migula, 1900.
D. Cells, surrounded by a sheath and arranged in elongated filaments—Family 4, *Chlamydobacteriaceæ* Migula, 1900.
E. Cells short or long cylindrical or filamentous, often clavate, cuneate, or irregular, with enclosed granules. Filaments without a sheath—Family 5, *Mycobacteriaceæ* Chester, 1901.

The Chlamydobacteriaceæ do not concern us, but the other families require some consideration.

FAMILY COCCACEÆ Zopf, 1885, *emendavit* Migula, 1900.

Definition.—Eubacteriales in which the free cells are usually globular, though in division they become somewhat elliptical.

Type Genus.—*Micrococcus* Hallier, 1866, *emendavit* Cohn, 1872, and Winslow and Rogers, 1905.

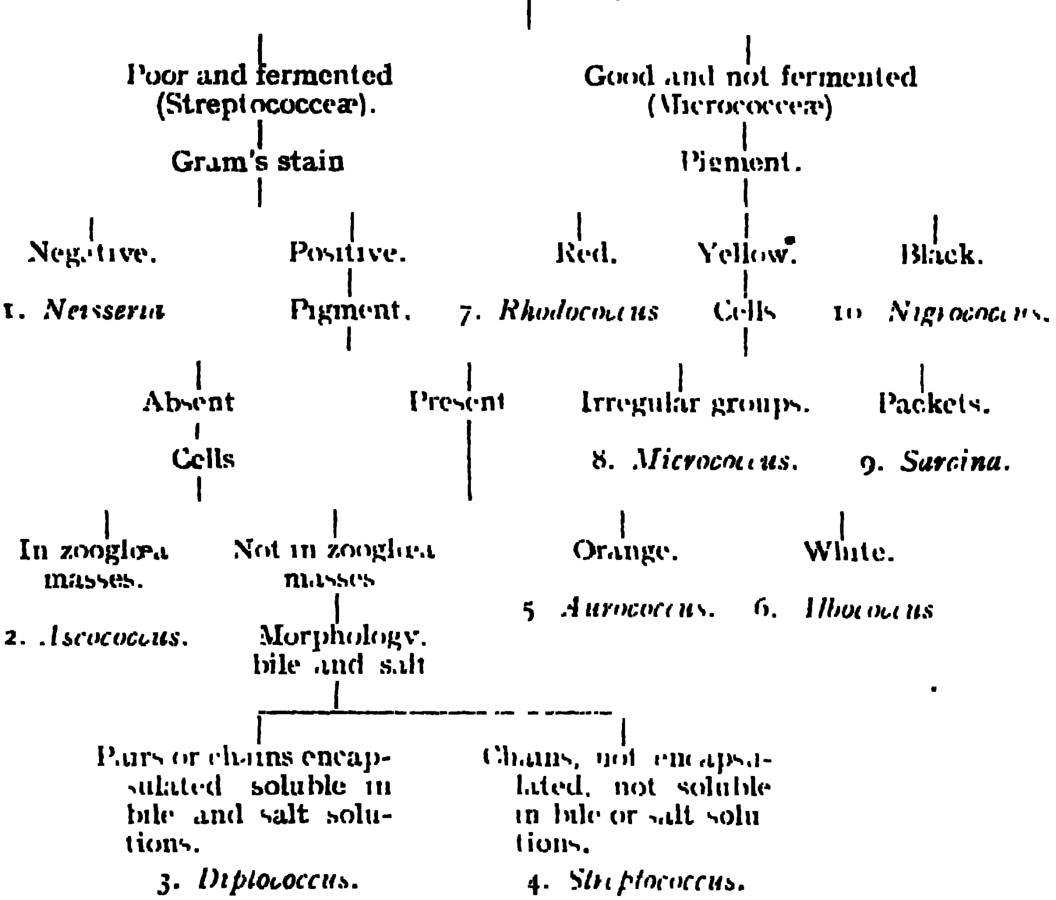
Classification.—This family, which contains forms of importance to us, may be divided into two tribes as follows:—

A. **Parasitic on plants and animals, often growing best anaerobically but frequently with difficulty and in small amount, or even not at all, on artificial media; in pairs or chains, generally but not always staining by Gram, and often producing acidity in glucose and lactose media, and when pigmented generally white or orange—Tribe I., *Streptococceæ* Trevisan, 1889, *emendavit* Winslow and Rogers, 1905.**
B. **Facultative parasites or saprophytes growing best under aerobic conditions and well on artificial media; in cell groups, packets or zoogloea masses and often Gram-negative, and when pigmented usually yellow or red—Tribe II., *Micrococceæ* Trevisan, 1889, *emendavit* Winslow and Rogers, 1905**

The two tribes may be divided into genera as set forth in the following table:—

DIAGNOSTIC TABLE OF THE FAMILY COCCACEÆ ZOPF, 1885.

Growth and Carbohydrates.



We are, however, only concerned with certain genera of the Streptococceæ, which are Neisseria, Diplococcus, Streptococcus, Aurococcus and one genus of the Micrococceæ—viz., Nigrococcus. As ***Micrococcus melitensis*** is often elongated (coccobacillus), we propose to place it under a separate heading, '*Incertæ Sedis*.'

TRIBE I. STREPTOCOCCEÆ TREVISAN, 1889, *emendavit* WINSLOW AND ROGERS, 1905.

Genus Neisseria Trevisan, 1885.

Synonyms.—*Micrococcus* Hallier, 1866, *pro parte*; *Diplococcus* Weichselbaum, 1887, *pro parte*.

Definition.—Streptococceæ growing best, and often only, aerobically, with or without pigment formation, usually present in pairs without a true capsule, and in exudates usually intracellular, and readily decolourized by Gram's method of staining.

Primary cultures grow poorly on usual laboratory media, but best on media containing glucose or blood serum. No lysis with bile. Ferment carbohydrates usually with but slight acid production.

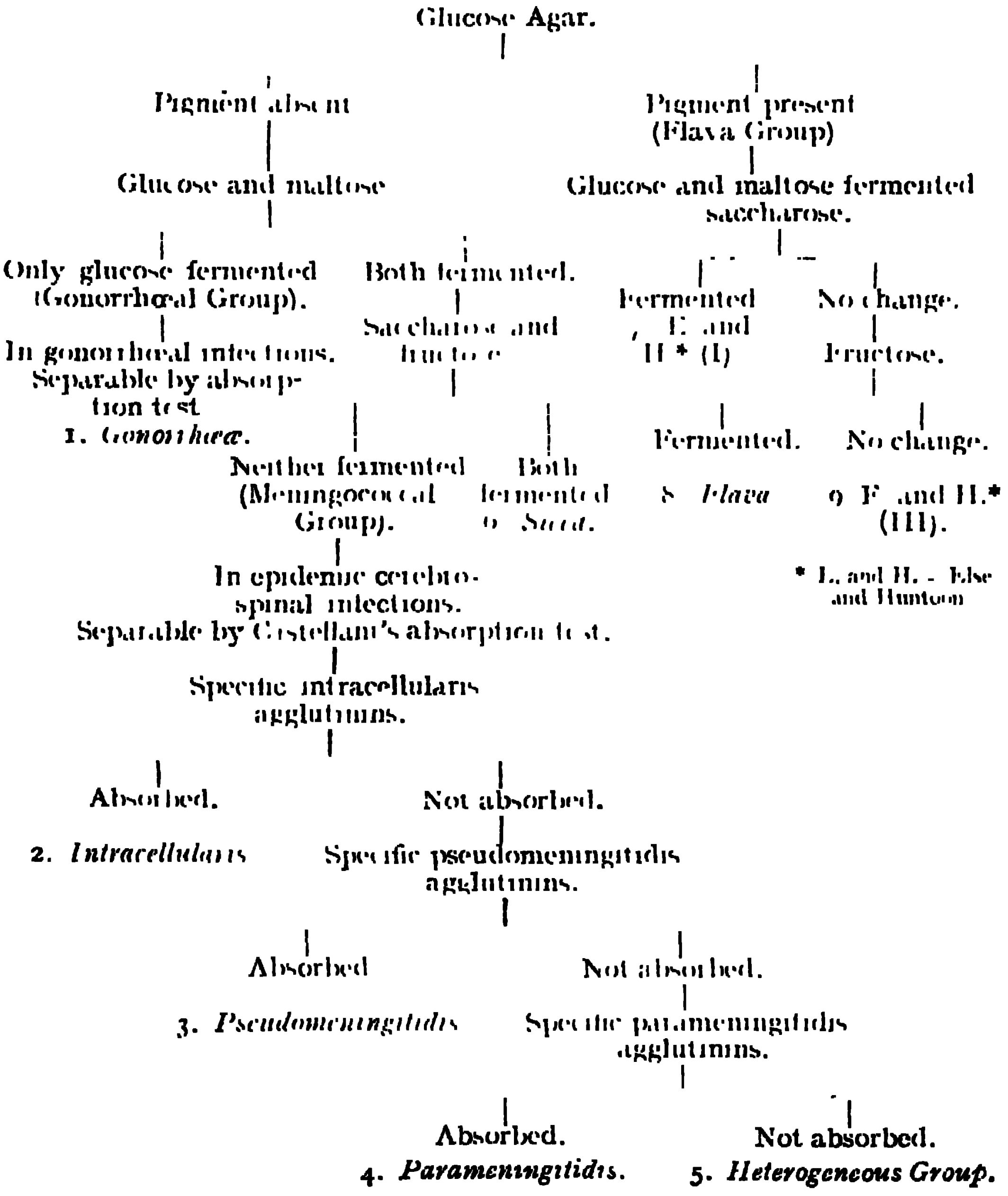
Type Species.—*Neisseria gonorrhϾ* (Bumm, 1885).

Classification.—The genus Neisseria includes the following species:

1. *N. gonorrhœæ* (Bumm, 1885), which is the cause of gonorrhœa.
2. *N. intracellularis* (Weichselbaum, 1887), which is one of the organisms causing epidemic cerebro-spinal meningitis.
3. *N. sicca* (von Lingelsheim, 1906).
4. *N. flava* (von Lingelsheim, 1906).
5. *N. pseudomeningitidis* (Elser and Huntoon, 1909).
6. *N. parameningitidis* (Dopter, 1909).
7. *A number of heterogeneous strains*, separable by the agglutination and absorption tests of specific immune sera.

These various strains and groups can be differentiated from one another by the tests set forth in the following diagnostic table:—

Diagnostic Table of the Genus Neisseria Trevisan, 1885


Glucose Agar.
Pigment absent
Glucose and maltose
Only glucose fermented (Gonorrhœal Group).
In gonorrhœal infections. Separable by absorption test
1. *Gonorrhœæ.*
Both fermented.
Saccharose and fructose
Neither fermented (Meningococcal Group).
In epidemic cerebro-spinal infections. Separable by Castellani's absorption test.
Specific intracellularis agglutinins.
Absorbed.
2. *Intracellularis*
Not absorbed.
Specific pseudomeningitidis agglutinins.
Absorbed
3. *Pseudomeningitidis*
Not absorbed.
Specific parameningitidis agglutinins.
Absorbed.
4. *Parameningitidis.*
Not absorbed.
5. *Heterogeneous Group.*
Both fermented
6. *Sicca.*
Pigment present (Flava Group)
Glucose and maltose fermented saccharose.
Fermented
7. E. and H.* (I)
No change.
Fructose.
Fermented.
8. *Flava*
No change.
9. E. and H.* (III).
* E. and H. - Elser and Huntoon

Genus Diplococcus Weichselbaum, 1886, *emendavit* Winslow and Rogers, 1905.

Definition.—Streptococceæ usually in encapsulated pairs, forming acid in glucose, lactose, saccharose, and inulin. Hæmolysis usually absent. Characteristic group serum reactions. Soluble in bile salts. Undergo autolysis in cultures and in emulsions of physiological saline.

Type Species. *Diplococcus pneumoniæ* Weichselbaum, 1886.

Remarks.—The genus contains the organisms associated with pneumonia, of which there are many strains separable by serum reactions. The genus requires further study before a definite classification can be given.

Two groups are recognized viz., those which exhibit a diplococcal form and are usually oval or lanceolate in shape (Pneumonia group), and those which are in chains and rounded in form (Mucosus group). These groups can be further differentiated by serological tests and by complement fixation.

Genus Streptococcus Rosenbach, 1884, *emendavit* Winslow and Rogers, 1905.

Definition. Streptococceæ parasitic in short or long chains or pairs, forming a large quantity of acid in fermented sugars. Hæmolysis present or absent. Without characteristic group serum reactions.

Type Species. *Streptococcus erysipelatos* Fehleisen, 1883.

Remarks.—Streptococci are frequently found in disease in the tropics, as primary agents causing the pathological changes, and as secondary or terminal infections in the course of illnesses due to other causes.

They are responsible for several types of puerperal fever, of abscesses, of septicæmias and of skin diseases.

Natural Habitat. Most streptococci are found as parasites (or saprophytes) of the nose, nasopharynx, and alimentary canal of vertebrate animals, but they can also be found in the alimentary tract of the invertebrata, and apparently also, but to a less extent, living on or in plants.

From these natural homes they may pass to air, soil, milk, or water, and so may be conveyed from one animal to another, as they are extremely resistant against heat and drought.

Thus *S. salivarius* Andrewes and Horder, 1906, lives in normal human saliva; *S. bovinus* Broadhurst, 1915, in bovine fæces, and is found in the cow-dung plastered on walls and floors of native huts; while *S. versatilis* Broadhurst, 1915, is found in equine and bovine fæces.

Researches with regard to certain human passages have shown how quickly these become infected with streptococci after birth.

It would appear that man quickly obtained his normal streptococcal flora from the animals by which he is surrounded, and that so long as they abide in their natural habitats they do no harm, but if they depart therefrom they become pathogenic.

Classification.—This is difficult, and perhaps should not be carried further than groups which may be recognized as follows:—

DIAGNOSTIC TABLE OF STREPTOCOCCAL GROUPS.

A. *Parasitic on plants.* Grow in broth but not on agar or gelatine—*I. Sphagni group.*

B. *Parasitic in animals.* Grow in broth and on agar and usually on gelatine:—

  I. Obligatory anaerobes—*II. Fœtidus group.*

  II. Aerobes, facultative anaerobes:—

    (*a*) *Pigment present—III. Sanguineus group.*

    (*b*) *Pigment absent*:—

      1. Gelatine actively liquefied—*IV. Gracilis group.*

      2. Gelatine usually not or rarely slightly liquefied, inulin usually not fermented:—

        (A) *Gas produced V. Gasogenous group.*

        (B) *Gas not produced*:—

      NON-FERMENTERS:—

        (*a*) Glucose and other sugar media not fermented—*VI. Non-fermenting group.*

      MONOSACCHARIDE FERMENTERS—*Equine Fæcal Type*:—

        (*b*) Glucose usually and other sugar media generally fermented.

        1. Glucose alone or with saccharose and salicin, but not with lactose, fermented—*VII. Equine group.*

      DISACCHARIDE FERMENTERS—*Human Fæcal Type*.—

        2. Lactose, glucose, saccharose, and salicin, but not mannitol fermented *VIII. Erysipelatos group.*

        3. Lactose, glucose, saccharose, salicin, mannitol, and sometimes raffinose fermented—*IX. Fæcalis group.*

      TRISACCHARIDE FERMENTERS—*Bovine Fæcal Type*.—

        4. Raffinose, lactose, saccharose, usually glucose sometimes salicin and rarely inulin, but not mannitol fermented—*X. Salivarius group.*

If desired the investigation can be extended, but in our experience only Groups II., VII., VIII., IX., and X. are of tropical importance, and therefore we shall limit our remarks to them:—

II. FŒTIDUS GROUP.

Definition.—Streptococcus parasitic in animals, obligatory anaerobes growing well at 37° C., and poorly or not at all at 20° C.:—

I. Fœtid gas produced; milk usually acidified and slowly clotted—*S. fœtidus.*

II. Fœtid gas not produced; milk unchanged—*S. anaerobius.*

Both these organisms have been known to cause puerperal fever.

VII. EQUINE GROUP.

Definition.—Streptococcus parasitic in animals, aerobe facultative anaerobe, without pigment, not liquefying gelatine nor producing gas, and being a monosaccharide fermenter. Glucose, salicin, and usually saccharose, are fermented, but not lactose, and with feeble or no growth at 20° C. Milk not clotted.

Classification.—By the action upon raffinose and inulin the group may be divided into two subgroups—*i.e.*, a typical, in which these are not fermented, and an atypical, in which one or both are fermented.

A. Raffinose and inulin not fermented and neutral red not reduced—*Typical subgroup.*
  I. Saccharose fermented—*S. equinus.*
  II. Saccharose not fermented—Andrewes and Horder, Winslow and Palmer, Broadhurst (A), Fuller and Armstrong.

B. Raffinose or inulin fermented or neutral red reduced—*Atypical subgroup.*

We have found *S. equinus* Andrewes and Horder, 1906, in a case of septicæmia in the tropics.

VIII. Erysipelatos Group.

Definition.—Streptococcus parasitic in animals, aerobe facultative anaerobe, without pigment; does not liquefy gelatine or produce gas; ferments lactose, glucose, saccharose, and salicin, but not mannitol or raffinose.

Classification.—The group may be differentiated into strains as follows:—

A. Colonies on agar large, white, and opaque, at the end of forty-eight hours resembling those of an albococcus; milk clotted. Hæmolytic action unknown—*S. puerperalis.*

B. Colonies on agar small, translucent, not resembling, at the end of forty-eight hours, those of an albococcus:—
  I. Hæmolysis present:—
    (*a*) Milk clotted:—
      1. Some kind of a capsule present, colonies on agar typical—*S. epidemicus.*
      2. Capsule absent, growth on agar may be absent or in the form of very fine or at times watery colonies, but typical on ascitic agar—*S. equi.*
    (*b*) Milk not clotted—
      Capsule absent, colonies on agar typical:—
      1. Found in cases of erysipelas—*S. erysipelatos.*
      2. Found in dermatitis cupoliformis—*S. tropicalis.*
  II. Hæmolysis absent:—
    (*a*) Milk clotted—*S. mitior.*
    (*b*) Milk not clotted—*S. mitis.*

S. puerperalis Furneaux-Jordan and Mackay, 1912, was found in twenty-one cases of puerperal fever in England.

S. equi Schutz, 1888, is the same as *S. coryzæ contagiosæ equorum* Eisenberg, and as *S. equi* Capelletti-Vivaldi, 1899, and *S. capellettii* Chester, 1901, and causes strangles, etc., or adenitis in horses.

S. erysipelatos Fehleisen, 1883, is the type species of the genus Streptococcus. It is the same as *S. pyogenes* Rosenbach, 1884, and *S. puerperalis* Arloing, 1884, and it may be the same as *S. puerperalis* Furneaux-Jordan and Mackay, though there are differences.

S. tropicalis Castellani, 1914, is the cause of *Dermatitis cupoliformis*, which is a type of tropical ecthyma (see p. 2034).

It may be that *S. mitior* Schottmüller, 1903, is the same as *S. mitis* Andrewes and Horder, 1906. It has been found in cases of puerperal fever.

IX. FÆCALIS GROUP.

Definition.—Streptococcus parasitic in man, facultative anaerobe, growing in broth and upon agar and blood serum without the formation of pigment, and well upon gelatine at 22° C., without producing liquefaction; fermenting glucose, saccharose, lactose, mannitol, and salicin; sometimes raffinose, but typically not inulin, and generally, but not always, clotting milk; variable as regards neutral red reduction and sulphuretted hydrogen formation, and usually producing relatively large amount of acidity in glucose media tested quantitatively.

Remarks. This is an important pathogenic group in the tropics, being found in all sorts of conditions. Its various strains may be differentiated as follows:

A. Glucose, saccharose, lactose, salicin, and mannitol fermented—Typical subgroup
  I. Raffinose not fermented *S. fæcalis* Andrewes and Horder, 1906.
  II Raffinose fermented *S. versatilis* Broadhurst, 1915.
B Suppression of one of the characters of the typical subgroup or with the addition of the fermentation of inulin Atypical subgroup.
  I Raffinose not fermented -Variants of *S. fæcalis*
  II. Raffinose fermented Variants of *S. versatilis*.

X. SALIVARIUS GROUP.

Definition. Streptococcus parasitic in animals, facultative anaerobe, growing in broth and on agar without pigment or gas formation; with slight or no growth at 22° C. in gelatine which is not liquefied, and capable of fermenting glucose, saccharose, lactose, and raffinose; may ferment inulin, but not mannitol, and generally capable of clotting milk. Habitat, human saliva, human fæces, bovine and equine fæces.

Classification. This group can be divided into a typical subgroup, and an atypical subgroup containing varieties of the typical group, in which there is suppression of some important character, which is not inulin fermentation.

TYPICAL SUBGROUP.- Glucose, saccharose, lactose, and raffinose, and at times inulin fermented.

A. Salicin not fermented: -
  I. Hæmolysis marked- -*S. anginosus*.
  II. Hæmolysis absent- *S. salivarius*.
B. Salicin fermented.
  I. Hæmolysis marked *S. actuosus*.
  II. Hæmolysis absent - *S. bovinus*.

ATYPICAL SUBGROUP.- Contains varieties of *S. anginosus*, *S. salivarius*, *S. actuosus*, and *S. bovinus*, in which there is suppression of some character but as these suppressions are generally only temporary it is not necessary to specially characterize them.

Remarks.—These streptococci are frequently found in sore throat and other infections in the tropics.

Shottmüller's Classification of the Genus Streptococcus.—This is very simple, and is based on the characters of colonies on blood-agar plates.

1. Colonies surrounded by a clear zone of hæmolysis—*S. hæmolyticus* (=*S. pyogenes* = *S. erysipelatos* = *S. erysipelatosus*).
2. Colonies not surrounded by a clear zone of hæmolysis; of a peculiar greenish colour—*S. viridans* (= *S. mitior*).
3. Colonies whitish, slimy, somewhat adherent to the medium (cocci capsulated)—*S. mucosus*.

Genus Aurococcus Winslow and Rogers, 1905.

Definition.—Streptococceæ parasitic, producing pigment, and in irregular groups or in non-capsulated groups of four, or in pairs, but never in zooglœa masses. Growth good. Sugars fermented with formation of a moderate amount of acid, but no gas. May or may not reduce nitrates and liquefy gelatine.

Type Species.—*Aurococcus aureus* (Rosenbach, 1884).

Classification.—Winslow and Rogers, after a long discussion of synonyms, have recognized only three types, which may be differentiated as follows:—

A. Nitrates not reduced:—
   (1) Gelatine strongly liquefied—*Aurococcus aureus* (Rosenbach, 1884).
   (2) Gelatine not liquefied—*Aurococcus aurantiacus* (Cohn, 1872).
B. Nitrates reduced:—
   (3) Gelatine may or may not be liquefied—*Aurococcus mollis* (Dyar 1895).

Remarks.—This group is of great interest in the tropics; as its members are the cause of boils and pyosis in various parts—*e.g.*, *Aurococcus mollis* causes Nile boils and pyosis Corletti.

With regard to 'pyosis Mansoni,' Castellani in Ceylon showed it to be caused by a species of aurococcus, which Clegg and Wherry in 1906 called *Micrococcus pemphigicontagiosi*, which seems to be the same as that named *Micrococcus pemphigineonatorum* by Almquist in 1901, and both may be *Aurococcus mollis*. *Aurococcus tropicus* Chalmers and O'Farrell, 1913, found in Castellani's 'pyosis tropica,' appears to be different, as its vaccine was without effect on a case of Nile Boils, but, unfortunately, it was not possible to test it on nitrates and gelatine.

TRIBE II. MICROCOCCEÆ Trevisan, 1880, *emendavit* Winslow and Rogers, 1905.

Genus Rhodococcus Winslow and Rogers, 1905.

Definition.—Micrococceæ, usually saprophytes, rarely parasites, with cells in groups or regular packets. Generally more or less decolourized by Gram. Growth on agar abundant, with the formation of red pigment. Very slight fermentative action. Gelatine rarely liquefied. Generally reduce nitrates to nitrites.

Type.—*Rhodococcus roseus* (Flügge, 1886), *emendavit* Dyar, 1895.

Remarks.—Winslow and Rogers recognize, in addition to the type, *R. fulvus* Cohn, 1875, and they leave the rest in groups to await further investigation.

We add *Rhodococcus castellanii*, discovered by Castellani and which Chalmers and O'Farrell in 1913 named and more fully described. It is found in *Trichomycosis rubra*, and we differentiate the three species as follows:—

A. Does not ferment glucose—*Castellanii*.
B. Produces slight acidity in glucose:—
  I. Nitrates reduced to nitrite.—*Roseus*.
  II. Nitrates not reduced—*Fulvus*.

Genus Nigrococcus Castellani and Chalmers, 1918.

Definition.—Micrococceæ saprophytic, rarely parasitic, producing black or bluish-black pigment.

Type.—*Nigrococcus nigrescens* (Castellani, 1911).

Classification.—The type is found in *Trichomycosis nigra*, along with *Cohnistreptothrix tenuis* Castellani; other forms are *N. fuscus* Adametz (1888), in water; *N. cyaneus* Schroeter, 1870, in air and water; and they may be differentiated as follows:—

A. Gelatine liquefied—*Fuscus*
B. Gelatine not liquefied:—
  I. Pigment indigo blue—*Cyaneus*.
  II. Pigment black—*Nigrescens*.

INCERTÆ SEDIS.

The so-called *Micrococcus melitensis* Bruce, 1886, which is the causal agent in Mediterranean, Malta, or undulant fever, is difficult to classify, because elongated forms are seen at times in cultures, and because it seems to have no affinity with the Gram-negative cocci; but, on the other hand, is very like the typhoid-colon group of organisms in certain respects. It does not ferment sugars, nor produce indol; does not liquefy gelatine, nor show polar-staining; while milk becomes alkaline.

FAMILY BACILLACEÆ Fischer, 1894.

Definition.—Eubacteriales with cells long or short, flagellate or non-flagellate, sporogenous or non sporogenous, but always cylindrical and straight. They divide in one direction only.

Type Genus.—*Bacillus* Cohn, 1872.

Remarks.—The enormous numbers of species and varieties gathered together under the names *Bacterium* and *Bacillus* form such an unwieldy mass, that we have endeavoured to simplify matters by formulating a number of tribes with genera.

Classification.—The family 'Bacillaceæ' may be classified into tribes as follows:—

Growth in ordinary laboratory media:—
A. Entirely or almost entirely absent—Tribe 1, *Nitrobactereæ*.
B. Poor, Gram-negative, grow best on blood media—Tribe 2, *Hæmophileæ*.
C. Extremely slow and scanty growth on ordinary and blood media—Tribe 3, *Graciloideæ*.
D. Growth good:—
  I. Endospores present—Tribe 4, *Bacilleæ*.
  II. Endospores absent:—

- (*a*) Fluorescent or chromogenic—Tribe 5, *Bacteridieæ*.
- (*b*) Neither fluorescent nor chromogenic:—
  - 1. Obligatory anaerobes—Tribe 6, *Bacteroideæ*.
  - 2. Aerobes often facultative anaerobes:—
    - (1) Gelatine liquefiers—Tribe 7, *Proteæ*.
    - (2) Gelatine non-liquefiers:—
      - (i.) Without capsules:—
        - (A) With polar staining—Tribe 8, *Pasteurelleæ*
        - (B) Without polar staining—Tribe 9, *Eberthieæ*
      - (ii.) With capsules—Tribe 10, *Encapsulateæ*.

THE TRIBES.

This is obviously not the place to enter into a prolonged discussion with regard to these tribes, but in order that there may be no doubt as to our meaning, we give the following table showing the type genus and type species which we propose for each tribe:—

Tribe.	*Type Genus.*	*Type Species.*	*Original Name of Type Species.*
Nitrobacterieæ.	*Nitrobacterium* Castellani and Chalmers, 1918.	*Nitrobacterium nitrobacter* (Winogradsky, 1892).	*Nitrobacter* Winogradsky, 1892.
Hæmophileæ.	*Hæmophilus* Castellani and Chalmers, 1918.	*Hæmophilus influenzæ* (Pfeiffer, 1892).	Bacillus of influenza, Pfeiffer, 1892.
Graciloideæ.	*Graciloides* Castellani.	*Graciloides albofaciens.*	*Bacillus albofaciens* Castellani 1904.
Bacilleæ.	*Bacillus* Cohn, 1872, *pro parte.*	*Bacillus subtilis* (Ehrenberg, 1833).	*Vibrio subtilis* Ehrenberg, 1833.
Bacteridieæ.	*Bacteridium* Schroeter, 1872.	*Bacteridium prodigiosum* (Ehrenberg, 1838).	*Monas prodigiosa* Ehrenberg, 1838.
Bacteroideæ.	*Bacteroides* Castellani and Chalmers, 1918.	*Bacteroides fragilis* Veillon and Zuber.	*Bacillus fragilis* Veillon and Zuber.
Proteæ.	*Proteus* Hauser, 1885.	*Proteus vulgaris* Hauser, 1885.	*Proteus vulgaris* Hauser, 1885.
Pasteurelleæ.	*Pasteurella* Toni and Trevisan, 1889.	*Pasteurella gallinæ* Toni and Trevisan, 1889.	Microbe du choléra des Poles, Pasteur, 1880.
Ebertheæ.	*Eberthus* Castellani and Chalmers, 1918.	*Eberthus typhosus* Zopf, 1885.	Bacillus of Eberth auctores.
Encapsulateæ.	*Encapsulatus* Castellani and Chalmers, 1918.	*Encapsulatus pneumoniæ* (Friedlaender, 1883).	Pneumococcus. The micrococcus of pneumonia. Friedlaender, 1883.

Of all these, the most important from our present point of view is *Eberthea*, which contains many intestinal organisms.

TRIBE ENCAPSULATEÆ CASTELLANI AND CHALMERS, 1918.

Definition.—Bacillaceæ growing well on ordinary laboratory media, without endospores; neither fluorescent nor chromogenic aerobes, not liquefying gelatine, possessing capsules in animal tissues.

Type Genus.—*Encapsulatus* Castellani and Chalmers, 1918.

Genus Encapsulatus Castellani and Chalmers, 1918.

Definition.—Encapsulateæ with the tribal characters.

Type Species.—*Encapsulatus pneumoniæ* (Friedlaender, 1883).

Remarks.—This genus is the only one at present in the tribe, and it includes the old group of encapsulated bacilli which have been reviewed by Fricke in 1896, Clairmont in 1902, Perkins in 1904, Abel and Hallwachs in 1912, and Fitzgerald in 1914.

The species are mostly short, non-motile, Gram-negative, encapsulated pleomorphic organisms, which ferment glucose and lactose; but as regards the latter sugar, they may give rise to acid only, though more usually they form acid and gas.

Classification.—The various species of this genus may be recognized as follows:—

A. Glucose completely fermented with the formation of acid and gas; lactose fermented partially with the formation of acid, but no gas. Milk clotted—*Pneumoniæ*.

B. Glucose and lactose completely fermented with the formation of acid and gas. Milk clotted:—

  I. Inosite not fermented—*Acidi lactici*.

  II. Inosite fermented with the formation of acid and gas—*Lactis aerogenes*.

TRIBE EBERTHEÆ CASTELLANI AND CHALMERS, 1918.

Definition.—Bacillaceæ growing well on ordinary laboratory media; not forming endospores, aerobes, and often facultative anaerobes; without fluorescence, pigment formation, or gelatine liquefaction; without polar staining; Gram-negative, without a capsule.

Type Genus.—*Eberthus* Castellani and Chalmers, 1918.

Classification.—The tribe may be divided into genera, which may be recognized as follows:—

A. Glucose and lactose either not at all or only partially fermented with the production of acid, but no gas:—

  I. Milk not clotted.

    (*a*) Glucose and lactose not fermented—Genus 1, *Alcaligenes* Castellani and Chalmers, 1918.

    (*b*) Glucose partially fermented with the production of acid and no gas, lactose not fermented:—

      1. Motile—Genus 2, *Eberthus* Castellani and Chalmers, 1918.

      2. Non-motile—Genus 3, *Shigella* Castellani and Chalmers, 1918.

    (*c*) Lactose and glucose partially fermented with the production of acid, but no gas—Genus 4, *Dysenteroides* Castellani and Chalmers, 1918.

II. **Milk clotted :—**

Glucose partially fermented with the production of acid, but no gas; lactose not fermented (no gas in any sugar)—Genus 5. *Lankoides* Castellani and Chalmers, 1918.

B. Glucose completely fermented with the production of acid and gas; lactose not fermented:—

I. Milk not clotted—Genus 6, *Salmonella* Lignières, *emendavit* Castellani and Chalmers, 1918.

II. Milk clotted—Genus 7, *Balkanella* Castellani and Chalmers, 1918.

C. Glucose completely fermented with the production of acid and gas; lactose partially fermented with the production of acid and no gas:—

I. Milk not clotted—Genus 8, *Wesenbergus* Castellani and Chalmers, 1918.

D. Glucose and lactose completely fermented with the production of acid and gas:—

I. Milk not clotted—Genus 9, *Enteroides* Castellani and Chalmers, 1918.

II. Milk clotted—Genus 10, *Escherichia* Castellani and Chalmers, 1918.

In order to be quite definite, we give the following table showing the type species for each genus:—

Genus.	*Type Species.*	*Original Name of the Type Species.*
Alcaligenes.	*Alcaligenes faecalis* (Petruschky, 1896).	*Bacillus faecalis alkaligenes* Petruschky, 1896.
Eberthus.	*Eberthus typhosus* (Zopf, 1885).	Bacillus of Eberth auctores.
Shigella.	*Shigella dysenteriae* (Kruse, 1899).	*Bacillus dysenteriae* Kruse, 1899.
Lankoides.	*Lankoides pyogenes* (Passet, 1902).	*Bacillus pyogenes foetidus* Passet, 1902.
Dysenteroides.	*Dysenteroides metadysentericus* (Castellani, 1917).	*Bacillus metadysentericus* Castellani, 1904.
Salmonella.	*Salmonella paratyphi* (Schottmuller, 1902).	*Bacillus paratyphosus A* Schottmuller, 1902.
Balkanella.	*Balkanella coagulans* (Castellani, 1916).	*Bacillus coagulans* Castellani, 1916.
Wesenbergus.	*Wesenbergus wesenbergi* (Castellani, 1913).	*Bacillus wesenberg* Castellani, 1913.
Enteroides.	*Enteroides entericus* (Castellani, 1907).	*Bacillus entericus* Castellani, 1907.
Escherichia.	*Escherichia coli* (Escherich, 1886).	*Bacterium coli commune* Escherich, 1886.

Genus Alcaligenes Castellani and Chalmers, 1918.

Definition.—Ebertheæ which do not ferment glucose or lactose, and are characterized by their general lack of fermentative power and by actually increasing the alkalinity of the media. Milk is not clotted, and is rendered alkaline.

Type.—*Alcaligenes fæcalis* (Petruschky, 1896), *emendavit* Castellani and Chalmers, 1918.

Here also comes *Alcaligenes vivax* (Archibald, 1918), which was obtained from the blood of a case of enteroidea in the Anglo-Egyptian Sudan, produced acidity in galactose and mannitol and was characterized by its marked motility.

Classification.—These various organisms can be differentiated as follows:—

A. Non-motile—*Metalkaligenes.*
B. Motile:—
  I. No acidity in any sugar—*Fæcalis.*
  II. Acidity in mannitol—*Vivax*

Genus Eberthus Castellani and Chalmers, 1918.

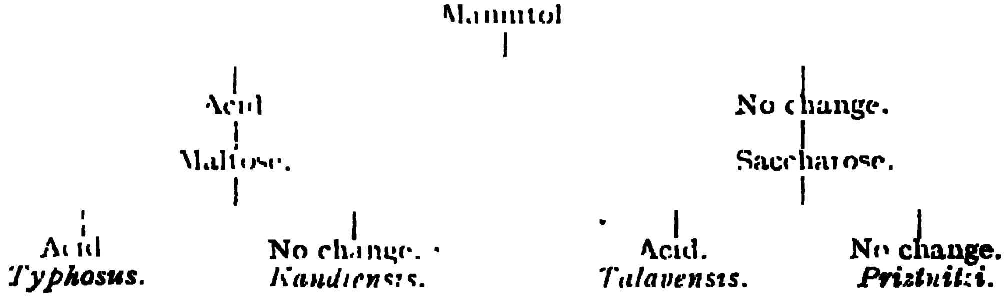
Definition.—Bacillaceæ motile, partially fermenting glucose with the production of acid and no gas. Lactose not fermented. Milk not clotted.

Type Species.—*Eberthus typhosus* (Zopf, 1885).

Remarks.—This genus has as its type species the organism which causes that variety of enteric fever which is called typhoid fever, as well as a number of species which are the causal agents of forms of enteroidea.

Classification.—The genus contains the following species, in addition to the type: *E. kandiensis* Castellani, *E. talavensis* Castellani, *E. priztnitzi* Castellani.

They may be differentiated biochemically as follows, though they can be distinguished in addition, by their serological reactions:—



Genus Shigella Castellani and Chalmers, 1918.

Definition.—Ebertheæ non-motile, partially fermenting glucose with the production of acid, but no gas; lactose not fermented. Milk not clotted.

Types.—*Shigella dysenteriæ* (Kruse, 1899).

Remarks.—This genus includes a number of forms which are associated with bacillary dysentery, but in going through those which have been described, we have rejected all with very imperfect descriptions which will never permit of their recognition.

Classification.—The species belonging to this genus may be divided for purposes of recognition into:—

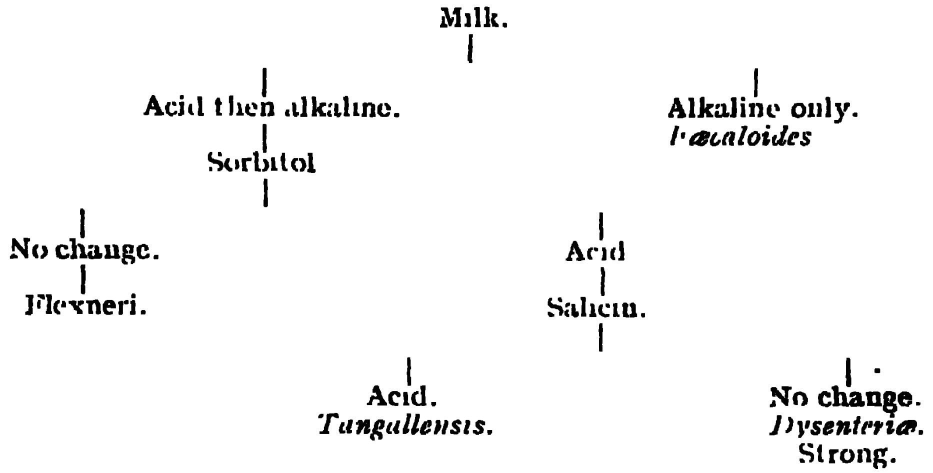
A. *Mannitol fermented*—Subgenus *Flexnerella* (Flexner group *sensu lato*).
  I. Maltose fermented—*Flexner group*.
  II. Maltose not fermented—*Pseudodysentery group*.
B. *Mannitol not fermented*—Subgenus *Shigella*

The forms belonging to these divisions and sections may be recognized by the following tables:—

Subgenus Flexnerella Castellani and Chalmers, 1918.

(Mannitol Partial Fermenters.)

Flexner Group: Maltose Partial Fermenters.

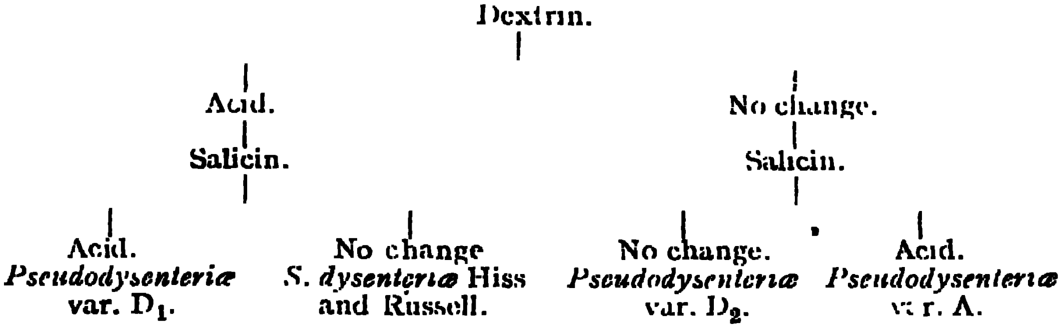


- Milk.
  - Acid then alkaline.
    - Sorbitol
      - No change.
        - Flexneri.
      - Acid
        - Salicin.
          - Acid. *Tangallensis.*
          - No change. *Dysenteriæ.* Strong.
  - Alkaline only. *Fæcaloides*

Subgenus Flexnerella Castellani and Chalmers, 1918.

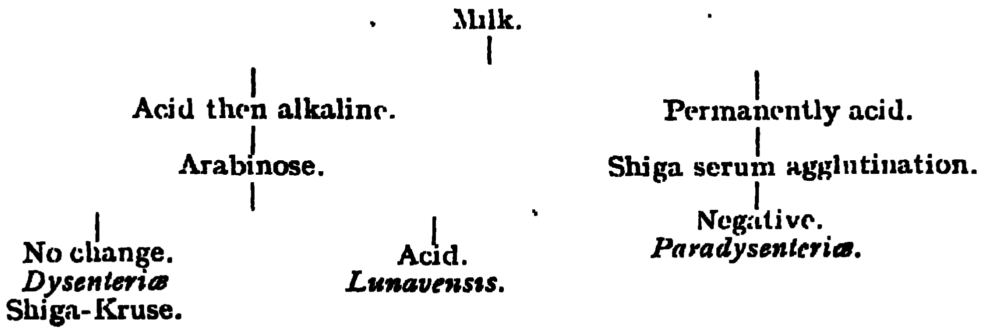
(Mannitol Partial Fermenters.)

Pseudodysentery Group: Maltose Non-Fermenters.



- Dextrin.
  - Acid.
    - Salicin.
      - Acid. *Pseudodysenteriæ* var. D_1.
      - No change *S. dysenteriæ* Hiss and Russell.
  - No change.
    - Salicin.
      - No change. *Pseudodysenteriæ* var. D_2.
      - Acid. *Pseudodysenteriæ* var. A.

Shiga-Kruse Division: Mannitol not Fermented.



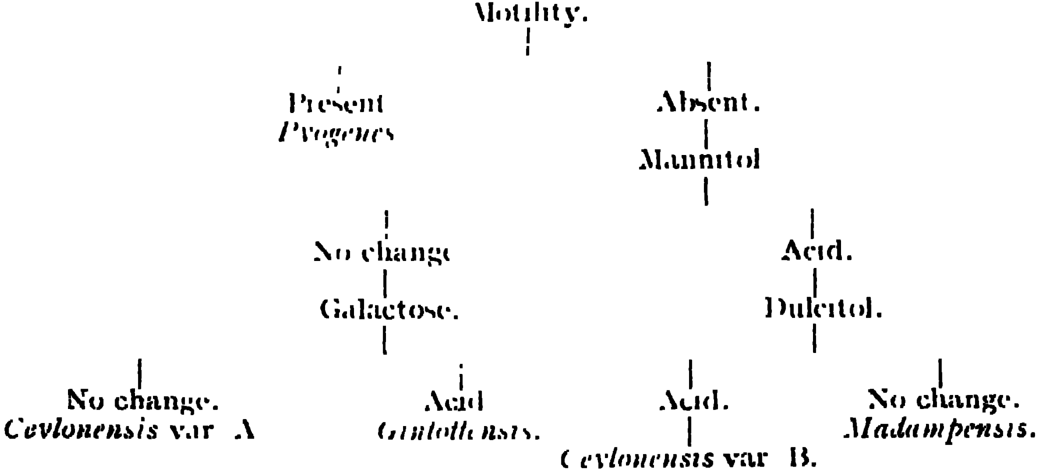
- Milk.
  - Acid then alkaline.
    - Arabinose.
      - No change. *Dysenteriæ* Shiga-Kruse.
      - Acid. *Lunavensis.*
  - Permanently acid.
    - Shiga serum agglutination.
      - Negative. *Paradysenteriæ.*

Genus Lankoides Castellani and Chalmers, 1918.

Definition.—Ebertheæ fermenting glucose partially with the production of acid, but no gas; lactose not fermented or only partially, without gas production. Milk clotted.

Type Species.—*Lankoides pyogenes* (Passet, 1902).

Classification.—The species classified in this genus may be recognized as follows:—

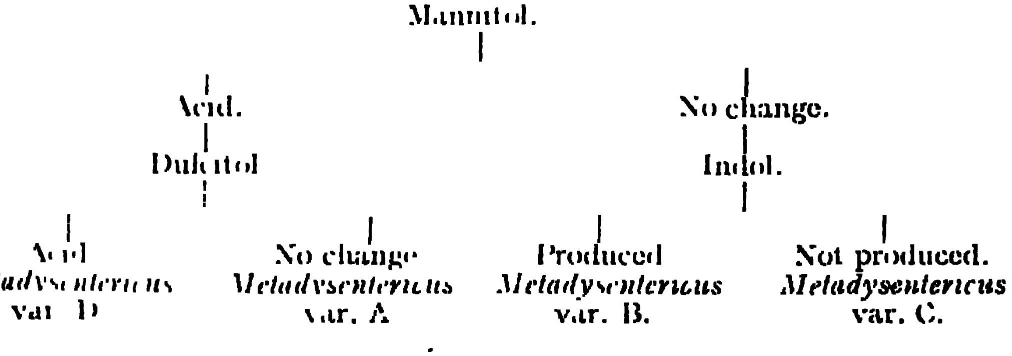


Genus Dysenteroides Castellani and Chalmers, 1918.

Definition.—Ebertheæ fermenting glucose and lactose partially, with the production of acid, but no gas. Milk not clotted.

Type Species.—*Dysenteroides metadysentericus* (Castellani, 1917).

Remarks.—This genus contains the organisms of the Metadysenteric group, which may be differentiated as follows:—



Genus Salmonella Lignières, *emendavit* Castellani and Chalmers, 1918.

Definition.—Ebertheæ which completely ferment glucose, but do not ferment lactose, and partially or completely ferment mannitol, in addition to other carbohydrates. Milk not clotted.

Type Species.—*Salmonella paratyphi* (Schottmüller, 1902).

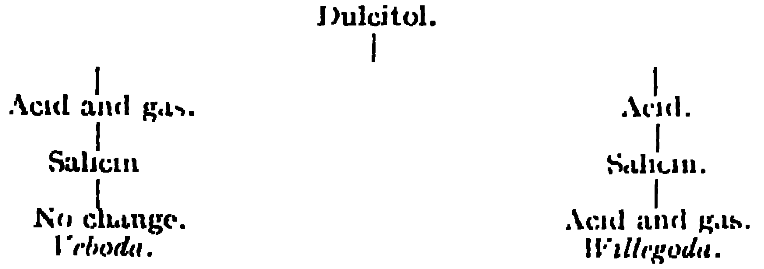
Remarks.—This genus contains a large number of species, which may be divided into groups as follows:—

A. Mannitol not fermented—*Morgan group*.
B. Mannitol partially fermented with the production of acid, but no gas —*Veboda group*.
C. Mannitol completely fermented with the production of acid and gas—*Paratyphoid-Asiaticus group*.

The Morgan group only contains *Salmonella morgani*, which is the same as Morgan I. of older nomenclature.

VEBODA GROUP.

This group contains two organisms viz., *Salmonella veboda* Castellani, 1909, and *S. willegoda* Castellani, 1911. They may be distinguished as follows:—



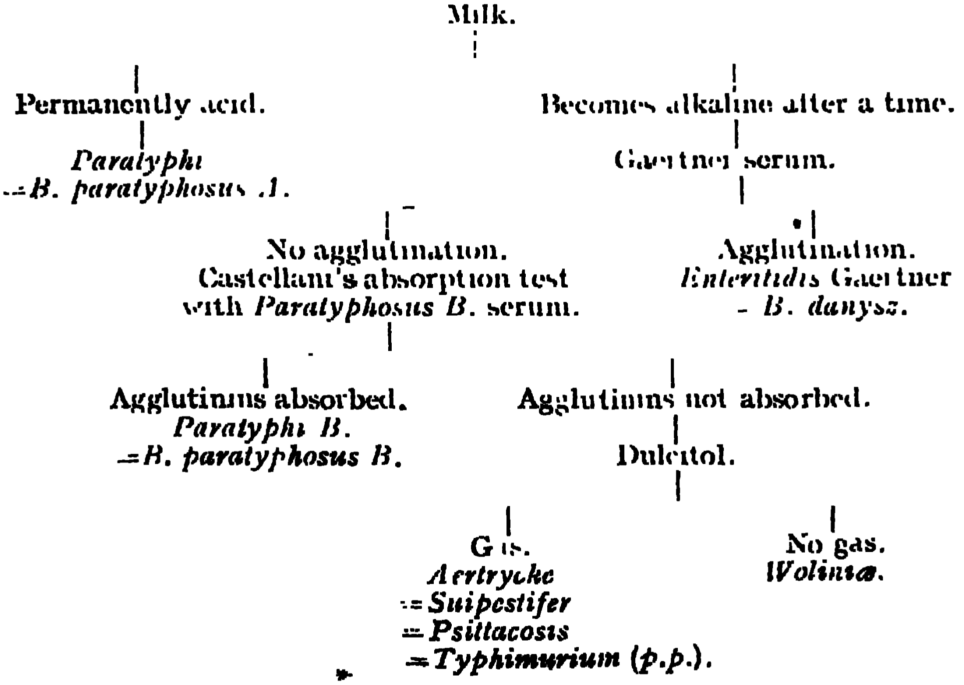
PARATYPHOID-ASIATICUS GROUP.

This group contains a number of forms, some of which are of tropical importance. It may be classified as follows:—

A. Indol not produced -*Paratyphoid division*.
B. Indol produced *Asiaticus division*.

The first subgroup contains *S. paratyphi A*, *S. paratyphi B*, *S. aertrycke*, *S. wolinia*. The term *S. paratyphi C* has been applied by various authors to indicate different germs, one of which is identical serologically with *S. enteritidis*.

PARATYPHOID DIVISION: INDOL NON-PRODUCERS.



ASIATICUS DIVISION: INDOL FORMERS.

Saccharose.
- No change.
  - Voges-Proskauer.
    - Positive. *Archibaldi* Castellani and Chalmers.
    - Negative
      - *Carolina* Castellani
- Acid and gas.
  - Salicin.
    - Acid and gas. *Pseudo-asiatica* Castellani.
    - No change.
      - Motility.
        - Present. *Asiatica* var. *mobilis* Castellani.
        - Absent. *Asiatica* Castellani.

Genus Balkanella Castellani and Chalmers, 1918.

Definition.—Eberthcæ which ferment glucose completely with the production of acid and gas; lactose not fermented. Milk clotted.

Type Species. *Balkanella coagulans* Castellani, 1916.

Remarks.—There are two species—viz., the type and *B. carolinoides* Castellani—which may be separated as follows:—

Saccharose.
- No change. *Coagulans.*
- Acid and gas. *Carolinoides*

Genus Wesenbergus Castellani and Chalmers, 1918.

Definition.—Eberthcæ which ferment glucose completely and lactose partially, producing acid, but no gas. Milk not clotted

Type Species.—*Wesenbergus wesenbergi* Castellani, 1913.

Remarks.—The type described by Castellani is motile, and produces acidity in litmus milk. It forms acid and gas in glucose and saccharose, but only acid in lactose, mannitol, and dulcitol. It is an indol producer.

To the same group belongs *Wesenbergus giumai* Castellani, which is non motile.

Archibald in the Anglo-Egyptian Sudan obtained an organism of this type from the blood of a case of enteroidea in Khartoum on the fifth day of the illness. It was motile, formed acid and gas in glucose, galactose, and rhamnose (iso-dulcite), dextrin, starch, mannitol, and sorbitol, but only acid in lactose, levulose, maltose, and dulcitol, while it failed to ferment saccharose, raffinose, inulin, salicin, glycerol, erythrol, or adonitol. It did not produce indol, gave a negative Voges-Proskauer reaction, but reduced nitrates and neutral red. Specific serum reactions separated it from *Eberthus typhosus, Salmonella paratyphi, S. paratyphosa*, and *S. gaertneri*, and it was well agglutinated by the patient's serum during convalescence. We name it *Wesenbergus fermentosus*.

Readers interested in this group will find some strains described by Alexander in 1914 in the supplement to the Annual Report of the Local Government Board, which may well be classified here.

The named species may be separated as follows:—

A. *Indol produced* :—
  I. Dulcitol fermented—*Wesenbergi.*
  II. Dulcitol not fermented—*Giumai.*
B. *Indol not produced—Fermentosus.*

Genus **Enteroides** Castellani and Chalmers, 1918.

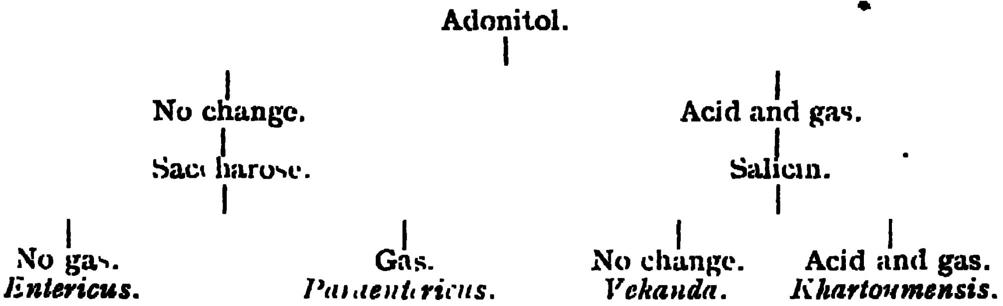
Definition.—Eberthеæ which ferment glucose and lactose completely with the production of acid and gas. Milk not clotted.

Type Species.—*Enteroides entericus* (Castellani, 1907).

Remarks.—Castellani isolated two organisms from cases of enteroidea and appendicitis in Ceylon—viz., the type and *E. paraentericus*—and later found another, *E. vekanda*, in the Balkans.

Chalmers and Macdonald obtained *E. khartoumensis* from cases of enteroidea in the Anglo-Egyptian Sudan.

Classification.—The various species of the genus may be recognized as follows:—



Genus **Escherichia** Castellani and Chalmers, 1918.

Definition.—Eberthеæ which ferment glucose and lactose completely; milk clotted.

Type Species.—*Escherichia coli* (Escherich, 1886).

Classification.—The number of species gathered together under this genus, even after the rejection of those so imperfectly described that they cannot be classified, is so large that they require to be divided into groups and sections as follows:—

A. Indol produced—*Smith's indol division.*
  I. Saccharolytic—*Communior section.*
  II. Non-saccharolytic—*Communis section.*
B. Indol not produced—*Smith's non-indol division.*

We recognize the mistake which has been made with regard to the organism called *Coscoroba*, which, as originally described, belongs to the genus *Pasteurella*—*i.e.*, among the hæmorrhagic septicæmias, being a cause of disease and death in swans. By some mistake, years ago quite a different organism belonging to the Colon group received this name. In order to prevent confusion, we propose to call the Colon type of Coscoroba by the name *Escherichia pseudocoscoroba* Castellani and Chalmers, 1918. The species may be recognized as follows:—

SMITH'S INDOL-PRODUCING DIVISION.

Durham's Saccharolytic Communior Section.

Dulcitol.

- Acid and gas.
  - Adonitol.
    - Acid and gas
      - Motility.
        - Absent. *Oxytocus.*
        - Present *Metacoli*
    - No change.
      - Motility.
        - Present
          - Pseudocoli serum
            - Agglutination. *Pseudocoli*
            - Non-agglutination (late fermentation of saccharose). *Coliformis.*
        - Absent
          - *Neapolitanus.*
- No change.
  - Motility.
    - Present.
      - Inosite.
        - Acid and gas. *Pseudocoloidella*
        - No change. *Pseudocoloides.*
    - Absent. *Pseudocoscoroba.*

SMITH'S INDOL-PRODUCING DIVISION.

Durham's Non Saccharolytic Communis Section.

Dulcitol.

- Acid and gas
  - Salicin.
    - Acid. *Cavicida.*
    - Acid and gas
      - Motility.
        - Absent.
          - Inosite.
            - No change. *Coloidella.*
            - Acid and gas. *Coloides.*
        - Present. *Coli.*
    - No change. *Metacoloides.*
- No change
  - Motility.
    - Absent
      - Maltose.
        - Acid and gas. *Colitropicalis.*
        - No change. *Vesiculosus*
    - Present.
      - Maltose.
        - Acid and gas. *Paragrünthali.*
        - No change. *Grünthali.*

SMITH'S NON-INDOL-PRODUCING DIVISION.

This division contains only one organism, *Escherichia coli mutabilis* Massini, insufficiently described.

TRIBE PASTEURELLEÆ CASTELLANI AND CHALMERS, 1918.

Definition.—Bacillaceæ with good growth on ordinary media, without endospores, aerobic, without fluorescence or pigment formation, unable to liquefy gelatine, and Gram-negative, but with polar staining.

Type Genus.—*Pasteurella* Toni and Trevisan, 1889.

Genus Pasteurella Toni and Trevisan, 1889.

Definition.—Pasteurelleæ with the tribal characters.

Type Species.—*Pasteurella cholerægallinarum* (Zopf, 1885).

Remarks.—This genus was formed by Toni and Trevisan, and includes all the organisms of the hæmorrhagic septicæmic group, and especially plague. It is to be noted that *Pasteurella coscoroba* (Trétrop, 1900) belongs to this genus, as well as *Pasteurella pestis* Kitasato and Yersin, 1894. The two great divisions, the animal and the human diseases, may be separated as follows:—

A. No growth on MacConkey's medium containing glucose, levulose galactose, or mannitol—*Animal group*.
B. Growth on MacConkey's medium containing the above-mentioned sugars—*Plague*.

This test must, however, be confirmed by animal inoculations.

TRIBE PROTEÆ CASTELLANI AND CHALMERS, 1918.

Definition.—Bacillaceæ growing well on ordinary laboratory media, not forming endospores, aerobic, without fluorescence or pigment formation, but liquefying gelatine.

Type Species.—*Proteus vulgaris* Hauser, 1885.

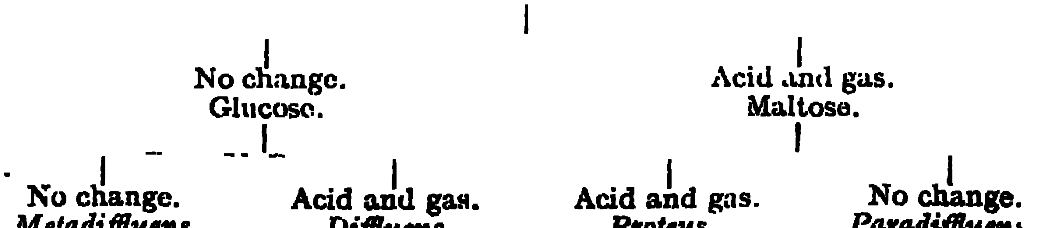
Classification.—The tribe may be divided into genera as follows:—

A. Rapid gelatine liquefiers; do not ferment lactose, mostly Gram-positive—*Proteus*.
B. Slow gelatine liquefiers; ferment lactose; Gram-negative—*Cloaca*.

Genus Proteus Hauser, 1885, *em.* Castellani and Chalmers, 1918.

Type Species.—*Proteus vulgaris* Hauser, 1885.

Remarks.—These organisms are of difficult classification, as the serological reactions are not always in accord with the biochemical characters. To this group belongs Proteus X_{19} (see page 1336). Some species may be separated as follows:—



Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. *acidi lactici* Hüppe	0	0	0	0	AC	AG	0	0	AG	AG	AG	AG	AG	AG	AG
B. *aertrycke* De Nobele	+	0	0	0	A, Alk	0	0	AG	AG	AG	AG	0	0	AGs	0
B. *albofaciens* Castellani, 1905	0	0	0	0	AC	0	0	0	0	A	0	—	—	—	—
B. *archibaldi* Castellani and Chalmers, 1918	+	0	0	0	A, Alk	0	0	AG	AG	AG	AG	—	0	—	0
B. *asiaticus* Castellani, 1905	0	0	0	0	A, Alk	0	AG	0	AG	AG	AG	AG	AG	AG	0
B. *asiaticus mobilis* Castellani, 1914	+	0	0	0	A, Alk	0	AG	0	AG	AG	AG	AG	AG	AG	0
B. *bentotensis* Castellani, 1912	+	0	0	0	A	A	A	As	0	A	A	0	As	0	0
B. *capsulatus* Pfeiffer	0	0	0	0	AC	AG	AG	0	AG	AG	AG	AG	AG	AG	AG
[illegible]*arolinus* Cas[illegible]llani	+	0	0	0	A, Alk	0	0	0	A or AG	A or AG	A or AG	—	AG	AG	—
[illegible]*vicida* Brieger	+	0	0	0	AC	AG	0	AG	AG	AG	0	AG	AG	AG	0
B. *ceylonensis A* Castellani, 1905	0	0	0	0	AC	0	0	0	0	A	0	0	0	0	0
B. *ceylonensis B* Castellani, 1905	0	0	0	0	AC	A	A	A	A	A	A	A	A	A	0
B. *cloacæ*, Jordan	+	0	+	+	AC	AG	AG	0	AG	AG	AG	AG	AG	AG	0

Inulin.	*Sorbite.*	*Galactose.*	*Lævulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
O	AG	AG	AG	O	O	—	—	O	—	+	O	Gt	Belongs to the capsulated bacilli; differs from *B. lactis aerogenes* in not fermenting inosite; differs from *B. coli tropicalis* in being capsulated and in fermenting adonite and not fermenting salicin.
O	AG	AG	AG	AG	O	O	AG	O	A	O or + s	O	Gt	Identical culturally and serologically with *B. suipestifer*; identical culturally with *B. enteritidis* Gaertner (differentiation by agglutination tests) and *B. paratyphosus B* (differentiation by Castellani's absorption test; agglutination not sufficient).
O	—	A	A	—	O	-	--	-	--	O	-	—	Very slow and scanty growth on agar.
O	—	AG	--	--		---	—	—	--	+	+	Gt	
O	AG	AG	AG	O	O	O	AG	O	AG	+ s	O	Gt	
O	AG	AG	AG	O	O	O	AG	O	AG	+ s	O	Gt	Differs from *B. asiaticus* only in being motile.
O	O	A	A	A	As	O	O	O	A	+	O	Gt	—
O	AG	AG	AG	AG	- -	-	-	--	—	±	+	Gt	Capsulated, probably identical with *B. lactis aerogenes*.
O	A	AG	AG	--	-	--	-		--	+	O	Gt or + P	—
O	—	AG	AG	O	A	--	--	—	--	+	O	-	Brieger described it at first as non-motile; differs from *B. coli* in not fermenting maltose.
O	O	O	O	O	O	O	O	O	O	O	O	Gt	—
O	A	A	A	O	O	O	A	O	A	+	O	Gt	—
O	AG	AG	AG	A or O	O	—	--	O	—	+	+	Gt	Liquefaction of gelatine very slow. The important intestinal liquefying bacilli may be grouped as follows: (1) lactose fermenters (*B. cloacæ*); (2) lactose non-fermenters, Gram + (*B. proteus vulgaris*); (3) lactose not fermenters, Gram O (*B. diffluens*).

Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. coagulans Castellani	O	O	O	O	AC	O	O	--	O	AG	AG	---	—	—	—
B. coli Escherich	+	O	O	O	AC	AG	O	AG	AG	AG	AG	AG	AG	AG	O
B. coli mutabilis Massini	O	O	O	O	AC	AG	O	O	--	-	—	---	—	—	O
B. coloides var. *A* Castellani	O	O	O	O	AC	AG	O	AG	—	AG	AG	---	—	--	—
B. coloides var. *B* Castellani	O	O	O	O	AC	AG	O	AG	—	AG	AG	—	--	...	—
B. colotropicalis Castellani, 1907	O	O	O	O	AC	AG	O	O	AG	AG	AG	AG	AG	AG	O
B. columbensis Castellani, 1905	+	O	O	O	Avs, O or Alk, Gvs D or A		O	AG	AG	AG	AG	As Gs	O	AG	O
B. coscoroba (= *B. pseudo-coscoroba*) Castellani and Chalmers	O	O	O	O	AC	AG	AG	O	AG	AG	AG	AG	AG	AG	O
B. danysz											--	—		-	—
B. diffluens Castellani 1915	+	O	+	+	Alk, D	O	O	O	O or A	AG	O	O	O	O or Avs	O
B. douglasi Castellani and Chalmers, 1918	O	O	O	O	Alk	O	O	A	A	A	A	—	--	--	—
B. dysenteriæ Flexner	O	O	O	O	A, Alk	O	O	O	A	A	A	A	A	A	O
B. dysenteriæ Hiss and Russell	O	O	O	O	A, Alk	O	O	O	A	A	O	A	A	A	O
B. dysenteriæ Shiga-Kruse	O	O	O	O	A, Alk	O	O	O	O	A	O	O or As	O	O	---
B. dysenteriæ Strong	O	O	O	O	AC	O	A	A	A	A	O	O	A	A	O
B. entericus Castellani, 1911	O	O	O	O	O	AG	O	AG	AG	AG	AG	AGs	OD	AG	O

Inulin.	*Sorbite.*	*Galactose.*	*Levulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
0	AG	AG	—	—	—	—	—	—	—	±	—	—	—
0	AG	AG	AG	0	AG	0	AG	0	AG	+	0	Gt	—
0	—	—	—	—	—	—	—	—	—	0	--	—	Incompletely described; late lactose fermenter (after six days); said not to produce indol.
—	—	—	--	0	AG	—	—	—	---	—	--	—	—
—	—	---	--	AG	AG	—	-	--	--	--	—	--	—
0	AG	AG	AG	0	AG	0	AG	0	AG	+			Differs from *B. coli* in being non-motile and in non-fermenting dulcite; from *B. neapolitanus* in not fermenting saccharose and dulcite.
0	AG	AG	AG	0	AG	0	AG	0	AG	+	0	Gt	—
—	AG	AG	--	A	-			-		0			Differs from *B. coli tropicalis* in fermenting saccharose; certain authors use the term *B. coscoroba* to indicate a different germ with all the characters of the fowl cholera bacillus (*pasteurella*).
—	--												Culturally and serologically identical with *B. enteritidis* Gaertner (Bainbridge).
0	-	AG	A or AG		0	--	-		A	0	--	Gt	See remarks on *B. cloacæ*. Some strains clot and peptonize milk.
--	--	—	--	-		--		--	-	+	---	-	--
0	0	A	A	--	0	0	0	0	0	+	-	--	--
0	0	A	A	-	0	0	0	0	0	+ or ±	—	---	
0	0	A	A	--	0	--	—	As	—	0	—	--	
0	A	A	A	—	0	0	A	0	0	+	—	—	—
0	AG	AG	AG	—	—	—	—	—	—	+	0	Gt Ps	-

Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. *enteritidis* Gaertner	+	O	O	O	A, Alk	O	O	AG	AG	AG	AG	AG	O	AG	O
B. *fæcalis alkaligenes* Petrushky	+	O	O	O	Alk	O	O	O	O	O	O	O	O	O	O
B. *fæcaloides* Castellani, 1915	+	O	O	O	Alk	O	O	O	A	A	A	A	O or A	O	O
B. *gasoformans nonliquefaciens*	O	O	O	—	AC	AG	AG	O	—	—	—	—	—	—	AG
B. *gintotensis* Castellani, 1910	O	O	O	O	D, AC	O	O	O	O	A	O	O	O	A	O
B. *giumai* Castellani, 1910	O	O	O	O	A, Alks	A	O	O	O	AG	AG	AGs	O	AG	O
B. *grunthali* Castellani	+	O	O	O	AC	AG	O	O	AG	AG	—	AG	AG	AG	O
B. *icteroides* Sanarelli	+	O	O	O	A, Alk	O	O	A or AG	AG	AG	AG	AG	O or A	A or AG	—
B. *kandiensis* Castellani, 1912	+	O	O	O	As, D, Alk	O	As	O	A	A	O	O	O	O	A
B. *khartoumensis* Chalmers and Macdonald, 1915	O	O	O	O	A	AG	O	AG	AG	AG	AG	O	O	AG	—
B. *lactis aerogenes* Escherich	O	O	O	O	AC	AG	AG	O	AG	AG	AG	AG	AG	AG	AG
B. *levans* Wolffin	+	O	+	—	AC	AG	O	O	AG	AG	—	AG	AG	AG	O
B. *lunavensis* Castellani, 1912	O	O	O	O	As, Alk	O	A	O	O	A	A	A	O	A	O
B. *madampensis* Castellani, 1911	O	O	O	O	AC	A	A	O	A	A	A	A	As	A	O
B. *meta alkaligenes* Castellani, 1915	O	O	O	O	Alk	Alk	Alk	Alk	Alk	Alk	Alk	—	—	—	—
B. *metacoli* Castellani 1915	+	O	O	O	AC	AG	AG	AG	AG	AG	AG	AG	AG	AG	O

Inulin.	*Sorbite.*	*Galactose.*	*Lævulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
O	AG	AG	AG	O	O	O	—	—	O	O	—	Gt	Identical culturally with *B. suipestifer* (=*B. aertrycke*) and *B. paratyphosus B;* differs serologically.
O	O	O	O	O	O	O	O	O	O	O	O	Gt	The typical *B. fæcalis alkaligenes* produces strong alkalinity in all sugar broths, but certain strains are said to produce slight acidity in glucose and maltose. Some strains peptonize milk.
O	A	A	A	—	O	O	—	O	—	O	O	Gt	—
O	--	—	—	A	—	—	—	—	..	O	+	--	Incompletely described. It is probably very similar to *B. colotropicalis,* but indol O.
O	O	A	O	O	O	O	O	O	O	O	O	Gt P	—
O	AG	AG	AG	O	AG	O	AG	O	As	+	O	Gt	—
O	AG	AG	AG	O	—	--	—	O	---	+	O	Gt	—
O	AG	AG	AG	—	—	--	—	--	--	±	O	Gt or Gt P	Considered to be identical with *B. suipestifer,* but complete serological tests have not been carried out.
O	O	A	A	A	O	O	A	A	A	O	O	Gt	—
O	AG	AG	AG	O	AG	O	—	—	AG	+	O	—	—
O	AG	AG	AG	AG	AG	—	--	.	--	O	+	Gt	Differs from *B. acidi lactici* in fermenting inosite.
AG	AG	AG	AG	O	AG	—	—	O	—	O	+	—	—
O	O	A	A	O	O	O	O	O	Avs	+	O	Gt	—
O	A	A	A	O	O	O	A	O	A	+	O	Gt	—
—	—	Alk	Alk	—	—	—	—	—	—	±	—	Gt	Differs from *B. fæcalis alkaligenes* in being non-motile.
O	AG	AG	AG	AG	AG	O	AG	O	AG	+	O	Gt	Differs from *B. pseudocoli* in fermenting inosite.

Bacteria.	Motility.	Gram.	Gelatine.	Serum.	Litmus Milk.	Lactose.	Saccharose.	Dulcite.	Mannite.	Glucose.	Maltose.	Dextrin.	Raffinose.	Arabinose.	Adonite.
B. metacoloides Castellani	+	O	O	O	AC	AG	O	G	AG	AG	AG	AG	AG	AG	O
B. metadiffluens Castellani	+	O	+	+	Alk	O	O	O	O	O	O	O	O	O or As	O
B. metadysentericus Castellani, 1904, var. *A*	O	O	O	O	A or Alk	A	A	O or As	A	A	A	—	—	—	—
B. metadysentericus Castellani, 1904, var. *B*	O	O	O	O	A, Alk	A	O or Avs	O or Avs	O or Avs	A	A	—	—	—	—
B. metadysentericus Castellani, 1904, var. *C*	O	O	O	O	A, Alk, D	As	O or Avs	O or Avs	O or Avs	A	As	—	—	—	—
B. metadysentericus Castellani, 1904, var. *D*	O	O	O	O	A, Alk	A	A	A	A	A	A	—	—	—	—
B. morgani Castellani and Chalmers, 1918	O	O	O	O	O, Alk, or As, Alk	O	O	O	O	AG	O or A	O or A	O	O or A	O
B. neapolitanus Emmerich	O	O	O	O	AC	AG	AG	AG	AG	AG	AG	AG	AG	AG	O
B. negombensis Castellani, 1910	O	O	O	O	O, Alk	O	O	O	O	A	O	O	O	O	O
B. oxytocus perniciosus Wyssokowitsch	O	O	O	O	AC	AG	AG	AG	AG	AG	—	AG	AG	AG	AG
B. para-aertryke Castellani, 1914	+	O	O	O	A, Alk	O	O	AG	AG	AG	AG	O	O	AG	O
B. para-asiaticus Castellani, 1916	O	O	O	O	O	O	O	AG	AG	AG	AG	AG	AG	AG	O
B. paracoagulans Castellani, 1914	O	O	O	O	AC	O	O	O	AG	AG	AG	—	AG	AG	—
B. paracolon Day	+	O	O	O	A, Alk,	O	O	A	AG	AG	AG	AG	AG	AG	—
B. paradiffluens Castel-	+	O	+	+	Alk D or	O	AG	O	O or A	AG	O	O	O	O	O

INTESTINAL BACILLI—*Continued.*

Inulin.	*Sorbite.*	*Galactose.*	*Levulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
O	AG	AG	AG	O	O	O	AG	O	AG	+	—	+	—
O	—	O or As	O	—	O	—	—	—	—	—	—	—	.
O	—	As	A	—	—	—	—	.	—	±	—	Gt	..
—	—	A	A	—	—		—	—	—	+	—	—	—
—	—	A	A		—		.		—	O	—	—	
—	—	A	A	—		—		.	—	+			
O	O	A or AGs	A or AGs	O	O	O	O	O	O	++	O	Gt	
O	AG	AG	AG	O	AGs	O	AGs	O	AGs	+	O	—	Differs from *B. coli* in being non-motile and in fermenting saccharose; from *B. pseudo-coli* in being non motile; from *B. colotropicalis* in fermenting dulcite and saccharose.
O	O	A	As	O	O	O	O	O	O	O	O	Gt	—
AG	AG	AG	AG	AG	AG	O	AG	O	AG	+	+	-	—
O	AG	AG	AG	AG	O	O	AG	O	AG	O	O	Gt	—
O	AG	AG	AG	O	O	O	AG	O	O	+s	O	Gt	Differs from *B. asiaticus* in not fermenting saccharose and in fermenting dulcite
O	A	AG	AG	—	—	.	.	—	—	+	O	Gt	—
—	AG	AG	AG	—	—	—	—	—	—	+	O	Gt	—
—	—	AG	AG	.	O	.	—		O	O	—	Gt	

Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. paradysentericus Castellani, 1904	O	O	O	O	A	O	O	O	O	O or A	O	O	O	O	O
B. para-entericus Castellani, 1914	+	O	O	O	A	AG	AG	AG	AG	AG	AG	AGs	AG	AG	O
B. paragrünthali Castellani	+	O	O	O	AC	AG	O	O	AG	AG	AG	AG	AG	AG	O
B. paratyphosus A Schotmüller	+	O	O	O	A	O	O	AG	AG	AG	AG	AG	O	AG	O
B. paratyphosus B Schotmüller	+	O	O	O	A, Alk	O	O	AG	AG	AG	AG	AG	O	AG	O
B. paratyphosus C	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
B. pneumoniæ Friedlaender	O	O	O	O	AC	A	AG	AG	AG	AG	AG	AG	AG	AG	AG
B. pritnitzi Castellani	+	O	O	O	A	O	O	O	O	A	A	A	O	O	O
B. proteus vulgaris Hauser	+	+	+	+	C or P	O	AG	O	O	AG	AG	O	O	O	O
B. pseudo-asiaticus Castellani, 1913	O	O	O	O	A, Alk	O	AG	AGs	AG	AG	AG	AG	AG	AG	O
B. pseudo-asiaticus mobilis Castellani, 1915	+	O	O	O	A or O, Alk	O	AG	AG	AG	AG	AG	AG	AG	AG	O
B. pseudo-carolinus Castellani, 1917	O	O	O	O	O	O	O	O	AG	AG	AG	—	AG	AG	—
B. pseudo-coli Castellani, 1909	+	O	O	O	AC	AG	AG	AG	AG	AG	AG	AGs	AG	AG	O
B. pseudo-coliformis Castellani, 1917	+	O	O	O	AC	AG	O, AG	AG	AG	AG	AG	AG	AG	AG	O

Inulin.	*Sorbite.*	*Galactose.*	*Levulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
—	—	O or As	O	O	O	O	O	O	O	±	...	Gt	Milk rendered permanently acid.
O	AG	AG	AG	—	—	—	—	—	—	+	O	Gt Ps	*B. badullensis* Castellani, 1911; culturally identical, differs serologically.
O	AG	AG	AG	O	AG	O	AG	O	AG	±	—	Gt	Differs from *B. grünthali* in fermenting maltose.
O	AG	AG	AG	O	O	O	AG	O	O or As	O	O	Gt	—
O	AG	AG	AG	AG	O	O	AG	O	O	O	O	Gt	Certain strains, serologically typical, may produce at times only A instead of AG; some strains do not ferment inosite (Weiss and Rice).
—	—	—	—	—	—	—	—	—	—	—	—	—	Cover several germs, one identical with *B. enteritidis*.
O	AG	AG	AG	AG	AG	—	—	O	—	O	O	—	—
A	O	A	A	O	A	O	O	O	O	O	—	Gt	—
O	O	AG	A or AG	O	O	—	—	—	O or As	+	—	Gt	Cultures emit a disagreeable odour. Hauser distinguished at first three varieties of proteus: *P. vulgaris* (rapid liquefaction of gelatine), *P. mirabilis* (slow liquefaction), *P. zenkeri* (no liquefaction); later abandoned this differentiation).
O	AG	AG	AG	O	AG	O	AG	O	AG	+	O	Gt	Differs from *B. asiaticus* in fermenting dulcite.
O	AG	AG	AG	O	AG	O	AG	O	AG	+	O	Gt	—
O	A	AG	AG	—	—	—	—	—	—	+	O	Gt P	—
O	AG	AG	AG	O	AG	O	AG	O	AGs	+	O	Gt Ps	Differs from *B. coli* in fermenting saccharose, belonging to the group Communior of coliform bacilli.
O	AG	AG	AG	O	AG	O	AG	O	AG	+	O	Gt	Differs from *B. pseudo-coli* serologically and in fermenting saccharose only after several days.

Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. pseudo-coloides Castellani, 1916	--	---	—	—	—	—	--	O	—	--	—	—	--	—	—
B. pseudo-coloides, var. *B*, Castellani	--	--	--	---	--	--	—	O	—	—	—	—	—	—	—
B. pseudo-columbensis Castellani, 1917	O	O	O	O	O	O	O	AG	AG	AG	AG	AGs	O	AG	O
B. pseudo-morgani Castellani	+	O	O	O	O, Alk	O	O	O	O	AG	O	O	O	O	O
B. pseudo-[illegible]e-senbergi Castellani, 1918	O	O	O	O	O	O	AG	O	O	AG	—	—	—	—	—
B. psittacosis Nocard	+	O	O	O	A, All.	O	O	AG	AG	AG	AG	AG	AG	AG	O
B. pyogenes fœtidus Passet	+	O	O	O	AC	A	A	A	A	A	A	A	A	A	—
B. schaefferi von Freudenreich	O	O	O	---	AC	AG	O	AG	—	—	--	---	--		O
B. suipestifer Kruse	+	O	O	O	A, Alk	O	O	AG	AG	AG	AG	O	O	AGs	O
B. talavensis Castellani, 1909	+	O	O	O	Alk, D	O	A	O	O	A	O	O	O	O	O
B. tangallensis Castellani, 1911	O	O	O	O	As, Alk	O	A	A	A	A	A	A	A	A	O
B. tardus Castellani, 1917	O	O	O	O	DP	O	O	O	O	As	O	—	-	--	
B. typhi murium Loeffler	+	O	O	O	A, Alk	O	O	AG	AG	AG	AG	AG	O	AG	O
B. typhosus Eberth	+	O	O	O	A	O	O	O	A	A	A	A	As	O	O
B. voboda Castellani, 1909	+	O	O	O	A, Alk	O	O	AG	A	AG	AG	AG	AG	AG	O
B. vekanda Castellani	+	O	O	O	A	AG	O	AG	AG	AG	AG	O	O	AG	AG
B. vesiculosis Henrici	O	O	O	O	AC	AG	O	O	—	--	—	—	—	—	O

Inulin.	*Sorbite.*	*Galactose.*	*Levulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
—	—	—	—	O	—	—	—	—	—	+	—	—	Differs from *B. pseudo-coli* in not fermenting dulcite.
—	—	—	—	AG	—	—	—	—	—	±	—	—	Differs from *B. pseudocoloides* in fermenting inosite.
O	AG	AG	AG	O	AG	O	AG	O	AG	+	O	Gt	—
O	O	A	A or AG	O	O	O	O	O	O	+	O	Gt	—
—	—	—	—	—	—	—	—	—	—	+	—	Gt	—
O	AG	AG	AG	—	O	—				O	O	Gt	Identical with *B. aertryke*, according to Bainbridge.
—	—	A	A	—		—			—	+	O	Gt	—
O	O	—	—	O	—	—	—		—	+	O	Gt	Incompletely described.
O	AG	AG	AG	O or AG	O	O	AG	O	As	+s	O	Gt	Identical with *B. aertryke*. Other synonyms for *B. suipestifer* are *B. choleræ suis*, bacillus of hog-cholera, Salmon and T. Smith, 1885.
O	O	A	A	A	A	O	O	O	A	+	O	Gt	—
O	A	A	A	O	A	O	A	O	A	+	O	Gt	
O	—	O	O or As	—	O		—	—	—	O	—	—	Very slow and scanty growth on agar.
O	AG	AG	AG		O	O	—	—	O	O	O	Gt	Bainbridge has found out that the name is applied to different organisms, some strains being serologically identical with *B. aertryke*, others with *B. enteritidis* Gaertner, others with *B. paratyphosus B.*
O	A	A	A	O	O	O	O	O	As	O	O	Gt	Certain strains, milk A, Alk.
O	AG	AG	AG	AG	O	O	A	O	O	O	—	Gt	—
O	AG	AG	AG	O	O	O	AG	O	AG	O	—	Gt	—
O	—	—	—	O	—	—	—	—	—	+	O	—	—

Bacteria.	*Motility.*	*Gram.*	*Gelatine.*	*Serum.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*
B. watareka Castellani	+	O	O	O	A	O	O	AG	AG	AG	AG	O	AG	AG	O
B. werahensis Castellani	+	O	O	O	A	O	O	AG	A	A	AG	AG	AG	AG	—
B. wesenbergi Castellani	+	—	O	O	A	A	AG	A	A	AG	—	—	—	—	—
B. wesenbergoides Castellani, 1916	+	O	O	O	O	O	AG	O	O	AG	AG	—	—	—	—
B. willegodai Castellani	+	O	O	O	A, Alk	O	O	A	A	AG	AG	AG	AG	AG	O
B. wolinia Castellani, 1916	+	O	O	O	A or A, Alk	O	A or Alk	O	AG	AG	AG	O	O	O	O
B. zeylanicus Castellani, 1910	+	O	O	O	Alk	Alk	Alk	Alk	Alk	Alk	Alk	Alk	Alk	O or Alk	O or Alk

Abbreviations used in the above Table.—A=acid; G=gas; C=clot; D=decolorized; Peptonized (milk) pellicle (broth); VS=very slight; O negative result—viz., neither acid liquefaction of gelatin or serum as the case may be; + positive result; ± =sometimes The new nomenclature has not been used in this table.

Inulin.	*Sorbite.*	*Galactose.*	*Levulose.*	*Inosite.*	*Salicin.*	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Broth.*	*Remarks.*
O	AG	AG	AG	AG	O	O	AG	O	A	+	—	Gt	—
—	—	O	O	—	A	O	AG	—	O	+s	—	Gt	—
—	—	—	—	—	—	—	—	—	—	+	—	Gt	—
—	—	—	—	—	—	—	—	—	—	+	—	Gt	—
—	—	AG	A	—	AG	O	AG	—	O	+s	—	Gt	—
O	O	A or AG	O	O	O	—	—	—	A	O	—	Gt	-
Alk	O or Alk	Alk	Alk	O or Alk	O or Alk	O or Alk	O or Alk	O or Alk	O or Alk	O	O	Gt or P	Classification difficult, the germ being polymorphic, vibrio-like, bacillus-like, leptothrix-like, spirilloides-like, hence its various generic names: bacillus, vibrio, spirobacillus, vibriothrix, p. 1068

Alk=Alkaline; S=slight; A, Alk - Acid then alkaline; Gt=general turbidity; P= nor clot in milk, neither acid nor gas in sugar media, non-production of indol, non-positive, sometimes negative.

Genus Cloaca Castellani and Chalmers, 1918.

Type Species.—*Cloaca cloacæ* Jordan, 1890.

Remarks.—Two species are known, *C. cloacæ* Jordan and *C. levans* Wolffin, but they are not important in tropical medicine. They may be recognized as follows:—

Saccharose.

Acid and Gas.	No change.
Cloacæ.	*Levans.*

TRIBE BACTERIDIEÆ CASTELLANI AND CHALMERS.

Definition.—Bacillaceæ growing well on ordinary laboratory media, without endospores, and either fluorescent or chromogenic.

Type Genus. *Bacteridium* Schroeter, 1872.

Remarks.—Two distinct groups belong to this tribe—viz., the fluorescent and the chromogenic—but we are only concerned with the latter, to which the type genus belongs.

Genus Bacteridium Schroeter, 1872.

Definition.—Bacteridieæ which are chromogenic.

Type Species. *Bacteridium prodigiosum* (Ehrenberg, 1838).

Remarks.—Although we are not particularly concerned with this genus as a whole in the tropics, still there is one species—*Bacteridium pyocyaneum* Gessard, 1882, synonym *Bacterium æruginosum* Schroeter, 1872—which is the organism of bluish-green pus.

It is a common intestinal parasite in the tropics, and is moderately common in pus in Ceylon, India, and the Anglo-Egyptian Sudan.

It is a small motile rod, which becomes pleomorphic if grown on media containing carbolic or boric acids. It only produces its bluish-green pigment when grown aerobically.

It produces acid, but no gas, in glucose, and no change in maltose, dulcitol, or salicin. Litmus milk is rendered alkaline and not clotted.

TRIBE GRACILOIDEÆ CASTELLANI AND CHALMERS 1918.

Definition.—Bacillaceæ growing very slowly and scantily on ordinary and blood media, without endospores or capsules, neither fluorescent nor chromogenic.

Type Genus.—*Graciloides* Castellani.

Genus Graciloides Castellani, 1917.

Definition.—*Graciloideæ* with the tribal characters.

Type Species.—*Graciloides albofaciens* Castellani, 1904.

Classification.—Two species have been so far described, which may be recognized as follows:—

A. Litmus milk rendered acid and clotted—*Albofaciens.*
B. Litmus milk decolorized or peptonized—*Tardus.*

TRIBE BACTEROIDEÆ CASTELLANI AND CHALMERS.

Definition.—Bacillaceæ with good growth on ordinary laboratory media, without endospores, fluorescence, or pigment formation, and obligatory anaerobes.

Type Genus.—*Bacteroides* Castellani and Chalmers, 1918.

Genus Bacteroides Castellani and Chalmers, 1918.

Definition.—Bacteroideæ with the tribal characters.

Type Species.—*Bacteroides fragilis* Veillon and Zuber.

The type is found in abscesses from various parts of the body. Another species is the well-known *Bacteroides fusiformis* of Le Dantec and Vincent, found in hospital gangrene, and in Vincent's angina and many other conditions, as well as in the mouths of healthy persons and in the tartar on teeth.

Some of the intestinal forms are given on p. 960.

TRIBE BACILLEÆ CASTELLANI AND CHALMERS, 1918.

Definition.—Bacillaceæ growing well on ordinary laboratory media and possessing endospores.

Type Genus.—*Bacillus* Cohn, 1872, *parte*.

Genus Bacillus Cohn, 1872.

Definition.—Bacilleæ with the tribal characters.

Type Species.—*Bacillus subtilis* (Ehrenberg, 1833).

Classification.—The genus may be divided into two groups as follows:—

A. Aerobes—*Subtilis group*.
B. Obligatory anaerobes—*Tetanus group*.

Only the latter concerns us at present.

TETANUS GROUP.

The group may be divided into subgroups as follows:—

A. Gelatine liquefied:
  I. Inspissated blood serum not liquefied:—
    (*a*) Little or no gas in milk; white of egg not sensibly affected. Usually motile—*Subgroup Quarter Evil*.
    (*b*) Much gas in milk; white of egg slightly affected. Usually non-motile—*Subgroup Saccharolytic*.
  II. Inspissated blood serum liquefied:—
    White of egg digested—*Subgroup Proteolytic*.
B. Gelatine not liquefied:—
  Inspissated blood serum not liquefied. White of egg not digested—*Subgroup Non-liquefactive*.

SUBGROUP QUARTER EVIL.

Synonym.—Rauschbrand group.

Definition.—Tetanus group usually motile, liquefying gelatine, non-proteolytic, and do not liquefy inspissated blood serum. Clotting milk without much shrinkage. Citron and bladder forms occur. Spores usually central.

Classification.—The organisms of this group may be recognized as follows:—

A. Long threads present—*Vibrion septique*.
B. Long threads absent:—
  I. Saccharose fermented—*Feseri*.
  II. Saccharose not fermented:—
    (*a*) Spores rare in animals—*Novyi*.
    (*b*) Oval end spores present—*End-sporing types*.

Bacteroides.	*Motility.*	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Glucose.*	*Starch.*	*Indol.*	*Gelatine.*	*Egg Albumen.*	*Broth.*	*Gram.*	*Spores.*	*Appearance of Growth in Deep Glucose Agar.*	*Formation of Gas in Agar.*	*Remarks.*
B. brunei Distaso	O	O	O	O	O	O	O	O	O	+	+	O	Of a hairy appearance.	O	Takes black tint with iodine in the vegetative forms.
B. variabilis Distaso	O	O	S+	S	S+	O	+	O	O	T	O	O	Round and transparent.	+	—
B. pseudo-ramosus Distaso	O	C	S+	S+	S+	O	+	O	O	T	–	O	Round; non-transparent.	O	—
B. anaerobicus Distaso	+	O	O	O	S+	O	O	O	O	T	+	O	Almost invisible.	O	—
B. cornutus Distaso	O	O	O	O	S+	O	O	O	O	T	+	O	Almost invisible.	O	—
B. bullosus Distaso	+	O	O	O	S+	O	O	O	O	T	O	O	Minute colonies, pin-head sized.	O	—
B. tethaiotaomicron Distaso	+	C	+	O	+	O	+	O	O	T	O	O	Transparent, medium-sized.	S+	—
B. variegatus Distaso	+	C	S+	O	S	O	+	O	O	T	+	O	Minute colonies, pin-prick sized.	O	—
B. bifidus Tissier	O	C	+	+	+	O	O	O	O	T	+	O	Pleomorphic colonies; mainly round or crenated.	O	— —

Abbreviations used in the Table.—O=negative result; + =positive result; C=clotted; T=turbidity; S+ =slight positive.

Remarks.—*Bacillus feseri* [Trevisan, 1885, the causal organism of quarter-evil, is the same as *B. chauvœi* Arloing, Cornevin, and Thomas, 1887; *B. carbonis* Migula, 1900; *B. anthracis symptomatici* Kruse, 1896; and the *Bacillus of Rauschbrand auctores.*

The Vibrion septique of Pasteur is the same as the bacillus of Ghon and Sachs, and has been found in gas gangrene; it really covers a group of strains which agree in morphology and in cultural characters, as well as in pathogenicity, but their agglutinative reactions are different.

SUBGROUP SACCHAROLYTIC.

Synonyms.—*Welchii subgroup : Perfringens subgroup.*

Definition.—Tetanus group, liquefying gelatine, usually causing stormy fermentation in milk, in which spores are not formed. Do not blacken meat or liquefy blood serum.

Classification.—The following organisms belong to this group:—

1. *B. welchii* Migula, 1900. (*Synonyms* :—*B. perfringens* Veillon and Zuber, 1898; *B. aerogenes capsulatus* Welch and Nuttall, 1892; *B. phlegmonis emphysematosi* Fraenkel, 1902; *B. saccharobutyricus immobilis* Schattenfroh and Grassberger, 1900; *B. enteritidis sporogenes* Klein, 1915, *pro parte.* This organism is merely a mixture of *B. welchii* and *B. sporogenes*, Achalme's bacillus.)
2. *B. fallax* Weinberg, 1915.
3. *B. œdematiens* Weinberg and Sequin, 1915.
4. *B. aerofetidus* Weinberg, 1916.

They may be differentiated as follows: -

- A. *Non-motile* :—
  - Saccharose and lactose fermented, but salicin not fermented—*Welchii.*
- B. *Feebly motile in cultures, more motile in tissues* :—
  - I. Saccharose and salicin fermented, but lactose not fermented—*Fallax.*
  - II. Saccharose not fermented, but lactose and salicin fermented -*Aerofetidus.*
  - III. Saccharose, lactose, and salicin not fermented —*Œdematiens.*

SUBGROUP PROTEOLYTIC.

Definition.—Tetanus group liquefying gelatine and inspissated blood serum. Meat media blackened. Milk usually digested without forming a clot. Colonies grow out in long tangled filaments.

Classification.—The following organisms belong to this subgroup:—

1. *B. tetani* Flügge, 1886.
2. *B. sporogenes* Metchnikoff, 1908. (*Synonyms* :- -*B. cadaveris sporogenes* Klein, 1901; *B. œdematis maligni* Koch, 1881; *B enteritidis sporogenes* Klein, 1895, *pro parte* *B. putrificus coli* Bienstock, 1906)
3. *B. botulinus* van Ermengem, 1898.
4. *B. histolyticus* Weinberg and Sequin, 1916.

They may be differentiated as follows: -

- A. *Dense white balls in four to five days in meat media :*
  - Very few large subterminal spores in culture. Pathogenic for laboratory animals—*Histolyticus.*
- B. *No formation of white balls in meat media* :-
  - I. Non-pathogenic for laboratory animals:
    - Central, subterminal, or terminal spores a marked feature in cultures—*Sporogenes.*
  - II. Pathogenic for laboratory animals:—
    - (*a*) Spores oval, central, or terminal—*Botulinus.*
    - (*b*) Spores round and terminal—*Tetani.*

Subgroup Non-Liquefactive.

Definition.—Tetanus group, motile, not liquefying gelatine or inspissated blood serum, and do not blacken meat media.

Remarks.—This group includes:—

1. *B. tertius* Henry, 1917, found in gas gangrene. (*Synonyms:— B. Y. Fleming*, 1915; *B. von Hibler* IX.; *B. rodella* III.)
2. *B. von Hibler* VII.
3. *B. amylobacter* Gruber, 1887.

Classification.—These organisms may be recognized as follows:—

A. Attack milk slowly, forming a soft clot after a long period:—
  I. Spores usually central—*Von Hibler* VII.
  II. Spores typically terminal—*B. tertius*.
B. Attack milk, forming tough clot, broken by gas—*Amylobacter*.

FAMILY 8: SPIRILLACEÆ Migula, 1900.

Definition.—Eubacteriales with cells spirally curved or representing part of a spiral; division in one direction.

Type Genus.—*Spirillum* Ehrenberg, 1838.

Classification.—The family may be divided into the following genera:—

A. Non-motile, comma-shaped, or spirally curved filaments, rigid, without flagella—Genus 1, *Spirosoma* Migula, 1900.

B. Motile, short, slightly curved, rigid, comma-like, sometimes in chains, with one, rarely more, flagella at one end, seldom at both ends—Genus 2, *Vibrio* O. F. Muller, 1773, *emendavit* Loeffler.

C. Motile, long, spirally curved, usually with a bunch of polar flagella composed of long and short forms—Genus 3, *Spirillum* Ehrenberg, 1838, *emendavit* Loeffler.

Remarks.—We are only concerned with the genus Vibrio, which contains the cholera and paracholera organisms.

If the spirochætes were to be considered to be bacteria, they would be classified here under the name Spironema

Genus Vibrio O. F. Müller, 1773.

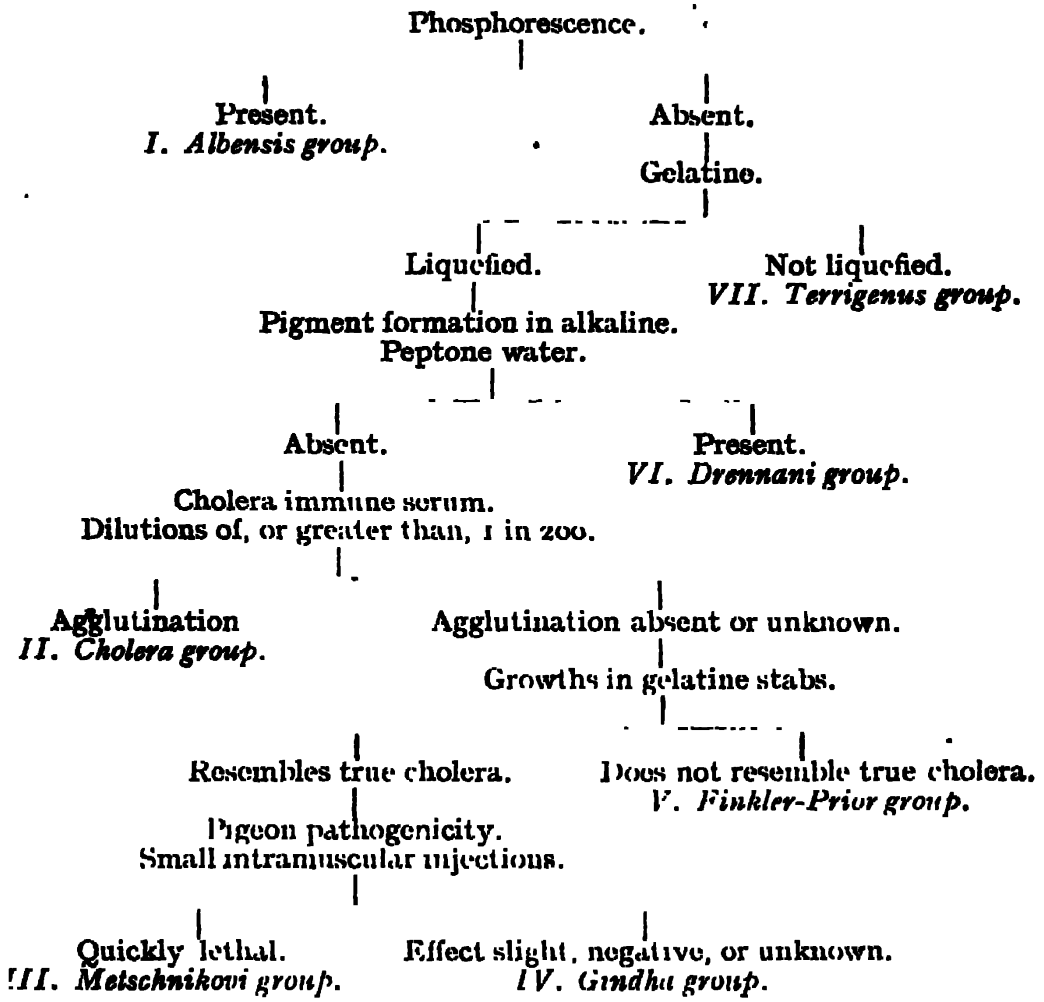
Definition.—Spirillaceæ motile, with short comma-like cells, possessing one, rarely more, flagellum at one, rarely at both ends.

Type.—It is difficult to decide which is the type of this genus so defined.

Remarks.—The important species is the *Vibrio comma* Koch, 1884, which is the cause of Asiatic cholera, but there are many other which cause paracholera—*e.g.*, *V. gindha*, Pfeiffer, 1896; *V. kegallensis* Castellani, 1913; *V. insolitus* Castellani, 1913, etc.

Classification.—The genus may be divided into aerobic groups as follows:—

The Aerobic Groups of the Genus Vibrio O. F. Müller, emendavit Loeffler.



nly the cholera and the gindha groups concern us.

CHOLERA GROUP.

Ruffer classifies the strains of the cholera group as follows:—

Series I.—A. Cholera immune serum.

1. Agglutination positive.
2. Castellani's saturation positive.
3. Pfeiffer's reaction positive.
4. Complement fixation positive.

B. *Hæmolysis negative.*

Series II., El tor vibrios.—A. Cholera immune serum.

1. Agglutination positive.
2. Castellani's saturation positive.
3. Pfeiffer's reaction positive.
4. *Complement fixation negative.*

B. Hæmolysis strongly marked.

Series III.—**A. Cholera immune serum.**

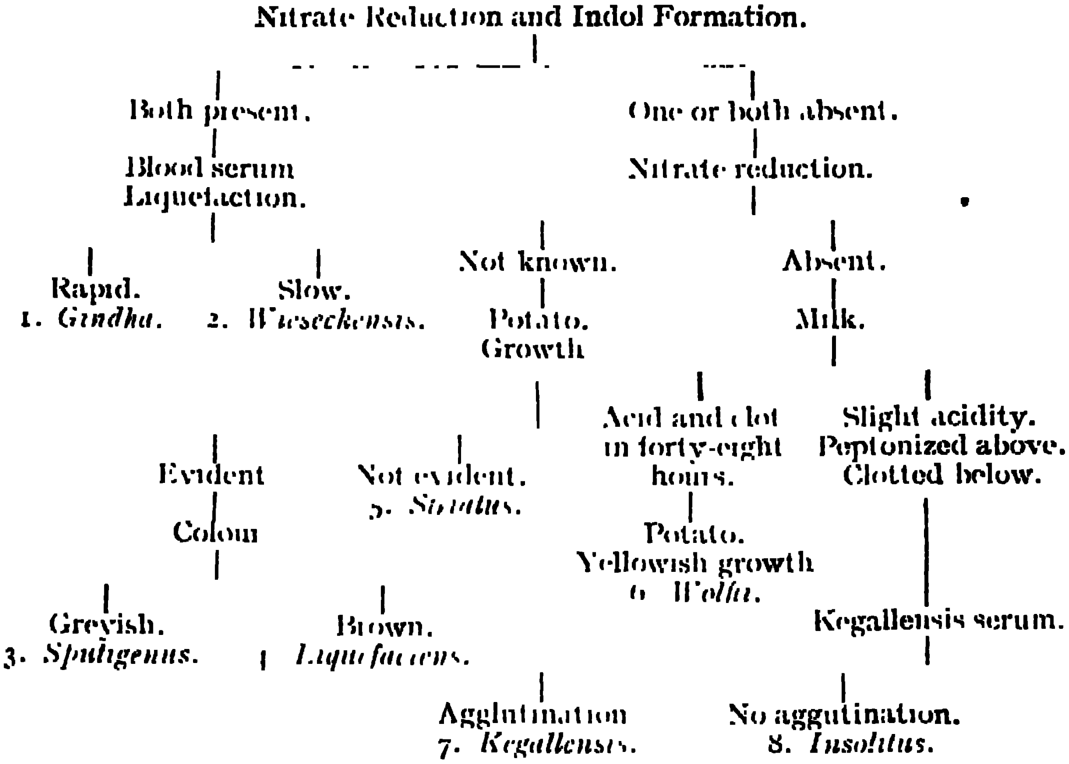
1. **Agglutination positive.**
2. ***Castellani's saturation negative.***
3. ***Pfeiffer's reaction negative.***
4. **Complement fixation positive.**

B. Hæmolysis feeble and late.

The bacteriological characters of the usual vibrio are to be found in every textbook on bacteriology.

GINDHA GROUP.

This group may be divided into species as follows:—



The names of the eight species so differentiated are:—

1. *V. gindha* (Pfeiffer, 1896).
2. *V. liquefaciens* (Migula, 1900).
3. *V. wiesseckensis* (Migula, 1900).
4. *V. striatus* (Migula, 1900).
5. *V. wolfii* (Migula, 1900).
6. *V. sputigenus* (Migula, 1900).
7. *V. kegallensis* vel *paracholeræ* (Castellani, 1913).
8. *V. insolitus* (Castellani, 1913).

Of these, the first and the last two have been associated with paracholera, to the exclusion of other organisms.

FAMILY MYCOBACTERIACEÆ Chester, 1901.

Definition.—Eubacteriales with short or long cells, cylindrical or filamentous, without a sheath, but often clavate, cuneate, or irregular, and often with enclosed granules.

Type Genus.—*Mycobacterium* Lehmann and Neumann, 1896.

Remarks.—Chester created this family to hold such forms as the diphtheria germ, the tubercle bacillus, and the nocardias.

The latter we classify with the Fungi Imperfecti, and probably the other organisms, especially the tubercle bacillus, should join them; nevertheless, for the time being, we keep them in Chester's family.

Mycobacterium becomes the only genus of the family, as Chester included with it the Corynebacterium of Lehmann and Neumann.

Genus Mycobacterium Lehmann and Neumann, 1896.

Definition. Mycobacteriaceæ with the characters of the family.

Type Species. - *Mycobacterium lepræ* (Hansen, 1874).

Remarks.- -From our point of view there are two divisions of the genus which are of importance viz:

A. Acid-fast when stained by Ziehl-Neelsen's method.
B. Not acid-fast when stained by Ziehl-Neelsen's method.

The former include the tubercle and the leprosy bacilli, which may be distinguished by the latter being present in very large numbers in the leprotic nodules, and being very resistant to decolourization, while the former are but few in a cell and relatively easier to decolourize. Moreover, the leprosy bacillus can be readily stained by Gram, while the tubercle is difficult to stain properly.

The tubercle bacillus can be cultivated, but so far there is a doubt as to the leprosy bacillus ever having been cultivated.

The other group contains the diphtheria bacillus. The names of these three organisms are: *M. lepræ* (Hansen, 1874); *M. diphtheriæ* (Klebs, 1883); and *M. tuberculosis* (Koch, 1882).

In addition the *Mycobacterium mallei* (Loeffler, 1886), the cause of glanders, may be mentioned, as Whitmore has described a fever in Rangoon characterized by broncho-pneumonic symptoms and often multiple abscesses, which is due to a closely allied organism introduced into the body while injecting morphine subcutaneously.

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CHAPTER XXXVII

FUNGACEÆ—PHYCOMYCETES

Preliminary—Fungaceæ—Phycomycetes—Zygomycetes—Mucorales—References.

PRELIMINARY.

THE study of fungi, or *mycology*, as it is often called, includes macroscopic and microscopic forms. The microfungi are those which principally cause disease, which, for this reason, is termed a *mycosis*. Thus 'otomycosis' means a mycosis of the ear, and 'mucormycosis' a disease caused by a mucor, which is a fungus known to Malpighi in 1686.

The study of the microfungi began in the days of Charles II., when Hooke in 1677, made a lens with which he examined the blighted or yellow specks on the leaves of the damask rose, and made excellent drawings of the microfungi which he saw. His book contains a chapter devoted to the 'Blue Mold and the First Principles of Vegetation arising from Putrefaction.'

Malpighi, in 1686, has a chapter devoted to 'Plantis quæ in alliis vegetant,' in which he refers to mucedo.

Ray, in 1706, in his 'Historia Plantarum,' describes *Pilobolus crystallinus*, one of the Mucoraceæ, which has beautiful crystalline sporangia on yellowish sporangiophores, and of which Plukenet in 1720 gave the first illustration.

Micheli, in 1729, named and gave a scientific account of the genus *Mucor*, as well as of *Aspergillus* and many other fungi.

Linnæus, in 1753, in his 'Species Plantarum,' made a résumé of knowledge up to that date; and Hudson, in 1762, described mucors in his 'Flora Anglica'; while Lightfoot in his 'Scottish Flora,' published in 1777, mentioned the ascomycete-sphæria. Pelham (1785), Withering (1795), Dickson (1785-1801), and Hill (1796), all contributed to the knowledge of microfungi, which was slowly growing, as did Batsch, in 1783, in Germany, and Bulliard, in 1791, in France.

This slow but sure progress now became very rapid, and the only way in which we can trace its evolution is by mentioning the great systematic works which are of use for reference.

They are Persoon (1801), 'Synopsis Methodica Fungorum'; Link (1824), 'Caroli Linné Species Plantarum,' Editio Quarto, tomus vi., p. 1; Fries (1821-1829), 'Systema Mycologicum'; Nees von Esenbeck and Henry (1837), 'Das System der Pilze; Kützing (1849), 'Species Algarum'; Charles Robin (1853), 'Végétaux Parasites'; Küchenmeister (1857), 'Animal and Vegetal Parasites of Man'; Fuckel (1869-1870), 'Symbolæ Mycologiæ'; Eidam (1872), 'Mycologie'; Naegeli (1877), 'Die Niederen Pilze.'

In 1881 Winter, Rehm, Fischer, and Lindau's 'Die Pilze Deutschlands,' etc., began to appear, and in 1886 Saccardo's great work of reference, the 'Sylloge Fungorum,' began. Both have continued down to the present period. In 1890 Zopf's oft-quoted work, 'Die Pilze,' was published, and in 1900 Engler and Prantl's 'Pflanzenfamilien.' In 1907 Vuillemin started his new classification in his paper, 'Les Bases actuelles de la Systematique en Mycologie.'

Leaving now the systematic study, we turn to the discovery of forms parasitic in man, beginning with the ringworm discoveries of Remak (1837), Schönlein (1837), Gruby (1842), and Malmsten (1845), and passing through the days of Carter and Manson to those of Sabouraud, Brumpt, De Beurmann, and Gougerot, down to the last, and by no means least, Pinoy, whose valuable researches are of such use in tropical medicine.

The above rather dry account will enable the reader of this and the two following chapters to realize the references and the names of the genera and species. Nomenclature is, however, very confused, and an author, before he gives a fungus a name, should read 'Règles Internationales de la Nomenclature Botanique,' published in 1912. Unfortunately, it has been decided that the nomenclature of the Fungi Imperfecti, which are so important in tropical medicine, should commence with Fries' work, while we are in accord with Vuillemin, who says that Saccardo's 'Sylloge' should be the basis for all fungi.

With this brief history we will pass on to consider the *Fungaceæ* Linnæus, 1737, which, as we have already seen, belongs to the Regnum Vegetabile, division Thallophyta.

SUBDIVISION FUNGACEÆ Linnæus, 1737.

Synonym.—*Fungi auctores.*

Definition.—Thallophyta thread-like, with apical growth producing cells (hyphæ) or rows of cells (hyphæ), which collectively are termed a mycelium, and reproducing by freely escaping spores, which are formed either acrogenously at the end of hyphæ or endogenously in special cells (sporangia), situate either at the apex of a free hypha, or are formed by sexual cells, which may be enclosed in a fruit or perithecium, formed by the interlacing of mycelial threads without chromatophores or chlorophyl.

Morphology.—Fungi are Thallophytes without chlorophyl, and do not contain starch or chromatophores. Their vegetative body, or thallus, consists generally of a mass of filaments or threads termed the 'mycelium.' The threads or filaments forming the mycelium are called 'hyphæ.' The mycelial threads or hyphæ may be *septate* or *non-septate*. Their walls do not consist of ordinary cellulose, but of a substance known as *fungus-cellulose*, which does not stain blue by iodine and sulphuric acid.

Nutrition.—The fungi, being unprovided with chlorophyl, cannot make use of the carbon dioxide of the air, and therefore derive their carbonaceous food material from complex organic compounds, as, for instance, decaying organic substances.

Mode of Life.—Fungi live as parasites or as saprophytes. They may live one way or the other, according to circumstances. Fungi are parasites of man, of the lower animals, and of plants.

Biological Characters.—Recent researches have shown the great biological analogies between fungi and bacteria as regards production of toxins, agglutination, and immunization phenomena, etc. Charrin and Ostrowsky, Concetti, Roger, and others, have obtained a soluble toxin from *Monilia albicans*. Auclair and Verliac have isolated from *Nocardia bovis* a toxic product soluble in ether, which they call 'actinomycetine.' They state that the injection of this substance produces the same lesions as the fungus. Ceni, Besta, Otto, and others, have obtained various toxins from fungi of the genus *Aspergillus*.

Macfadyen, by vaccinating animals with cultures of a saccharomyces, and G. H. Rogers and Concetti, using *Monilia candidans* Robin, have noticed a production of specific agglutinins and immune bodies. Similar results have been obtained by Quarelli using *Monilia balcanica* Castellani.

Plato, Bloch, Truffi, and others have prepared trichophyton vaccines by killing with heat, and triturating cultures of these fungi. By injecting these vaccines into patients suffering from trichophytoses, they have observed a general reaction, with fever, similar to the reaction obtained in tubercular patients by injecting tuberculin. De Beurmann has described a cuti-reaction in patients affected with sporotrichosis.

Widal and Abrami have introduced a general diagnostic method, 'sporo-agglutination,' based on the fact that the blood of patients suffering from diseases due to fungi contain specific agglutinins for the spores of such fungi. Non-specific coagglutinins may, however, be present in large amount.

Other biological reactions—complement fixation, etc.—have been described.

Reproduction.—The seeds of the Phanerogamia may be said to be represented in the fungi by the roundish or oval-shaped bodies called 'spores.' The spores multiply by budding, producing daughter spores, identical with the parent spores. Under certain conditions the spore, by a process of germination, gives rise to a true mycelial filament, which ramifies, producing mycelial hyphæ. Some of the terminal hyphæ are shorter and structurally different from the other hyphæ, and they become organs of fructification, which produce spores. The formation of spores upon these hyphæ takes place in various modes, of which five different types may be distinguished.

1. *Conidia or Exospores.*—These are non-sexual spores, which take origin by a process of budding or septation from the extremity of a germinal mycelial hypha or *sporophora*. The spores may all be of the same size, or, at other times, some are much larger, *macroconidia*, others smaller, *microconidia*. The conidia are at first always unicellular, but later they may divide and become multicellular.

2. *Chlamydospores or Endoconidia.*—These are asexual globular spores of great size, and provided with a thick membrane. Chlamydospores are terminal or intramycelial.

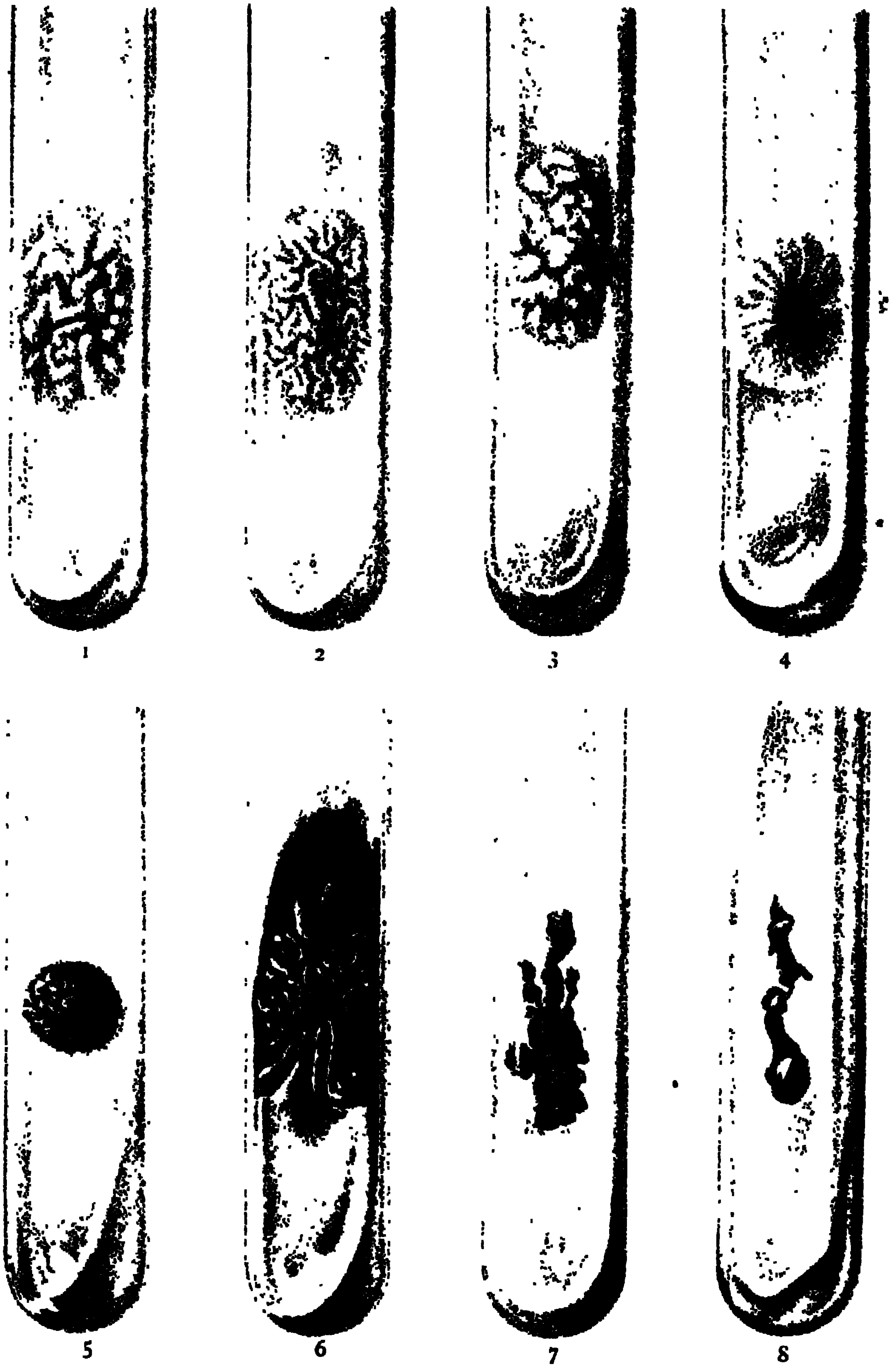
3. *Endospores or Gonidia.*—These spores take origin inside a special spore-case structure, or *sporangium*, which is often terminal and aerial. Endospores which are free and provided with organs of locomotion (cilia or flagella) are called *zoöspores*, and the sporangium is known under the name of *zoösporangium*.

PLATE V.

CULTURES OF SOME TROPICAL FUNGI.

1. ENDODERMOPHYTON CONCENTRICUM Blanchard, 1901, *emendavit* Castellani, 1911.
   Typical culture on glucose agar three weeks old.
2. ENDODERMOPHYTON TROPICALE Castellani, 1914.
   Old culture on glucose agar.
3. ENDODERMOPHYTON INDICUM Castellani, 1911.
   Fairly old culture on glucose agar.
4. ENDODERMOPHYTON INDICUM Castellani, 1911.
   Young culture on glucose agar.
5. EPIDERMOPHYTON RUBRUM Castellani, 1909
   Culture on glucose agar.
6. TRICHOPHYTON VIOLACEUM Bodin, 1902; VAR. DECALVANS Castellani, 1911.
   Culture on Sabouraud's agar.
7. CLADOSPORIUM MANSONI Castellani, 1905.
   Culture on Sabouraud's agar.
8. NIGROCOCCUS NIGRESCENS Castellani, 1910.
   Culture on Sabouraud's agar.

PLATE V.



CULTURES OF SOME TROPICAL FUNGI.

Geo. Waterston & Sons, Ltd. Edin.

To face page 970

***Ascus Fructifications*, or *Asci*, are special sporangia, containing four or eight or a multiple of eight spores arranged in a single line. These spores are called *ascospores*. Each ascospore presents two membranes, *one internal, one external*. The external membrane frequently shows a pore, which is called the *germinating pore*.**

***Basidia Fructifications*.**—Basidia are large elongated cells, each of which supports at its apex two or four slender processes (sterigmata), each terminating in a small roundish conidium or basidio-spore.

4. *Zygospores*.—These are the product of a process of conjugation or modified sexual act between two special hyphæ. These hyphæ give rise to small club-shaped branches, which come into contact and fuse together, forming a new large cell, which presents a very resistant double wall. The special branches (*gametes*) which come into contact and unite to produce the *zygospore* do not show any apparent sexual differentiation.

5. *Oöspores*.—These are formed by a complete sexual act or fertilization, and can therefore be compared with a fertilized ovum.

The female element (*oösporangium, oögonium*) contains one or more roundish protoplasmatic masses (macrogametes or *oöspheres, female gametes*), and presents a thick wall pierced by several *pores*. The male gamete (*antheridium*), which originates on a delicate special hypha, comes into contact with the oösporangium, sending a protoplasmatic process through it. In other cases the *antheridium* divides into several motile bodies called *microgametes, antherozoids*, or *spermatozoids*, which come into contact with the oösporangium, and fertilization takes place. In some rare cases the transformation of the oösporangium into an oöspore is in reality a process of parthenogenesis.

Classification.—The Fungaceæ may be arranged in two divisions, viz.:—

A. Vegetative body a multinucleate naked plasmodium—*Myxomycetes*.
B. Vegetative body usually filamentous—*Eumycetes* Schroeter, 1892.

We are only concerned with the Eumycetes.

Eumycetes Schroeter, 1892.

The Eumycetes may be classified as follows:—

A. Mycelium continuous in the vegetative stage—Class I., *Phycomycetes* De Bary, 1856.
B. Mycelium septate:—
    I. Spores in asci—Class II., *Ascomycetes* Berkeley.
    II. Spores in basidia—Class III., *Basidiomycetes* De Bary, 1856.
    III. Spores not in asci or basidia, but on conidiophores, naked or in pycnidia or unknown—Class IV., *Fungi Imperfecti* Fuckel, 1869.

The fungi parasitic in man are practically all found among the Phycomycetes, the Ascomycetes, and the Fungi Imperfecti. Only one species of importance is found among the Basidiomycetes, and none among the Myxomycetes.

CLASS I. PHYCOMYCETES DE BARY, 1856.

Definition.—Eumycetes with mycelium continuous in the vegetative stage.

Type Genus.—*Mucor* Micheli, 1729.

Classification.—The Phycomycetes may be divided into subclasses as follows:—

A. Sexual spores when present isogamous (similar gametes)—Subclass 1, *Zygomycetes*.
B. Sexual spores when present heterogamous (dissimilar gametes)—Subclass 2, *Oomycetes*.

ZYGOMYCETES.

Definition.—Phycomycetes with similar gametes.

Classification.—The Zygomycetes may be divided into two orders:—

A. Several asexual spores in sporangia—Order 1, *Mucorales*.
B. Solitary asexual spore, a true conidium, on conidiophore—Order 2, *Entomophthorales*.

Only the first order is of interest to us.

ORDER MUCORALES.

Definition.—Zygomycetes with several asexual spores in a sporangium, which in some genera are conidia like bodies.

Type Genus.—*Mucor* Micheli, 1729.

Classification.—The Mucorales may be divided into the following families:—

A. Asexual spores in typical sporangia, in some genera few spored.
   I. Columella present, zygospores naked and thinly covered—Family 1, *Mucoraceæ*.
   II. Columella absent, zygospores closely covered by hyphæ—Family 2, *Mortierellaceæ*.
B. Asexual spores not in typical sporangia—Families *Choanephoraceæ*, *Chætocladiaceæ*, *Piptocladiaceæ*.

Only the Mucoraceæ are of importance to us.

FAMILY MUCORACEÆ.

These organisms have a ramified thallus, branches taking origin laterally or by dichotomy. Some species are provided with *rhizoids*, root-like hairs by which they are attached to the surface on which they grow. From the surface of the mycelium some aerial branches called 'gonidiophores' take origin, each of which supports on its distal extremity a pear-shaped, globular, or claviform sporangium called *gonidangium*. The *sporangium* is at first separated from the gonidiophore by a septum, which later protrudes into the lower portion of the sporangium to form a variously shaped structure termed the *columella*.

Inside the sporangium or gonidangium *endospores* or *gonidia* develop by free cell-formation.

The sporangial protoplasm not used in the formation of endospores gives rise to a peculiar mucilaginous substance, which at a later period, by absorption of water, causes the bursting of the sporangium. Each endospore or gonidium, when it has become free, gives rise to a mycelial tube by germination. This mycelial tube ramifies, and a new mycelium is formed.

In some species, under certain conditions, a sexual reproduction may take place. This consists in the conjugation of undifferentiated non-motile gametes, which leads to the formation of zygospores.

Many species, when vegetating in unfavourable media, reproduce only by formation of conidia and chlamydospores.

The Mucoraceæ are extremely common as parasites or saprophytes of plants and animals. A mycosis due to these parasites is often termed 'mucormycosis.'

Mucoraceæ can be easily grown on sugar culture media—for instance, Sabouraud's maltose agar—or even on ordinary agar. The optimum temperature for their growth is between 35° and 40° C. The Mucoraceæ require plenty of oxygen, and therefore the media tubes must never be closed with rubber caps. When there is not enough oxygen, the Mucoraceæ lose their characteristics, and give rise to monilia-like or yeast-like forms.

Classification.—Four genera of Mucoraceæ are found to contain species parasitic on man:—

Family Mucoraceæ	Mycelium ramified, no rhizoids—*Mucor*. Mycelium non-ramified, with or without rhizoids; the peduncle supporting the sporangium terminates in a special formation encircling the base of the columella—*Lichtheimia*. Mycelium with rhizoids, columella ovoid—*Rhizomucor*. Mycelium with rhizoids; columella hemispheric, shaped like a mushroom—*Rhizopus*.

Genus Mucor Micheli, 1729.

Ramified mycelium; absence of rhizoids.

Mucor mucedo Linnæus, 1761.

Synonyms.—*Mucor vulgaris* Micheli, 1729; *M. sphærocephalus* Bulliard, 1791

The hyphæ carrying sporangia (sporangiophores) are long and erect; the sporangium is globular, 100 to 200 μ in diameter; its colour brownish; its surface covered by fine, minute crystals of oxalate of calcium. The spores (gonidia) are elliptical, with a smooth surface. The columella is ovoid-shaped, and generally yellowish. Occasionally very large zygospores may be observed.

M. mucedo L. is very common, living in organic substances in decomposition—for instance, horse-dung. It is the cause of a deadly disease in bees—the so-called 'mucorine,' or May's disease—but is seldom found in man. Fürbringer has observed it twice in cases of pulmonary infarcts. A case of broncho-pulmonary mucormycosis has been observed by Castellani in the Balcanic Zone.

Mucor pusillus Lindt, 1886.

Mycelium at first white, then yellowish. The hyphæ carrying sporangia are much shorter than in the preceding species. The sporangium is globular, at first pale greyish, then dark greyish. Its diameter varies between 50 and 80 μ. The columella is claviform, ovoid or spherical, yellowish or brownish. The spores are smooth, spherical, 3 to 3·5 μ in diameter.

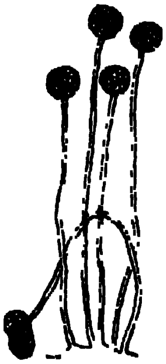


FIG. 479.—*Mucor mucedo* LINNÆUS.

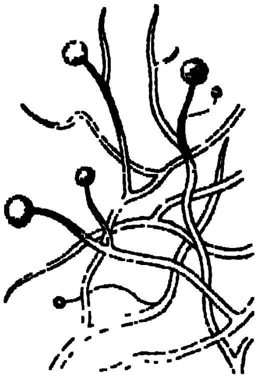


FIG. 480.—*Mucor pusillus* LINDT. (After Lindt.)

M. pusillus is often found in bread which has been soaked in water. It is very pathogenic to rabbits: it has once been found in man in a case of otomycosis by Jakowski.

Genus Lichtheimia Vuillemin, 1904.

Non-ramified mycelium; rhizoids may be present or not; peduncle supporting sporangium terminates in a formation encircling the base of the columella.

Lichtheimia corymbifera Cohn, 1884.

Synonym.—*Mucor corymbifer* Cohn, 1884.

Mycelium at first white, then yellowish. The sporangia are pear-shaped, 10 to 70 μ in diameter: columella conical, dark greyish or brownish: spores elliptical, 2 to 3 μ. The hyphæ carrying sporangia are ramified in corymbiform formation. This parasite has been observed several times in man, giving rise to a mycosis of the ear (Hückel, Siebenmann, Graham), of the nose (Siebenmann), of the lungs (Podack). A case of generalized infection has been recorded by Paltauf (see p. 977).

Lichtheimia ramosa Lindt, 1886.

Synonyms.—*Mucor ramosus* Lindt, 1886; *Lichtheimia ramosa* Vuillemin, 1904.

Closely resembles *L. corymbifera*, but rhizoids are often present. The spores are larger, ovoidal, 4 to 7 μ in length. The columella is always smooth.

This species has been observed in man by Jakowski in a case of otomycosis. According to Vuillemin, it is frequently found in the nasal mucosa of horses.

Genus Rhizomucor Lucet and Costantin, 1900.

Rhizoids generally present, columella of ovoid shape.

Rhizomucor parasiticus Lucet and Costantin, 1900.

Mycelium at first greyish, later brownish. Sporangium globular, 35 to 80 μ. Hyphæ carrying sporangia are often ramified, and are between 1 and 2 centimetres in length. They are often provided at their basal portion with rhizoids.

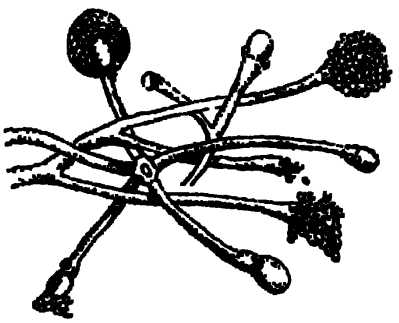


FIG. 481.—*Lichtheimia corymbifera* VUILLEMIN. (After Lichtheim.)

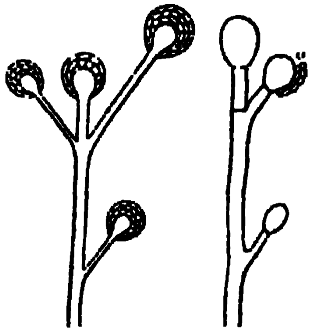


FIG. 482.—*Rhizomucor parasiticus* LUCET AND COSTANTIN. (After Lucet and Costantin.)

The columella is ovoid or pyriform; dark brownish; spores ovoid; longitudinal diameter, 4 μ, transverse diameter, 2·5 μ.

R. parasiticus is pathogenic for guinea-pigs and rabbits. It was found in the expectoration of a woman by Lucet, Costantin, and Lambry. The patient had been considered at first to be suffering from tuberculosis. She recovered under a potassium iodide and arsenical treatment.

Rhizomucor septatus von Bezold, 1889.

Synonyms.—*Mucor septatus* von Bezold; *Rhizomucor septatus* Lucet and Costantin, 1889.

Rhizoids present; sporangia of a brownish-greyish colour, spherical, with a smooth, or occasionally slightly moriform surface; diameter about 30 to 35 μ columella spherical, brownish; spores roundish or slightly oval, from 2·5 to 4 μ.

The spores are of a yellowish or brownish colour; spherical or ovoid, with a smooth surface.

This species was found by Siebenmann in a case of otomycosis.

Genus Rhizopus Ehrenberg, 1820.

Rhizoids present; columella hemispheric; mushroom-like.

This genus contains only one species.

Rhizopus niger Ciaglinski and Hewelke, 1893.

Synonym.—*Mucor niger* Ciaglinski and Hewelke, 1893

The mycelial filaments are provided with abundant rhizoids forming a snow-white mass. Sporangia globular, of black colour when ripe. Spores ovoid, smooth. Columella is at first globular, but later takes a cylindrical shape, and when the spores have become detached, shows a peculiar mushroom-like appearance.

FIG. 483.—*Rhizomucor septatus* VON BEZOLD. (After Siebenmann.)

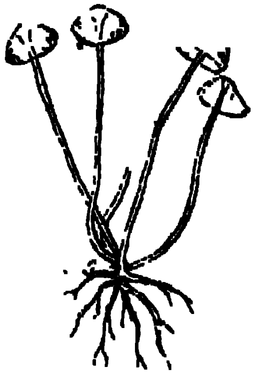


FIG. 484.—*Rhizopus niger* CIAGLINSKI AND HEWELKE. (After Ciaglinski.)

This species was discovered by Ciaglinski and Hewelke in a case of black mycosis of the tongue.

General Remarks on Mycoses due to Species of the Family Mucoraceæ.

These mycoses are generally called mucormycoses. They have been recorded several times in man.

MUCORMYCOSIS OF THE NOSE.—Several cases are on record in which species of Mucoraceæ (generally *Lichtheimia corymbifera*) were found in various affections of the nose. Their pathogenic rôle in such affections has not been demonstrated with certainty.

MUCORMYCOSIS OF THE TONGUE.—Ciaglinski and Hewelke, and later Seniyiak, have described cases of so-called 'black tongue,' due to *Rhizopus niger*.

MUCORMYCOSIS OF THE EAR—OTOMUCORMYCOSIS.—Several cases are found in the literature (Siebenmann, Böke, Hückel, etc.). Almost always *Lichtheimia corymbifera* was present. In the tropics we have observed two cases in which *L. ramosa* occurred. When the fungus is in great quantity, the patient complains of tinnitus aurium and deafness—the same symptoms as those produced by a plug of cerumen in the external auditory meatus.

MUCORMYCOSIS OF THE LUNGS.—This condition is rare. Fürbringer has described two cases in which *L. corymbifera* was found at the autopsy in some hæmorrhagic foci in the lungs. Lucet, Costantin, and Lambry described a case of bronchitis in a woman due to *Rhizomucor parasiticus*. The expectoration was rather scanty and mucopurulent, but without blood. Mycelial threads and spore-like bodies were present. Cultures were made, and the fungus grown. The condition lasted several months. Potassium iodide was given, and later, owing to the symptoms of iodism, various arsenical preparations. Castellani has recorded a case of bronchomucormycosis due to *Mucor mucedo*, in the Balcanic Zone.

General Mucormycosis.—One case only is on record—that of Paltauf. The patient during life presented fever, slight jaundice, enlargement of the spleen and liver, with signs of diffuse bronchitis and obscure nervous symptoms. At the post-mortem the brain presented several foci of a friable, yellowish substance; the other internal organs showed nodules of various size, some rather hard; others had undergone a purulent change. In all these formations mycelial threads were found; in the lung-nodules fructifications (sporangia) were also present, which enabled Paltauf to determine the fungus as *Lichtheimia corymbifera*. According to him, the infection must have originated from the intestine, which showed several ulcerative lesions containing the same fungus.

REFERENCES.

Current Literature.

This is very scattered, but references can usually be found in the *Bulletin de l'Institut Pasteur*, while original papers may be found in the *Archives de Parasitologie*, edited by R. Blanchard; in the *Centralblatt f. Bakteriologie*, in the principal journals of dermatology, such as the *British Journal of Dermatology*, the *Archiv für Dermatologie und Syphilis*, the *Annales de Dermatologie*, *Il Giornale Italiano delle Malattie della Pelle*, and *Lo Sperimentale*.

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CHAPTER XXXVIII

ASCOMYCETES AND BASIDIOMYCETES

Preliminary—Classification—Protoascomycetes—Saccharomycetales—Saccharomycetaceæ—Endomycetaceæ—Euascomycetes—Gymnoascaceæ—Aspergillaceæ—Pyrenomycetes—Basidiomycetes—References.

PRELIMINARY.

THIS chapter includes an account of the fungi parasitic on man which belong to the Ascomycetes. These fungi are characterized by their mode of reproduction—viz., by spores originating inside special cells called *asci*. The spores (ascospores, endospores, gonidia) inside the asci are generally four or eight or a multiple of eight. While these fungi live a parasitic life, no asci are found, and reproduction takes place by germination and conidia. The fungi belonging to this order are often pleomorphic, their morphological characters changing according to the medium on which they live.

Classification.—The Ascomycetes are divided into subclasses as follows:—

- A. Asci with varying number of spores, usually numerous—*Hemiascomycetes*.
- B. Asci with a definite number of spores:—
  - I. Asci separate or scattered—*Protoascomycetes*.
  - II. Asci approximate, usually forming a hymenium—*Euascomycetes*.

SUBCLASS PROTOASCOMYCETES.

This subclass contains a single order, the Saccharomycetales.

ORDER SACCHAROMYCETALES.

This order is divided into two families as follows:—

- A. Vegetative cells single or loosely attached in irregular colonies—*Saccharomycetaceæ*.
- B. Vegetative cells forming a mycelium—*Endomycetaceæ*.

FAMILY SACCHAROMYCETACEÆ REES, 1870.

Definition.—Protoascomycetes with vegetative cells single or loosely attached in irregular colonies; mycelium not usually developed; asci isolated, not differentiated from vegetative cells.

Remarks.—These organisms are generally round or ovoid cells, presenting a cell wall of single or double contour; the internal protoplasmatic mass often shows granules and vacuoles. During active vegetation as parasites they reproduce by a ***budding process***, hence the name of ***budding fungi***; when living on artificial media, under unfavourable nutritive conditions, or in the absence of oxygen, they multiply also by formation of endospores or ascospores. Each cellular element may become an ascus containing 1-4, sometimes more, up to 12 spores (ascospores).

The organisms are, as a rule, unicellular plants, but at times the cells elongate, and a rudimentary mycelium may be formed. This occurs, for instance, when the organisms are cultivated in certain fluid culture media—for example, fluid beer-wort. In such cases side-buds, which separate into conidia-like bodies, may also develop on the hyphæ.

Classification.—The family contains thirteen genera, of which only two—*Saccharomyces* Meyen, 1837, and *Willia* Hansen, 1904—contain species parasitic on man; while, in regard to *Schizosaccharomyces* Beyerinck, 1893, it appears doubtful to us whether this really should be placed in this family, as it reproduces by division instead of by budding. The various genera may be recognized as follows:—

- A^1. Vegetative cells globose, ovoid, or pyriform, without lemon-shaped extremities:—
  - B^1. *Vegetative cells increase by budding*:—
    - C^1. Vegetative cells without large fat globule; asci 3-4 spored:—
      - D^1. *Ascospores globose or ovoid*:—
        - E^1. On germination spores form typical yeast cells:—
          - F^1. *Ascus formation not preceded by zygosis*:—
            - G^1. Spore membrane single:—
              - H^1. Spore membrane verrucose—*Debaryomyces* Klöcher.
              - H^2. Spore membrane verrucose and possessing a superficial elevated linear process, dividing the surface into two unequal portions—*Schiönniomyces* Klöcher.
              - H^3. Spore membrane without verrucosities or crest—*Saccharomyces* Meyen, 1838.
            - G^2. Spore membrane double—an inner, *endosporium*, and an outer, *exosporium*—*Saccharomycopsis* Schiönning.
          - F^2. Ascus formation preceded by zygosis:—
            Ascospores have a smooth membrane—*Zygosaccharomyces* Barker, 1901.
        - E^2. On germination spores form a poorly developed promycelium, multiplication by a process intermediate between budding and transverse division—*Saccharomycodes* Hansen, 1904.
      - D^2. Ascospores pileiform or limoniform; costate with bowler-hat shape. No alcoholic formation, but ethers produced, with pleasant fruity odour, in sugar media—*Willia* Hansen, 1904.
      - D^3. Ascospores spherical, hemispherical, or irregularly shaped. Thick pellicle with air-bubbles on sugar liquid media—*Pichia* Hansen, 1904.
    - C^2. Vegetative cells large, spherical, each containing a large fat globule as in torula. D. Asci 8-spored—*Torulaspora* Linder.
  - B^2. *Vegetative cells increase by fission*:—Asci 8-spored—*Schizosaccharomyce* Beyerinck, 1893.
- A^2. Vegetative cells oval, with one or both extremities lemon-shaped. Asci 1-spored—*Hansenia* Linder.
- A^3. Vegetative cells elongate, cylindrical, spores filiform.
  Asci 1-spored—*Monospora* Metchnikoff.
  Asci 8-spored; ascospores flagellate—*Nematospora* Peglion.

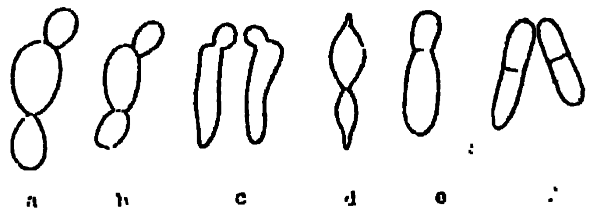


FIG. 485.—TYPES OF YEASTS.
a, Saccharomyces cerevisiæ; *b*, S. ellipsoideus; *c*, S. pastorianus; *d*, S. apiculatus; *e*, Saccharomycodes; *f*, Schizosaccharomyces.
(After Lindner.)

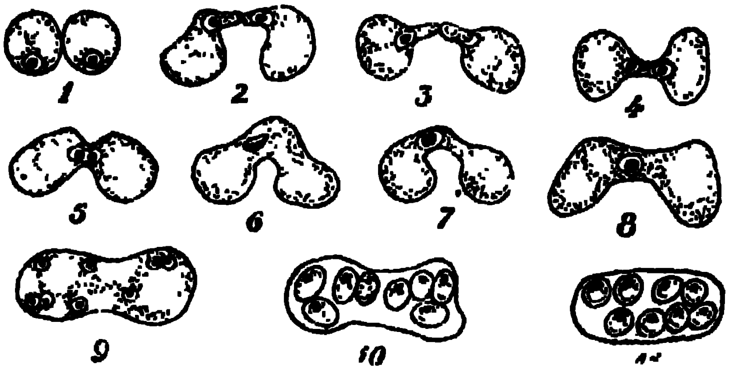


FIG. 486.—ZYGOSIS AND FORMATION OF AN ASCUS IN *Zygosaccharomyces octosporus*.
(After Guilliermond.)

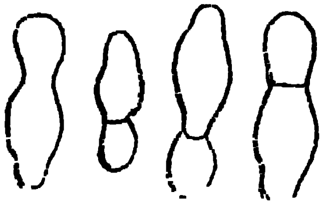


FIG. 487. — REPRODUCTION OF SACCHAROMYCODES.

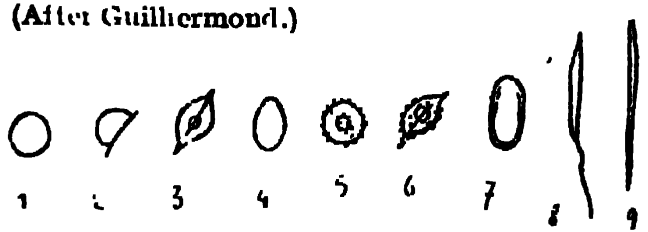


FIG. 488.—TYPES OF ASCOSPORES.
1, Saccharomyces; 2-4, Willia; 5, Debaryomyces; 6, Schwanniomyces; 7, Saccharomycopsis; 8, Monospora; 9, Nematospora.
(After Guilliermond.)

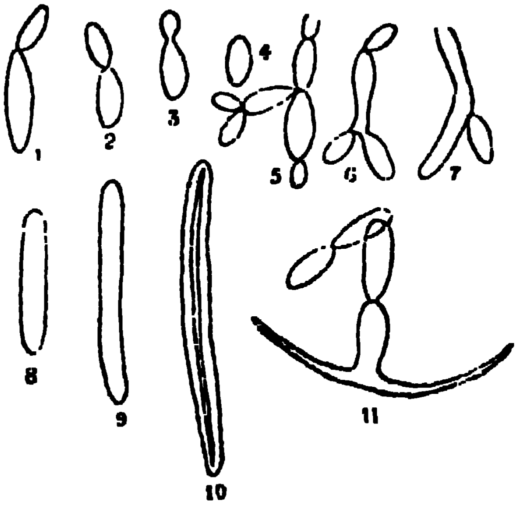


FIG. 489.—*Monospora cuspidata.*
1-7, Budding cells; 8-9, Ascus formation; 10, Ascospore germinating.
(After Metchnikoff and Guilliermond.)

Genus Saccharomyces Meyen, 1838.

Definition.—No proper thallus. Reproduction by budding and ascospores; fermentation of glucose and saccharose, and often of other carbohydrates. Ascospores with one membrane. No trace of any copulative process. Occasionally rudimentary mycelial tubes present, with transverse septation.

Remarks.—As already stated, the fungi of this genus, as well as of the genera *Cryptococcus*, *Monilia*, *Oidium*, and *Coccidioides*, are usually called Blastomycetes, and the diseases induced by them blastomycoses.

The fungi of the genera *Saccharomyces*, *Cryptococcus*, and *Coccidioides* have a great importance in dermatology, as they give rise to peculiar ulcerative affections of the skin, often resembling a syphilide or a tuberculide. The first cases of blastomycosis were observed in America by Posadas, Wernike, and others, who at first believed them to be a protozoal infection. Later Gilchrist, Ricketts, and others recognized the true nature of the parasites. By some authors (Sanfelice, Roncali, etc.), cancer has been considered to be of blastomycetic origin.

Fungi of the genus Saccharomyces are very important from an industrial and agricultural standpoint, being the cause of alcoholic fermentation. The best-known yeast is the brewer's yeast, *S. cerevisiæ*, which is slightly ovoid, 8 to 9 μ in diameter.

Saccharomyces blanchardi Guiart, 1906.

Found at an operation by Blanchard, Schwartz, and J. Binot, on a patient who had been considered to be suffering from tubercular peritonitis. The fungus had produced in the peritoneum a large, whitish, gelatiniform mass, weighing about 1 kilogramme. The fungus grew well on all sugar media.

On maltose agar it produced crateriform colonies of a snow-white colour. Presence of asci with eight spores. On gelatine mucoid-like, of greyish colour. Slow liquefaction of the medium. On potato mucoid growth, whitish, darkening after a long time. On carrot growth viscid, abundant; pathogenic to rabbits, in which it induced a general mycosis, terminating fatally.

Saccharomyces granulatus Vuillemin and Legrain, 1900.

Observed by Vuillemin and Legrain in a tumour of the submaxillary bone. Cells ovoid, 4 to 5 μ in length, and 3 to 4 μ in breadth. Cultures pinkish or pinkish-red; ascospores and chlamydospores present. Gelatine not liquefied. Sugar reactions not given.

Saccharomyces tumefaciens Curtis, 1896.

Synonym.—*Saccharomyces subcutaneus tumefaciens* Curtis, 1896.

Found by Curtis in a myxomatous tumour. It appeared in the tissues in the shape of spherical bodies 16 to 20 μ in diameter, each surrounded by a zone of amorphous substance. Grows well on all sugar media; in very old cultures asci are seen, with 1–4 spores.

Gelatine with surface growth whitish; no liquefaction. Said to ferment saccharose, but not maltose or lactose. Its action on glucose is not mentioned. Pathogenic to rats and dogs.

Saccharomyces samboni Castellani, 1907.

Cells roundish 6 to 8 μ in diameter—easily grown on various media, producing white colonies, which rapidly coalesce. Found by Castellani in Ceylon in a few cases of intertriginous dermatitis of the cruro-scrotal region. A similar or identical organism has been observed by Whitfield in England in a case of the same dermatitis. Ferments glucose, levulose, and maltose. Gelatine is not liquefied. In very old cultures asci present.

Saccharomyces ellipsoides Rees, 1870.

Found by Maggiora and Gradenigo in two cases of chronic otitis media. The cells are elliptical, about 6 μ in maximum diameter; presence of asci. Maggiora and Gradenigo do not consider this fungus to be pathogenic. The yeast is found on ripe grapes, and has been carefully described by Hansen, *Asci ellipsoide* containing 1-4 spores each. The fungus often produces a pellicle in sugar fluid media. Ferments glucose, maltose, and saccharose.

Saccharomyces hominis Klein and Gordon, 1903.

Isolated in some cases of tonsillitis clinically resembling diphtheria. Roundish or oval cells, 5 to 7 μ in diameter. Pathogenic to guinea-pigs and rabbits. Sugar reactions unknown.

Saccharomyces anginæ Achalme and Troisier, 1895.

Found by Achalme and Troisier in a case of tonsillitis showing white patches; *in situ* cells ovoid, 8-15 × 5-6 microns. In cultures asci, 4-spored, present. On gelatine surface growth white. Ferments saccharose, but other reactions not given.

Saccharomyces balzeri Balzer, Burnier, and Gougerot, 1911.

Synonym.—*Parendomyces balzeri* Balzer, Burnier, and Gougerot, 1911.

Grows on culture media under the type of oval or roundish yeast-like cells, proliferating by budding. Isolated by Balzer, Burnier, and Gougerot from a gummatous affection. Sugar reactions unknown.

FIG. 490.—CRATERIFORM COLONIES *Saccharomyces blanchardi* GUIART. (After Blanchard, Schwartz, and Binot, from Brumpt.)

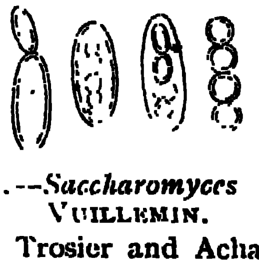


FIG. 491.—*Saccharomyces anginæ* VUILLEMIN. (After Trosier and Achalme.)

Saccharomyces roseus Maggiora and Gradenigo, 1890.

Found by Maggiora and Gradenigo in the Eustachian tube, and considered by them to be non-pathogenic. Cultures of pink colour. Sugar reactions unknown.

Genus Willia Hansen, 1904.

Definition.—Saccharomycetaceæ with ascospores lemon-shaped or hat-shaped (see Fig. 492). As a rule do not produce alcoholic fermentation, but produce various ethers. Cultures present a pleasant fruity odour.

Species in Man.—*Willia anomala* Hansen, 1904.

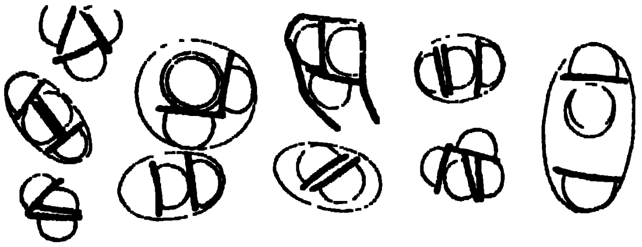


FIG. 492.—ASCOSPORES OF *Willia anomala* HANSEN. (After Guilliermond.)

Willia anomala Hansen, 1904.

Rather small oval cells. In sugar liquid media it forms a well-marked membrane, containing air-bubbles. Asci with 2-4 spores of the so-called hat-like type. Glucose fermented, but not saccharose or maltose. Ferments beer-wort, with production of ethers. Found by Beauverie and Lesieur in the sputum of a tubercular patient.

FAMILY ENDOMYCETACEÆ.

Definition.—Mycelium usually well developed, multiseptate; asci 4-8 spored; spores one-celled.

- A. Mycelium poorly developed—*Podocapsa.*
- B. Mycelium well developed:—
  - I. Asci formed after zygosis—*Eremascus.*
  - II. Asci formed asexually:—
    - (*a*) Asci 4-spored—*Endomyces.*
    - (*b*) Asci 8-spored—*Oleina.*
    - (*c*) Asci with a large number of spores—*Coccidioides.*

Only Endomyces and Coccidioides concern us.

Genus Endomyces Rees, 1870.

Definition.—Endomycetaceæ with mycelium abundant, ramified or not, simple or septate. Presence of budding and asci with four spores. Reproduction by external spores, ascospores, and spores situated inside the mycelial tubes.

Remarks.—Vuillemin believed at one time that the thrush fungus belonged to this genus. Researches carried out by Castellani have demonstrated that the condition known as *thrush* may be caused by various fungi. These fungi, as a rule, do not reproduce by ascospores, and, as justly remarked by Pinoy and Vuillemin himself, belong to the genus *Monilia* (see p. 1079). For the fungus isolated once by Vuillemin, which has all the characteristics of the genus *Endomyces*, Landrieu has suggested the term *Endomyces vuillemini.*

Endomyces vuillemini Landrieu, 1912.

Synonym.—*Endomyces albicans* Vuillemin, 1898.

Found by Vuillemin in 1898 in thrush patches.

Parasitic Life.—This fungus forms white patches on the tongue and buccal mucosa. The patches are easily detached. A particle examined under the microscope shows septate mycelial threads, simple or ramified, the articles of which are straight or somewhat bent. Each article or cell is about 20 μ in length, and 3 to 5 μ in breadth. At the terminal portion of each mycelial thread three or four shorter ovoid elements are found which reproduce by budding. Some similar ovoid or roundish globular refringent cells can be observed, originating laterally at the septations of the mycelium. These globular elements, which were at first considered to be spores, become detached, and reproduce by germination.

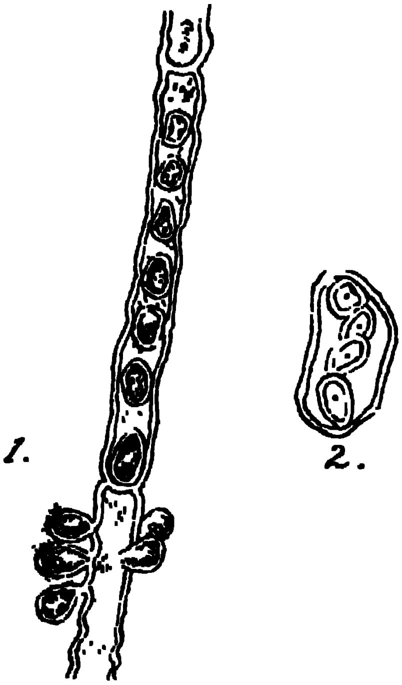


FIG. 493.—*Endomyces vuillemini* LANDRIEU.

(From a culture. After Vuillemin.)

1, Mycelial threads, with endospores and conidia; 2, ascus fructification.

Saprophytic Life--Culture Characters. - The fungus grows well on slightly acid, Sabouraud's, and other media; does not grow abundantly in alkaline media; does not ferment lactose and is Gram-positive.

In cultures the fungus appears under two forms: (1) A filamentous form, showing the mycelial threads simple or ramified. (2) A globular form, morphologically similar to a typical yeast, and reproducing by budding. Both forms may be found in the same culture.

The fungus in cultures reproduces by:—

1. Chlamydospores or external spores; large globular cells 10 to 20 μ in diameter, with thick resistant walls. The chlamydospores are situate at the terminal extremity of some mycelial hyphæ, and represent modified mycelial articles.
2. Asci containing four ascospores.
3. Internal spores. These are oval cells with membrane, protoplasm, and nucleus similar to the external spores. The internal spores are arranged in a single string inside some mycelial tubes.

Pathogenicity.—The fungus was found by Vuillemin in a case of *thrush*, a condition generally due to fungi of the genus *Monilia* (see p. 1079).

Genus Coccidioides Rixford and Gilchrist, 1896.

Definition.—Endomycetaceæ with mycelium well developed and asci containing a large number of spores, with intermediate characters between *Saccharomyces* and *Monilia*. One species only: *Coccidioides immitis* Rixford and Gilchrist, 1896.

Coccidioides immitis Rixford and Gilchrist, 1896.

Synonyms.—*Coccidioides pyogenes* Rixford and Gilchrist, 1896; *Oidium coccidioides* Ophüls, 1905; *O. protozoides* Ophüls, 1905; *Posadasia esferiformis* Cantón, 1898; *Oidium immite* Verdun, 1907.

Definition.—Coccidioides with a large number of spores in the asci.

Discovered by Wernicke in 1882 in America in a patient with patches resembling a tuberculide, and gummata. In the lesions roundish bodies are seen of various sizes, 3 to 80 μ in diameter, with a well-defined thick membrane. Inside some of the bodies numerous spores may be seen. This genus is not well defined.

Cultures.—The fungus grows under two types: (1) a saccharomyces-like type, reproducing by budding; (2) a filamentous type. The colonies are roundish, slightly elevated, but deepening into the medium. They are grey or white, but when old often become brownish. In old cultures chlamydospores may be present. The biochemical properties of the fungus are not known.

Pathogenicity.—The fungus induces in man a type of blastomycosis (see p. 2084). It is pathogenic to monkeys, mice, guinea-pigs, and rabbits. It probably lives saprophytic in nature.

SUBCLASS EUASCOMYCETES.

Definition.—Ascomycetes with asci not separate or scattered, but approximate, usually forming a hymenium, and with a definite number of spores in an ascus.

Classification.—According to Stevens, the following orders may be recognized:—

- A. Asci approximate, no definite ascoma, but an indefinite hymenium—*Protodiscales*.
- B. Asci grouped in a definite ascoma:—
  - I. Asci not in a cylindrical or globose perithecium—*Helvellales*, *Pezizales*, *Phacidiales*, *Hysteriales*, *Tuberales*.
  - II. Asci in a cylindrical or globose perithecium:—
    - (*a*) Perithecium sessile:—
      - 1. Asci arising from a common level in the perithecium—*Perisporiales*, *Hypocriales*, *Dothidiales*, *Sphæriales*, *Pyrenomycetes*.
      - 2. Asci arising at different levels in the perithecium—*Aspergillales*.
    - (*b*) Perithecium on a short pedicle—*Laboulbeniales*.

Only the Aspergillales and the Pyrenomycetes interest us. The latter differ from the former by having their asci arranged in a hymenium within the closed ascocarp.

ORDER ASPERGILLALES.

Definition.—Euascomycetes with asci gathered into definite cylindrical or globose perithecia.

Type Family.- Aspergillaceæ.

Classification.- The order contains a number of families, which may be recognized as follows:—

A. Peridium of loose floccose hyphæ— *Gymnoascaceæ* Baranetsky, 1872.
B. Peridium compact:—
  I. Perithecia small:—
    (*a*) Perithecia mostly sessile:—
      1. Peridia closed—*Aspergillaceæ*.
      2. Peridia open—*Trichocomaceæ*.
    (*b*) Perithecia mostly stalked—*Oxygenaceæ*.
  II. Perithecia large—*Elaphomycetaceæ* and other families

Only the Gymnoascaceæ and the Aspergillaceæ concern us.

FAMILY GYMNOASCACEÆ BARANETZKY, 1872.

Definition.—Aspergillales with the peridium composed of loose hyphæ, at the extremities of which the asci are situate, or without perithecial or ascal formation, and reproducing (as far as is known), as a rule, by mycelial or conidial spores.

Type Genus.- *Gymnoascus* Baranetzky, 1872.

Classification.- From the definition given above, it is obvious that the family is capable of being divided into two tribes, as follows:—

A. *Ascomycetes type* :—
  With perithecia and asci—Tribe 1, *Gymnoasceæ* Castellani and Chalmers, 1918.
B. *Fungi Imperfecti type* :—
  Without perithecia or asci. Reproduction asexual by mycelial and conidial spores—Tribe 2, *Trichophytoneæ* Castellani and Chalmers, 1918.

The first tribe includes the genera *Myxotrichum* Künze, 1823; *Gymnoascus* Baranetzky, 1872; *Ctenomyces* Eidam, 1880; ***Amauroascus*** Schroeter, 1893; *Arachniotus* Schroeter, 1893; and ***Eidamella*** Matruchot and Dassonville, 1901; but these are not directly concerned with tropical medicine, and will only receive a passing notice as required in the following pages.

The second tribe is, however, of considerable importance, and must be considered in some detail; but we must first inquire why the genus Trichophyton and its allies, which are included in this tribe, should be classified here.

It must be pointed out that Vuillemin would classify all these genera as follows:—***Class***, Fungi Imperfecti; ***Order***, Thallosporales; ***Suborder*** 1, Blastosporineæ; ***Family***, Oösporaceæ; ***Genus***, Achorion; ***Suborder*** 2, Arthrosporineæ; ***Genera***, Microsporum, Trichophyton, etc.

We, however, classify them as given above, and our reasons for so doing may be set forth in a short historical statement.

Historical.—In 1844 Gruby discovered the parasite of ringworm, and this was verified in 1845 by Malmsten, who proposed two generic names for the new fungus—*i.e.*, 'Trichophyton' or 'Trychomyces'—and one specific name, 'Tonsurans.' The first generic name has become established, and the genus, the systemic position of which we are about to review, is now known as *Trichophyton* Malmsten, 1845; very often the date given is 1848, which is that of the publication of the German translation, and not the date of the original Swedish work, the name being derived from *θρίξ*, 'hair,' and *φυτόν*, 'a plant.'

Malmsten believed the genus *Trichophyton* to be closely related to the genus *Torula* Persoon, 1801, and especially to the species *T. olivacea* Corda, 1837, and *T. abbreviata* Corda, 1837.

This relationship was adopted by Charles Robin in his celebrated work 'Histoire Naturelle des Végétaux Parasites,' published in 1853. His classification is as follows: Fungi: Division *Arthrosporei*; Tribe, *Torulacei*; Genus, *Trichophyton* Malmsten.

In 1886 Hallier regarded the relationship to be closely allied to the genus *Penicillium* Link, 1809.

In 1875 Grawitz made a new assertion, claiming that the relationship was with *Oospora* Wallroth, 1833 a view which was adopted by Baumgarten in his 'Pathologischen Mykologie' in 1890.

Later researches by Duclaux in 1886, by Verujsky in 1887, and still later by Sabouraud, indicated that some of the species should be classified near to *Sporotrichum* Link, 1809, which suggestion has been adopted by Saccardo in his 'Sylloge Fungorum,' though he goes further, making Trichophyton merely a synonym of *Sporotrichum*.

Bodin (1899-1902) brought forward views tending to show that the relationship is complex, some of the species being allied to *Endoconidium* Prillieux and Delacroix, 1891 (a genus which lately disappeared, having become *Stromatinia* Prillieux, 1897), while other species were held to be more closely related to *Acladium* Link, 1809, and to *Haplaria* Link, 1809. These views are based upon a study of the sporulation, and indicate that *Trichophyton* is a genus belonging to Fuckel's class *Fungi Imperfecti*, and, adopting the older methods of classification, to the subclass *Hyphomyceteæ* Martius, 1817, the family *Mucedinaceæ* Link, 1809, subfamily *Amerosporeæ* Saccardo, 1886, tribe *Macronemeæ* Saccardo, 1886, and subtribe *Botrytideæ* Saccardo, 1886

In June, 1899, Matruchot and Dassonville published a paper entitled 'Sur la Position systématique des Trichophytons,' and followed it later in the same year by another paper entitled 'Sur le *Ctenomyces serratus* (Eidam) comparé aux Champignons des teignes.' Briefly stated, their view is that the genus *Trichophyton* Malmsten, 1845, belongs to the Ascomycetes of De Bary, if this is taken to include Hemiascomycetes of Brefeld. In either case, whether these classifications or Schroeter's more detailed arrangement of the Ascomycetes be adopted does not concern our present purpose, as both contain the family Gymnoascaceæ (often written Gymnoasceæ), in which Matruchot and Dassonville place the genus *Trichophyton*.

Their reasons for this classification are:—

1. *Ctenomyces serratus* Eidam, 1880, is a fungus found on the feathers of birds, which, when cultivated on Sabouraud's proof media, produces growths strikingly analogous to those of species of Trichophyton.

2. *Ctenomyces serratus*, when inoculated into animals, gives rise to lesions, resembling a *Trichophyton* eruption, in which it appears in a filamentous form.

3. A fungus closely resembling a ctenomyces, which they found in a ringworm in a dog, when cultivated gave rise to perithecia. For this fungus they created a new genus, *Eidamella* Matruchot and Dassonville, 1901, calling the given species *Eidamella spinosa* Matruchot and Dassonville, 1901.

Against this view Sabouraud has pointed out that in the cultures of this fungus they found intercalary chlamydospores but neither fusiform bodies nor the conidia usually seen in Trichophyton cultures, and therefore he considers their demonstration to be still incomplete.

Chalmers and Marshall in 1914 pointed out that they had found oval perithecia in very old cultures of *Trichophyton currii*. The peridium was at first loose, but hardened later, and contained a number of asci situate at different levels, but these were degenerate and did not contain ascospores. The perithecia were judged to belong to the Trichophyton, because there was no sign at any time of any other organism in or on the growth, macroscopically or microscopically, and the perithecia appeared at the same time all through the culture. When very old the peridium became compact and like that of the Aspergillaceæ, but at that stage they consisted of the outer wall only, the contents having all disappeared. They therefore considered that their observation supported the views of Matruchot and Dassonville.

We therefore classify the genus Trichophyton in the Gymnoascaceæ, but the very large number of species included in that genus exhibit such different characters that they can easily be arranged in groups, which appear to us to be of generic value, especially as we know that Malmsten meant only the form we now call 'endothrix' to be designated by his name Trichophyton, because he states:—'The mould formation appears in the root of the hair, and it occurs *only* inside of the hair, between its fibres, so that the epithelial layer is uninfected: besides, there is no mould formation to be found among the epidermal cells, so that one can say with good reason that the disease absolutely belongs to the hair.'

We have therefore distinguished the other groups by the generic names *Ectotrichophyton*, *Neotrichophyton*, and *Atrichophyton*, given below.

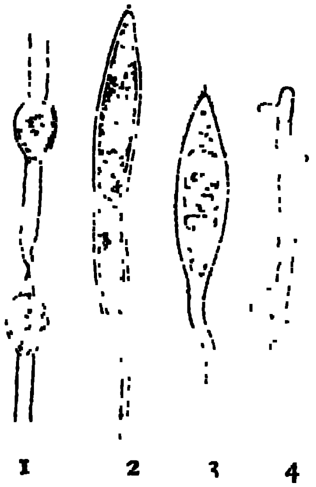


FIG. 494. -- *Microsporum audouini* GRUBY.

(After Bodin.)

1, Chlamydospores; 2, spindle; 3, pluri-septate spindle; 4, spore-bearing hypha; type Acladium.

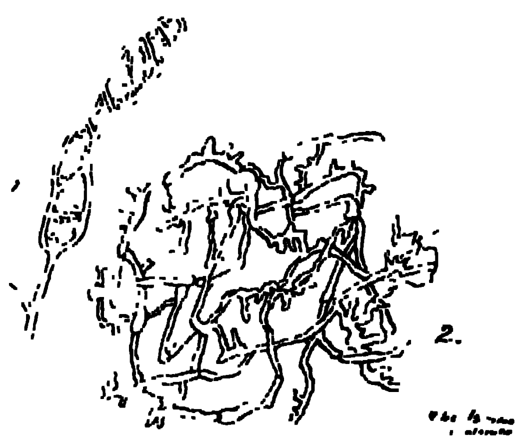


FIG. 495. — *Microsporum audouini* GRUBY.

(From cultures.)

1, Septate spindle body; 2, mycelium, with denticulated structures.

TRIBE TRICHOPHYTONEÆ Castellani and Chalmers, 1918.

Definition.—Gymnoascaceæ of the Fungi Imperfecti type.

Type Genus.—*Trichophyton* Malmsten, 1845.

Classification.—The various genera belonging to this tribe may be recognized as follows:—

A. *In lesions* only mycelial filaments and no spores present—Genus *Lophophyton* Matruchot and Dassonville, 1899.

B. *In lesions* mycelial filaments and spores present:—

I. In cultures no conidial-bearing hyphæ found. Do not attack hairs or hair follicles, but grow in the superficial or deep strata of the epidermis.

(*a*) Pluriseptate spindles present in cultures. Grow in the superficial strata of the epidermis, do not attack hairs. Cultures not faviform—Genus *Epidermophyton* Lang, 1879.

(*b*) Pluriseptate spindles unknown in cultures. Grow between the superficial and deep layers of the epidermis. Cultures faviform—Genus *Endodermophyton* Castellani, 1909.

II. In cultures conidial-bearing hyphæ present. May or may not attack hairs or hair follicles.

(*a*) Conidia only at the ends of hyphæ; large—Genus *Montoyella* Castellani, 1907.

(*b*) Conidia only at the sides of hyphæ; not large—Genus *Pinoyella* Castellani and Chalmers, 1918.

(*c*) Conidia at the ends and sides of hyphæ:—

1. In cultures fusiform bodies present as septate or non-septate spindles. Yellow favic scutula not present in lesions:—

(A) Conidia on short stalks:—

(1) Attack hairs or hair follicles:—

(i.) Grows in and on the surface of the hair. Is often pyogenic and of animal origin—Genus *Ectotrichophyton* Castellani and Chalmers, 1918.

(ii.) Grows mainly in the hair, but a few mycelial filaments and spores can be found outside the hair. Not pyogenic; of human origin—Genus *Neotrichophyton* Castellani and Chalmers, 1918.

(iii.) Grows entirely in the hair, and filaments and spores cannot be found outside it. Not pyogenic, except most rarely. Of human origin—Genus *Trichophyton* Malmsten, 1845.

(2) Do not attack hairs or hair follicles—Genus *Atrichophyton* Castellani and Chalmers, 1918.

(B) Conidia sessile—Genus *Microsporum* Gruby, 1843.

2. In cultures fusiform bodies present in the form of swollen claviform ends of filaments. Yellow favic scutula present in lesions—Genus *Achorion* Remak, 1845.

FIG. 496.—*Trichophyton currii*, CHALMERS AND MARSHALL, TO SHOW FUNGUS IN HAIR.

Genus Microsporum Gruby, 1843.

Definition.—Gymnoascaceæ with only Fungi Imperfecti forms known; producing in the lesions mycelial filaments and mycelial spores, which are small, roundish, and about 2-3 microns in diameter. In cultures hyphæ bearing sessile conidia may be seen and septate or non-septate fusiform bodies. The lesions in man do not produce yellow favic scutula.

Type Species.—*Microsporum audouini* Gruby, 1843.

Remarks.—The fungi belonging to this genus are generally parasitic in the hairs and hair follicles, but may attack glabrous parts. When parasitic in the hairs, they are characterized by the mycelial spores being roundish, small (2 to 3 μ), and irregularly arranged in a mosaic-like manner. They are easily cultivated on Sabouraud's and other sugar media (see Genus *Trichophyton*, p. 996). In cultures the microsporons proliferate by *sprouting* with branching of the mycelium: and also, often, by

1. *Spore-Bearing Hyphæ*—of type *Acladium*, the conidia being oval, 3 to 4 μ in length, and 2 to 3 μ in breadth. They are not supported by short sterigmata, as is the case in the genus *Trichophyton*.

2. *Terminal Septate or Non-Septate Spindles.*—These structures are found at the end of certain filaments, and may be considered to be modified terminal conidia. They are large fusiform structures, 30 to 60 μ in length, and 15 to 18 μ in breadth. They have granular contents, and may be septate or non-septate. The surface, especially at the apex, presents some peculiar hair-like formations which are not observed in the spindles of the fungi of the genus *Trichophyton*.

3. *Chlamydospores.*—Certain mycelial articles become expanse, ovoid, or ampulliform, 22 to 18 μ in length, and 6 to 8 μ in breadth. Their protoplasm may be granular, and the membrane may become much thicker and have a double contour. These elements are chlamydospores. They are generally found when the fungi vegetate under unfavourable conditions. Another structure often seen in fungi of the genus *Microsporum* are the so-called *denticulate* or *pectinate bodies*, which are mycelial segments, generally curved, showing on one side—the convex side as a rule—several small protruding processes. Bodin has demonstrated these processes to be mycelial tubes arrested in their development.

Pleomorphism.—After a time, and often rapidly, the cultures of microsporons lose their characteristics and become pleomorphic. This phenomenon is not very prominent, however, in the most important species—viz., *Microsporum audouini*—while it is very accentuated in some microsporons of animal origin, especially *M. minimum*, in which, according to the complete investigation carried out by Bodin, two types may be met with:—

1. THE DOWNY TYPE (*Acladium type*).
2. THE GLABROUS TYPE (*Endoconidium type*).

1. **The downy type** is found on the ordinary sugar media in which there is an abundant development of white duvet. Microscopically, fructifications of the type *Acladium* are seen, the spore-bearing hyphæ presenting numerous lateral sexile conidia. Subcultures will always give rise to the same downy type.

2. **The glabrous type** is observed on wort agar. The growth has a smooth surface, without duvet. Microscopically, short strings of hyaline, ovoid, or cylindrical conidia are seen inside the terminal segments of the fertile hyphæ. Lateral conidia are absent.

Mode of Infection.—Infection takes place from man to man in the case of microsporons of human origin; from the lower animals to man in the case of microsporons of animal origin. The human microsporons (*M. audouini*, *M. velveticum*, *M. umbonatum*, *M. tardum*) do not seem to be inoculable into the lower animals

Table showing Species of Microsporum Parasitic on Man.

Genus.		Species.
Microsporum Gruby, 1843	of human origin	M. audouini Gruby, 1843.
		M. velveticum Sabouraud, 1907.
		M. umbonatum Sabouraud, 1907.
		M. tardum Sabouraud, 1909.
	of animal origin	M. scorteum Priestley, 1914.
		M. minimum Le Calvé et Malherbe, 1898.
		M. lanosum Sabouraud, 1907.
		M. felineum C. Fox and Blaxall, 1896.
		M. fulvum Uriburu, 1907.
		M. pubescens Sabouraud, 1909.
		M. villosum Minne, 1907.
		M. tomentosum Pelagatti, 1909.
		M. iris Pasini, 1912.
		M. flavescens Horta, 1912.
		M. depauperatum Guéguen, 1912.

Some species (*M. audouini*, *M. velveticum*, *M. umbonatum*, *M. tardum*) seem to be parasitic on man only; others (*M. lanosum*, *M. felineum*, *M. minimum*, etc.) are parasitic on the lower animals, but occasionally infect man.

Microsporum audouini Gruby, 1843.

This parasite was described by Gruby in 1843, but his investigation was forgotten, till Sabouraud, in his classical researches on ringworm in 1892, demonstrated the plurality of species of the fungi found in this affection, and showed that a form of tinea capitis was due to the microsporon described by Gruby.

Parasitic Life.—Around the affected hairs the fungus forms by means of its mycelial spores a white opaque sheath, extending 2 or 3 millimetres above the opening of the hair follicle. The sheath is composed of a mosaic of small, roundish, or polyhedral spores, the diameter of which varies between 2 and 3 μ. In the interior of the hair a few mycelial filaments of the fungus may be observed. The fungus very seldom attacks glabrous parts of the body.

Saprophytic Life—Cultures.—*Microsporum audouini* grows well on Sabouraud's maltose agar and other media. The rate of growing is slow. In maltose agar the growth becomes evident about a week after inoculation under the appearance of a plaque of a so-called 'satiny aspect,' beneath the surface. In a few days more, aerial hyphæ develop, extending above the surface. When the development is complete—generally this takes about six to eight weeks—the growth is roundish, covered with short greyish duvet, and presents often a central knob, and some concentric rings of a whitish-greyish colour. The cultural characters, however, are variable, and pleomorphism occurs. The cultural characters have been thoroughly investigated by Sabouraud, Fox and Blaxall, Bodin, and others. The fungus very slowly liquefies gelatine; on potatoes it produces a brownish discoloration compared by Sabouraud to the colour of dried blood.

Reproduction.—This takes place—

1. By sprouts from the mycelial tubes.
2. By small terminal and lateral conidia, there being spore-bearing hyphæ of type Acladium (see Fig. 494).
3. By large unilocular or multilocular spindle conidia. These spindles are large structures 30 to 60 μ in length, and 15 to 18 μ in breadth. They may be septate or non-septate.
4. By formation of chlamydospores.

Pathogenicity.—*Microsporum audouini* causes the most obstinate form of tinea capitis. The patches affected are often large, scaly, and present stumps, provided with an opaque whitish sheath. It seldom attacks glabrous parts of the body. *M. audouini* is extremely common in England; but rare in the South of Europe (Italy), and extremely rare in the tropics. We have never seen cases of ringworm due to *M. audouini* in Equatorial Africa or Ceylon, but a few cases have been described in Brazil, in Madagascar, and in Senegal.

M. audouini seems to live only on the human subject, but closely allied species have been found by Fox in cats, by Bodin in dogs, and by Bodin, Fox, and others, in horses.

Microsporum velveticum Sabouraud, 1907.

Resembles closely *M. audouini*, but the cultures are more velvety, the duvet being white instead of greyish, and of closer growth. Not inoculable into guinea-pigs.. This species seems to be fairly common in North America.

Microsporum umbonatum Sabouraud, 1907.

Found by Sabouraud in two cases of microsporosis of the scalp contracted in Russia. The appearance of the growth when it has reached complete development (about twenty-five to thirty days after inoculation) has been compared by Sabouraud to the appearance of an ancient round shield, with a central conical formation representing the *umbo* of the shield. Not inoculable into guinea-pigs.

Microsporum tardum Sabouraud, 1909.

Found by Sabouraud in cases of microsporosis capitis clinically identical with the type caused by *M. audouini*. Differs from *M. audouini* by the growth being much slower and scantier, and the duvet being shorter.

Microsporum lanosum Sabouraud, 1907.

Synonym.—*Microsporon audouini* var. *canis* Bodin, 1897.

Commonly found in dogs. May affect man, causing a type of severe tinea capitis; may also produce forms of tinea barbæ and tinea corporis.

On Sabouraud's agar the growth is at first similar to *M. audouini*, only more abundant and more downy. Later—twenty-five to thirty days from inoculation—the central portion of the growth becomes umbilicated, the depression being surrounded by a ring of snow-white duvet, which in very old cultures may become yellowish. Pleomorphism is common.

Microsporum felineum C. Fox and Blaxall, 1896.

Common in the cat in England, North America, and Belgium; may infect man, attacking hairy and non-hairy regions of the body. On Sabouraud's agar the growth is rather abundant, discoid, with flattened surface, showing no furrows, and covered with a large amount of grey duvet. The fungus is easily inoculable into cats, dogs, and guinea-pigs.

Microsporum minimum Le Calvé and Malherbe, 1898.

Synonyms.—*Microsporon audouini* var. *equinum* Bodin, 1896; **Trichophyton minimum* Le Calvé and Malherbe, 1898.

Very common in foals; may infect man, giving rise to a mild type of tinea corporis, which gets cured spontaneously.

On Sabouraud's and glucose agar the growth is deeply furrowed, and, in contrast to all other microsporons, duvet is absent, or, when present, is very scanty, very short, and of a pinkish colour.

Microsporum fulvum Uriburú, 1907.

Found by Uriburú in cases of tinea capitis in the Argentine. It grows very rapidly on Sabouraud's agar, the growth presenting a central *umbo*, or projection, surrounded by a brownish powdery ring. The peripheral zone of the growth is covered with white duvet.

Microsporum pubescens Sabouraud, 1909.

Discovered by Sabouraud in a case of tinea capitis contracted in New York. It grows rapidly on Sabouraud's medium, the culture being characterized by the presence of abundant but very delicate silky duvet. At complete development—about thirty days from inoculation—the growth may have a flattened surface, or some furrows, radiating from the centre, may be present. The central portion, which is covered with rather long, white duvet, is encircled by a zone of powdery appearance; outside this there is the peripheral zone covered by the extremely delicate, characteristic, silky-like duvet.

Microsporum villosum Minne, 1907.

Found in Belgium by Minne in a child suffering from ringworm of the hair clinically identical with the type caused by *M. audouini*. On Sabouraud's agar the growth at complete development is about 6 centimetres in diameter; the central portion is flattened, with powdery, slightly brownish surface. This is surrounded by mammillary, downy formations, which decrease in size towards the periphery.

Microsporum tomentosum Pelagatti, 1909.

Found by Pelagatti in Sardinia in a case of microsporosis capitis, clinically identical with the usual type caused by *M. audouini*. It grows rapidly on Sabouraud's agar. The growth at complete development has a somewhat flattened appearance, but several furrows are present, originating from the central portion, which may be umbilicated. The whole surface is covered by thin white duvet.

Microsporum iris Pasini, 1911.

Discovered by Pasini in Italy in some cases of microsporosis capitis, clinically somewhat different from the usual type. The fungus grows well on Sabouraud's agar. At complete development -twenty-two to twenty-six days from inoculation- the growth presents a central knob covered with white duvet, and surrounded by white and brick-red rings, alternating.

The microsporosis capitis due to this microsporon is characterized by the hairs remaining nearly of normal length, and presenting a white-greenish discoloration.

Microsporum flavescens P. Horta, 1912.

Isolated by Horta from some circinate squamous patches situate on the neck of a child in Brazil. Grows rapidly on Sabouraud's agar: the growth is of a yellow colour; there is a depression at the centre, from which radiate four or five shallow furrows. Pleomorphic duvet appears quickly.

Microsporum depauperatum F. Guéguen, 1912.

Isolated by Guéguen from some circinate, dry, squamous patches. In cultures the membrane of some nuclear filaments presents peculiar thickenings. Spore-bearing hyphæ are not so well differentiated as in other species.

Microsporum scorteum Priestley, 1914.

This parasite resembles *M. fulvum* Uriburú, 1909, both morphologically and culturally, and may be identical therewith, as the descriptions given in Europe of Uriburú's parasite are scanty. It was found by Priestley in Townsville in Tropical Queensland; and occurred in two circular inflamed areas on the calf of a boy's leg. There was no scaliness, and the hairs were not visibly altered, though microscopically they contained mycelium and a few spores.

On Sabouraud's maltose agar it grew rapidly, producing a growth like a piece of chamois leather. It slowly digested milk, which it did not clot. Multiseptate spores were abundant, but lateral conidia were few, 3-4 × 2-3 microns in size, while chlamydospores were infrequent. Nodular bodies like those found by Sabouraud in *T. lacticolor* were found. Spirals were frequent and pectinate bodies rare. Duvet was formed.

Genus Trichophyton Malmsten, 1845.

Definition.—Trichophytoneæ with mycelial filaments and spores present in the lesions and conidial-bearing hyphæ in cultures, only attacking hairs and entirely of human origin. Almost never pyogenic.

Type Species.—*Trichophyton tonsurans* Malmsten, 1845.

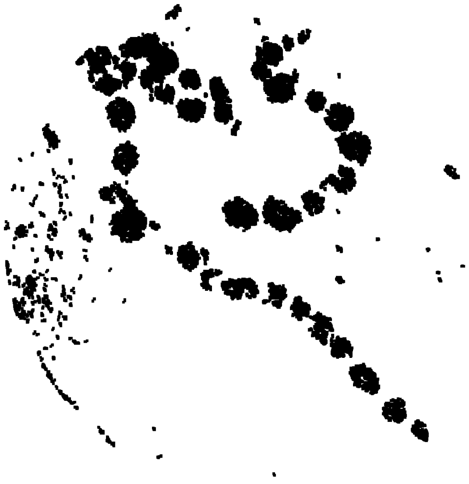


FIG. 497.—*Trichophyton currii*, TO SHOW MYCELIAL SPORES.

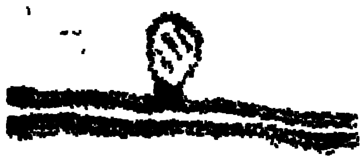


FIG. 498.—*Trichophyton currii*, TO SHOW CONIDIAL-BEARING HYPHA.

General Considerations.—During their parasitic life the species of the genus *Trichophyton* vegetate according to two types: (1) mycelial filaments; (2) mycelial spores.

The mycelial filaments consist of long cylindrical cells, separated by septa. The so-called mycelial spores are simply a modification of the mycelial filaments, due to the septa being much closer, so that the cells limited by them are almost as broad as they are long. The term 'mycelial spores' is incorrect, as they are not organs of reproduction, but only vegetative organs.

When the shape of these mycelial spores or sporulating mycelia is roundish or oval, the filament takes a moniliform appearance. Moreover, these cells are easily dissociated. Such a type is called 'fragile mycelium.' To this type belongs, for instance, *Trichophyton sabouraudi* R. Blanchard.

When the mycelial spores are square, the filament straight, and its articles long, the mycelium is called 'resistant.' This type is observed, for example, in *Trichophyton tonsurans* Malmsten.

Cultivation. Most *Trichophytons* can be cultivated, some cannot. The best medium is Sabouraud's maltose agar, the composition of which is the following:—

Maltose .. .	4 grammes.
Peptone Chassaing	1 gramme.
Agar .. .	1·50 grammes.
Distilled water .	100 c.c.

On this medium, however, pleomorphism is of frequent occurrence.

Pleomorphism. Cultures on maltose and other sugar agars of all *Trichophytons*, with the single exception of *T. sabouraudi*, becoming old, lose their characteristics and become covered with abundant white duvet. In these cultures, which can be considered degenerate, and are generally called 'pleomorphic,' organs of fructification are usually absent. By transplanting these cultures, the same pleomorphic, downy type of growth will be obtained: never again will the growth show the characteristics of the original *young* cultures directly obtained from the lesions. It is impossible to return to the original type, even by animal inoculations.

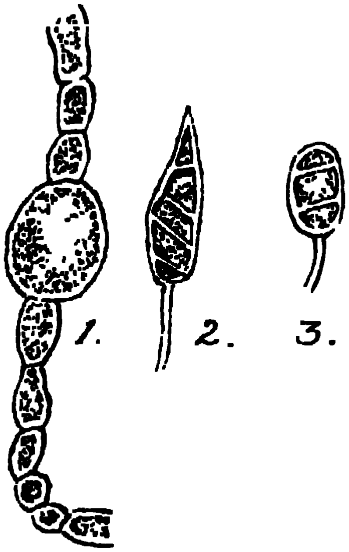


FIG. 499.—TRICHOPHYTON.

(Preparation from cultures, after Bodin.)

1, Chlamydospore; 2 and 3, septate spindle bodies.

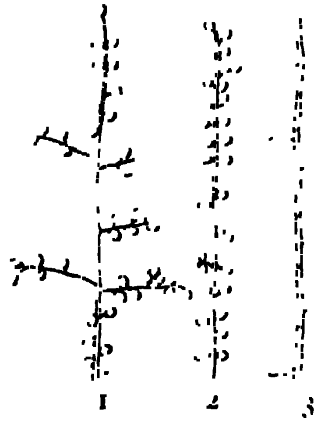


FIG. 500.—FRUCTIFICATIONS.

1, 2, Spore-bearing hyphæ (*Trichophyton*); 3, spore-bearing hypha (*Microsporum*).

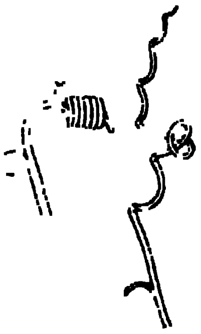


FIG. 501.—TRICHOPHYTON: SPIRAL BODIES.

To prevent pleomorphism, Sabouraud advises the following medium:—

Agar..	1·8 grammes.
Peptone Chassaing	3 to 5 grammes.
Water	100 c.c.

On this medium the growth of the various *Trichophytons* is much less abundant than on sugar media, but the cultures are fairly characteristic, and do not become pleomorphic.

Experimental Inoculations.—Certain *Trichophytons* can be easily inoculated experimentally into man and many of the laboratory animals—guinea-pigs, rabbits, etc. Sabouraud advises the inoculation of portions of the cultures to be made into a small flictena, artificially induced by burning, such as by applying to the skin a lighted match.

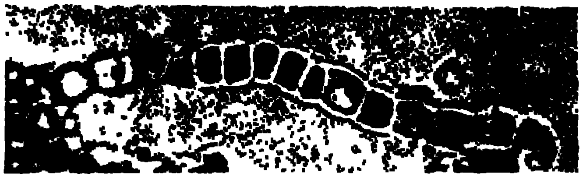


FIG. 502.—*Trichophyton currii*, TO SHOW LADDER-LIKE ROWS OF MYCELIAL SPORES.

The *intravenous* injection may induce generalized lesions of the internal organs.

The intraperitoneal injection as done by Citron may induce a type of peritoneal pseudo-tuberculosis.

Mode of Infection.—Infection may take place from man to man—this is generally the case with *Trichophytons* of the group *endothrix*—or from the lower animals to man. There is also little doubt that *Trichophytons* may live saprophytically in nature, this explaining sporadic cases of trichophytoses in man.

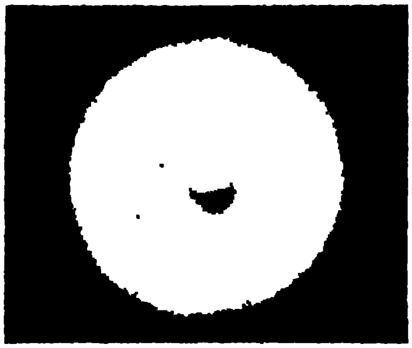


FIG. 503. — *Trichophyton currii*, FOUR DAYS' GROWTH ON SABOURAUD'S MALTOSE AGAR AT 34° C., TO SHOW WHITE GROWTH WITH KNOB-LIKE CENTRE.

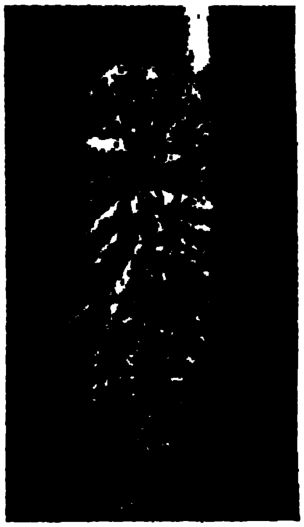


FIG. 504.—*Trichophyton violaceum* VAR. *khartoumense*.

(Note absence of acuminate centre and dark [violet] colour of the growth.)

Reproduction.—This takes place by—

1. Lateral and terminal conidia, supported by short sterigmata.
2. Chlamydospores; these are rare.
3. Large terminal septate and unseptate spindles.

Classification.—The principal species of the genus *Trichophyton* arranged chronologically are:—

1. *T. tonsurans* Malmsten, 1845.
2. *T. sabouraudi* R. Blanchard, 1895.
3. *T. violaceum* Bodin, 1902.
4. *T. sulphureum* C. Fox, 1908.
5. *T. glabrum* Sabouraud, 1909.
6. *T. fumatum* Sabouraud, 1909.
7. *T. effractum* Sabouraud, 1909.
8. *T. circonvolutum* Sabouraud, 1909.
9. *T. regulare* Sabouraud, 1909.
10. *T. umbilicatum* Sabouraud, 1909.
11. *T. exsiccatum* Uriburú, 1909.
12. *T. polygonum* Uriburú, 1909.
13. *T. soudanense* Joyeux, 1912.
14. *T. currii* Chalmers and Marshall, 1914.

These may be recognized as follows:—

A. Condition of mycelium in hair not definitely stated, but probably that of the Crateriform subdivision (see below)

(1) In cultures very convoluted—*Circonvolutum*

B. Condition of mycelium in hair definitely stated.

I. Mycelium in hair resistant to caustic potash, segments characteristically quadrangular in shape, with double contour, 4 to 6 μ in breadth, arranged in fairly straight ladder-like rows—*Crateriform subdivision*.

(*a*) *Cultures coloured and with craters: Tonsurans group*:—

(2) Yellow in centre white at periphery—*Tonsurans*.

(3) As 'tonsurans,' but, when old, cracked and dry—*Effractum*.

(4) Orange-red centre, remainder sulphur coloured—*Sulphureum*.

(5) Golden-yellow convoluted centre, becoming crateriform later—*Soudanense*.

(6) When old of a yellowish-brown colour—*Fumatum*.

(*b*) *Cultures white with craters: Umbilicatum group*:

(7) Deeply umbilicated with aureola—*Umbilicatum*.

(8) Slow growth, surface cracked with dry appearance—*Exsiccatum*.

(9) Growth at first roundish and then polygonal—*Polygonum*.

(*c*) *Cultures white with knob-like centre: Currii group*:

(10) Does not form duvet—*Currii*.

II. Mycelium in hair not resistant to caustic potash; segments rounded, 4·7 μ in diameter, not arranged as a rule in rows, but if a row is visible it resembles a string of beads and not a ladder—*Acuminate subdivision*.

(*a*) *Without acuminate centre: Violaceum group*:—

(11) Primary growth violet:—

(A) Most strains do not melt gelatine very rapidly:—

(i.) Ordinary amount of scaling on the head—*Violaceum*.

(ii.) Enormous numbers of scales, followed at times by permanent baldness—Var. *decalvans*.

(B) Melts strong gelatine very rapidly, beginning as soon as growth appears—Var. *khartoumense*.

(12) Primary growth white—*Glabrum*.

(*b*) *With acuminate centre: Sabouraudi group*:—

(13) Without duvet when old—*Sabouraudi*.

(14) With duvet when old—*Pilosum*.

Courmont's parasites cannot be easily classified.

Trichophyton tonsurans Malmsten, 1845.

Synonyms.—*Trichomyces tonsurans* Malmsten, 1845; *Oidium tonsurans* Zopf, 1890; *Trichophyton megalosporum endothrix* Sabouraud, 1894; *T. crateriforme* Bodin, 1902, which is the term in current use in dermatological literature.

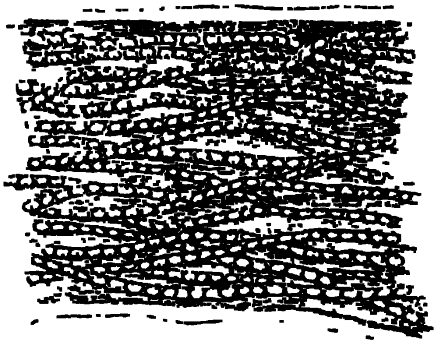


FIG. 505.—*Trichophyton tonsurans* MALMSTEN.

(Preparation of a hair in liquor potassæ, after Sabouraud.)

Causes a type of tinea capitis somewhat rare in England, but common on the Continent. The hairs are broken 2 to 4 millimetres from the scalp, and the stumps are variously bent. The diseased hairs have a powdery, greyish appearance, and on pulling them out the roots are not black, as in normal hairs. It belongs to the type Endothrix. The mycelial cells are large (4 to 5 μ), quadrangular (so-called resistant mycelium type). Grows well on maltose agar and other media; on maltose agar colonies are white or yellowish, often crateriform, and present a velvety surface at first, later powdery. In hanging-drop cultivations spore-bearing fructifications can be seen.

T. tonsurans, besides producing a type of tinea capitis, produces also a form of tinea corporis and a trichophytosis of the nails.

Trichophyton sabouraudi R. Blanchard, 1895.

Synonym.—*Trichophyton acuminatum* Bodin, 1902. This is the term commonly used in dermatological works.

This *Trichophyton* is of the type Endothrix. Mycelial threads have a moniliform appearance, and their articles become easily dissociated (so-called fragile mycelium). Grows well on maltose agar, giving rise to conical white colonies; often acuminate with central plumes, and occasionally may present yellowish or pinkish rings; older cultures may present a powdery surface of a dark pinkish colour. Pleomorphism always absent. In hanging-drop cultures aerial filaments with lateral conidia are seen.

T. sabouraudi causes a form of tinea capitis called by Sabouraud 'tondante peladoide,' and also a variety of tinea circinata.

The tinea capitis induced by this fungus is also known under the name of 'black-dotted ringworm.' The hairs get broken lower than in the type of ringworm caused by *T. tonsurans*. The stumps are on the same level as the surface of the scalp, and appear as black dots.

Trichophyton pilosum Sabouraud, 1909.

Very similar to *T. sabouraudi*, from which it differs only by the cultures being covered, when old, by a dense, short, white duvet.

Trichophyton soudanense C. Joyeux, 1912.

Endothrix: very similar to *T. tonsurans*. In the hairs the mycelial spores are generally rectangular, arranged in long strings. On Sabouraud's agar the growth appears three to four days after inoculation as a small yellow nodule; later, the peripheral portion of the growth appears white. It has been found by C. Joyeux in cases of tinea capitis in the Sudan.

Trichophyton violaceum Bodin, 1902.

Discovered by Sabouraud in cases of tinea barbæ; type Endothrix. The growth on maltose agar is of a light brownish or greyish colour, with moist surface, and later becomes violet.

This species is common in Italy and North Africa. In Ceylon a variety of this fungus produces a type of very common ringworm of the scalp in children, with white patches covered by enormous numbers of pityriasic squamæ. The patches often remain permanently bald. The Ceylon fungus is endo-ectothrix, and although culturally is hardly distinguishable from *T. violaceum*, is probably a different variety (var. *decalvans* Castellani, 1913), as it produces lesions generally different from those induced by *T. violaceum*. In the Sudan it apparently liquefies gelatine more rapidly (var. *khartoumense* Chalmers and Macdonald, 1915).

Trichophyton glabrum Sabouraud, 1909.

Closely allied to *T. violaceum*, but shows a more rapid growth, and no violet pigmentation develops. Surface smooth and moist.

Trichophyton sulphureum C. Fox, 1908.

Described by Colcott Fox in some cases of tinea capitis in England. Endothrix type. On Sabouraud's agar the growth is characterized by a central reddish nodule, which later becomes crateriform, assuming a speckled appearance. The rest of the culture has a delicate but distinct primrose or sulphur colour.

Trichophyton plicatile Sabouraud, 1909.

Colonies closely resemble those of *T. tonsurans*, but have a creased appearance. Found by Sabouraud in cases of sycosis. Sequeira has observed it in a case of trichophytic granuloma. We have placed the fungus in the genus Neotrichophyton (p. 1001).

Trichophyton circonvolutum Sabouraud, 1909.

Endothrix; somewhat similar to *T. plicatile*; the growth has a convoluted surface. Found by Sabouraud in cases of trichophytosis contracted in the Sudan and Dahomy.

Trichophyton exsiccatum Uriburú, 1909.

Found in Argentina by Uriburú. Endothrix; very slow growth; crateriform colonies, with surface finely cracked, and of a dry aspect

Trichophyton polygonum Uriburú, 1909.

Endothrix. The growth is at first roundish, then takes a characteristic polygonal outline. The central part is crateriform.

Trichophyton regulare Sabouraud, 1909.

Endothrix; very similar to *T. tonsurans*, the cultures being at first crateriform; then, the edges of the crater becoming undermined, the growth takes a peculiar pouch-like shape, with several radiating small sulci. The characters of the fungus show always the greatest regularity, never changing: hence the name *T. regulare* given to it by Sabouraud. This fungus was found by Dalla Favera.

Trichophyton umbilicatum Sabouraud, 1909.

Endothrix: cultures are deeply umbilicated: present at the periphery fine radiating hyphæ, forming a sort of aureola.

Trichophyton fumatum Sabouraud, 1909.

Cultures crateriform, taking when old a yellowish-brownish colour, compared by Sabouraud to the colour of a dead leaf. This *Trichophyton* is fairly common in some parts of Italy.

Trichophyton effractum Sabouraud, 1909.

Cultures at first very similar to those of *T. tonsurans*; being crateriform; when old, the growth becomes very dry, and the surface splits from the edge.

Trichophyton currii Chalmers and Marshall, 1914.

This fungus was found in an epidemic of ringworm in a Khartoum school. It is not the common fungus of the town, which appears to be *T. violaceum* var. *khartoumense*. *T. currii* is of the type endothrix, and grows aerobically, but not anaerobically. It forms ladder-like rows of mycelial spores in the hairs. These spores are usually 4·2 microns in breadth, and they and the mycelium resist the action of caustic potash. It forms neither acid nor gas in monosaccharids, disaccharids, trisaccharids, polysaccharids, glucosides, or alcohols. It does not alter litmus milk. It does not liquefy gelatine. On Sabouraud's agars it produces white growths with a central knob, a white plateau with a slight circular marking, and a peripheral fringe. It grows on carrot, potato, but was not characteristic on beetroot, and was poor on Buchanan's and Loeffler's media. Inoculations directly from the patients' heads failed in monkeys, cats, dogs, and mice. In man it gives rise to a type of tinea capitis tropicalis.

Genus Neotrichophyton Castellani and Chalmers, 1918.

Definition.—Trichophytineæ with mycelium and spores present in the lesions, and conidial-bearing hyphæ in cultures, attacking hairs, but with mycelial spores and filaments outside the hair shaft.

Type Species.—*Neotrichophyton flavum* Bodin, 1902.

Classification.—There are only two species, which may be distinguished as follows:—

A. Cultures cerebriform—*Flavum*.
B. Cultures crateriform and creased—*Plicatile*.

Neotrichophyton flavum Bodin, 1902.

Synonym.—*Trichophyton cerebriforme* Sabouraud, 1909.

Differs from *Trichophyton tonsurans* by the cultures being cerebriform, and by becoming creamy-white when old.

Pathogenicity.—Induces a type of tinea corporis and a form of sycosis. Inoculable into guinea-pigs.

Neotrichophyton plicatile Sabouraud, 1909.

Synonym.—*Tricophyton plicatile* Sabouraud, 1909.

Colonies closely resemble those of *Trichophyton tonsurans*, but have a creased appearance with white, powdery surface. Found by Sabouraud in cases of sycosis. Sequeira has observed it in a case of trichophytic granuloma.

Genus Ectotrichophyton Castellani and Chalmers, 1918.

Definition.—Trichophytoneæ with mycelium and spores present in the lesions, and conidial-bearing hyphæ in cultures; attack hairs and hair follicles, growing in and on the surface of the hairs; is often pyogenic and of animal origin.

Type Species.—*Ectotrichophyton mentagrophytes* Robin, 1853.

Classification.—The genus is capable of division into three subgenera by the following characters:

A. *Ectotrichophyton* :—

With small spores about 3 to 4 microns in diameter, forming a sheath outside the hair shaft, on dissociation of which they are seen to form chains; with sinuous and quadrangular hyphal segments, together with spores of varying diameter and air-bubbles, inside the hair shaft; with cultures easily obtainable, of rapid growth, and of considerable vitality, characterized by plaster-like or floury centres surrounded by a fringe, when grown on Sabouraud's proof media, and by successful inoculations into animals—Subgenus *Microtrichophyton*.

B. *Ectotrichophyton* :—

With large spores about 5 to 7 microns in diameter, forming a sheath outside the hair shaft, on dissociation of which they are seen to form chains, and with sinuous hyphal segments, together with large-sized spores and air-bubbles, inside the hair shaft; with cultures easily obtainable, but of slow growth in temperate climates, though much more rapid in tropical climates, characterized by their tendency to resemble (at all events when old) those of the Achorions, and capable of being inoculated into animals—

I. With early formation of a duvet—Subgenus *Ectotrichophyton*.
II. Culture sooner or later resembles that of *Achorion schoenleini*—Subgenus *Favotrichophyton*.

Ectotrichophyton (Favotrichophyton) Castellani and Chalmers, 1918.

Definition.—Ectotrichophyton with the characters given above for Favotrichophyton.

Type Species.—*Ectotrichophyton discoides* Sabouraud, 1909.

FIG. 506.—*Ectotrichophyton discoides*. NINETEEN DAYS' GROWTH ON SABOURAUD'S MALTOSE AGAR AT 32° C.

FIG. 507.—*Ectotrichophyton discoides*: FORTY-TWO DAYS' GROWTH ON SABOURAUD'S MALTOSE AGAR AT 32° C.

Classification. The Favotrichophyton species which are known are

E. verrucosum Bodin, 1902,
E. ochraceum Sabouraud, 1909,
E. album Sabouraud, 1909,
E. discoides Sabouraud, 1909,
E. luxurians Brault and Viguier, 1914,

which may be differentiated as follows:-

A. Condition of mycelium in hair not definitely stated. -
  I. Young cultures white in colour, and soon resembling those of *Achorion schoenleini*, but sunk into the medium—*Album*.
B. Condition of mycelium in hair that of an ecto-endothrix: -
  II. Cultures grey in colour, humid, with verrucose surface—*Verrucosum*.
  III. Young cultures of a yellow ochre colour—*Ochraceum*.
  IV. Cultures yellowish-brown or greyish-yellow, cupola-shaped, humid, with usually smooth surfaces, and not resembling the Achorion cultures until old—*Discoides*.
  V. Very rapid development—*Luxurians*.

Ectotrichophyton verrucosum Bodin, 1902

Synonym.—*Trichophyton verrucosum* Bodin, 1902.

Endo-ectothrix, megalosporon, faviform. This fungus, though producing typical trichophytic lesions when parasitic, shows cultural characters somewhat similar to an achorion, the growth, which is white, being often convoluted or cerebriform. It is found in donkeys, and may infect man. The same or similar species are found parasitic on the horse and on some birds, and may also infect man.

Ectotrichophyton ochraceum Sabouraud, 1909.

Synonym.—*Trichophyton ochraceum* Sabouraud, 1909.

Type Ectothrix, of animal origin; cultures somewhat similar to favus. On maltose and glucose agars the colonies are characterized by an ochre-yellow knob; portions of the growth may be covered by an extremely short, almost invisible, duvet. On ordinary agar the surface of the colonies is cerebriform. Optimum temperature, 25° C. It is easily inoculated into guinea-pigs.

Ectotrichophyton album Sabouraud, 1907.

Synonym.—*Trichophyton album* Sabouraud, 1907.

The cultures are extremely like favus, but are generally less bulging, more deeply umbilicated, and more regularly folded; the growth deepens in the medium; some white duvet present. Optimum temperature, 25 C. Can be inoculated into guinea-pigs.

Ectotrichophyton discoides Sabouraud, 1909.

Synonym.—*Trichophyton discoides* Sabouraud, 1909.

Endo-ectothrix, megalosporon, faviform. Somewhat similar to *E. album*, but the growth, which is almost a perfect disc, has a more flattened surface. There is often a central knob. The whole growth has a brownish-yellowish colour, with a moist surface, somewhat resembling the non-pigmented cultures of *Trichophyton violaceum*. It occurs in Egypt and in the Anglo-Egyptian Sudan, as described by one of us.

Ectotrichophyton luxurians Brault and Viguier, 1914.

Isolated from cases of kerion in Algeria. Very rapid growth with faviform appearance.

Ectotrichophyton (Microtrichophyton) Castellani and Chalmers, 1918.

Definition.—Ectotrichophyton with small spores 3-4 microns in diameter.

Type Species.—*Ectotrichophyton* (*Microtrichophyton*) *mentagrophytes* Robin, 1853.

Classification.—The following species are known:—

E. mentagrophytes Ch. Robin, 1853.
E. farinulentum Sabouraud, 1910.
E. persicolor Sabouraud, 1910.
E. granulosum Sabouraud, 1908.
E. lacticolor Sabouraud, 1910.
E. radiolatum Sabouraud, 1910.
E. felineum R. Blanchard, 1895.
E. denticulatum Sabouraud, 1910.

They may be differentiated as follows:—

- A. Grows best on agar without sugars—*Persicolor.*
- B. Grow best on agar with sugars:—
  - I. Growth white, elevated centre, powdery surface, radiating furrows.
    - (*a*) Furrows well marked. Pure white—*Mentagrophytes.*
    - (*b*) Furrows poorly marked. Not so white—*Radiolatum.*
  - II. Growth white, discoid, umbilicated, but later knob in centre; white powdery surface, radiating furrows—*Farinulentum.*
  - III. Growth white, yellowish, dotted with granular projections—*Granulosum.*
  - IV. Growth cream white to yellowish, not granular—*Lacticolor.*
  - V. Growth white, with umbilicated centre, with numerous radiating projections at periphery.
    - (*a*) Projections well marked—*Echineum.*
    - (*b*) Projections poorly marked—*Denticulatum*

Ectotrichophyton mentagrophytes Ch. Robin, 1853.

Synonyms.—*Microsporon mentagrophytes* Robin, 1853: *Sporotrichum mentagrophytes* Saccardo, 1886; *Trichophyton gypseum* Bodin, 1902; *T. asteroides* Sabouraud, 1909; *Trichophyton mentagrophytes* Robin, 1853.

Endo-ectothrix; mycelial spores are mostly situated outside the cuticle of the hair, while a few are found in the interior. The latter are 5 to 6 μ in size; those outside, forming the parasitic sheath, are of very unequal size (2 to 11 μ).

On Sabouraud's agar the growth is of white colour; the centre is somewhat elevated and covered by duvet; the rest of the growth has a powdery surface, and often presents several radiating furrows. At the periphery numerous tapering projections are observed. This *Trichophyton* is of animal origin, being found in horses, cows, dogs, and, perhaps, pigs and sheep. In man it is pyogenic, causing a type of trichophytic sycosis, kerion, and also a pustular type of tinea corporis.

The following five species are very closely allied to *E. mentagrophytes:*—

Ectotrichophyton farinulentum Sabouraud, 1910.

Synonyms.—*Trichophyton gypseum* Bodin, 1902, *pro parte; Trichophyton farinulentum* Sabouraud, 1910.

Found in cases of kerion by Sabouraud. On maltose agar the growth is at first discoid, umbilicated, with a white powdery surface and several radiating furrows. Later, the central part becomes raised, forming a knob covered with white duvet. On agar media not containing sugars the growth is at first smooth, without any duvet, of moist appearance and yellow colour; while later the central part becomes downy, and the peripheral portions take a powdery aspect.

Ectotrichophyton persicolor Sabouraud, 1910.

Synonym.—*Trichophyton gypseum* Bodin, 1902, *pro parte: Trichophyton persicolor* Sabouraud, 1910.

Found by Sabouraud in cases of pustular ringworm of the palms of the hands and of the beard. In contrast to all other species of *Trichophytons,* it grows better on agar without sugar than on sugar media. The cultures are of a pinkish-reddish colour. The appearance of the colonies has been aptly compared by Adamson to the skin of a very ripe peach.

Ectotrichophyton granulosum Sabouraud, 1908.

Synonym.—*Trichophyton gypseum* Bodin, 1902, *pro parte*, *Trichophyton granulosum* Sabouraud, 1908.

The growth on Sabouraud's agar is discoid, often umbilicated; powdery surface of a white-yellowish colour, with granular formations or prominences dotted all over.

This *Trichophyton* is found in the horse, in which it produces a peculiar type of trichophytosis, with extremely numerous, very small, patches. It has been observed in man in Italy by Dalla Favera.

Ectotrichophyton lacticolor Sabouraud, 1910.

Synonym.—*Trichophyton gypseum* Bodin, *pro parte*; *Trichophyton lacticolor* Sabouraud, 1910.

The cultures are discoid flattened, with shallow furrows radiating from the centre. The colour is cream-white, with occasionally a slight yellow tinge. In old cultures there is abundant pleomorphic duvet. Can easily be inoculated in guinea-pigs.

Ectotrichophyton radiolatum Sabouraud, 1910.

Synonym.—*Trichophyton gypseum* Bodin, *pro parte*. *Trichophyton radiolatum* Sabouraud, 1910.

Isolated by Sabouraud from cases of kerion. Very similar to *E. mentagrophytes*, from which it differs in culture by the colour being of less pure white, and by the radiating projections being less marked or absent. After three to four weeks abundant white pleomorphic duvet appears

Ectotrichophyton felineum R. Blanchard, 1895.

Synonyms. *Trichophyton niveum* Sabouraud: *T. radians* Sabouraud, 1909: *T. felineum* R. Blanchard, 1895.

Endo-ectothrix: causes often a pustular ringworm of the body; less frequently attacks the hairs. In the pustules free spores and a few mycelial elements are seen: in the affected hairs the spores forming the parasitic sheath are of large dimensions, 7 to 9 μ in diameter. The growth on Sabouraud's medium is umbilicated, with a white powdery surface and numerous radiating projections at the periphery.

Pathogenicity.—This fungus is found in the cat, and probably also in horses, cattle, dogs, sheep, and pigs. In man it causes a type of kerion celsi and also a type of vesiculo-pustular tinea corporis, called by Sabouraud 'trichophytosis circinata disidriformis,' and 'herpes iris vesiculosus' by Biett.

Ectotrichophyton denticulatum Sabouraud, 1910.

Synonym.—*Trichophyton niveum* Sabouraud, *pro parte*. *T. denticulatum*.

Almost identical with *E. felineum*, but in cultures the radiating projections are much shorter and more pointed.

Ectotrichophyton (Ectotrichophyton) Castellani and Chalmers, 1918.

Definition.—Ectotrichophyton with large spores about 5-7 microns.

Type Species.—*Ectotrichophyton* (*Ectotrichophyton*) *megnini* R. Blanchard, 1895.

Classification.—The following species are known:—

E. megnini (R. Blanchard, 1895).
E. equinum (Gedoelst, 1902).
E. vinosum (Sabouraud, 1909).
E. nodoformans (Castellani, 1912).

They may be distinguished as follows:—

A. Mycelial spores very large, 8-9 microns in diameter:—
  I. Old cultures pinkish—*Megnini*.
  II. Old cultures deep wine red—*Vinosum*.
B. Mycelial spores not large, 2-4 microns in breadth:—
  I. Surface growth abundant, dark red—*Equinum*.
  II. Surface growth scanty and colourless submerged portion brick red—*Nodoformans*.

Ectotrichophyton megnini R. Blanchard, 1895.

Synonyms.—*Trichophyton roseum* Bodin, 1902; *T. rosaceum* Sabouraud, 1902; *T. megnini* R. Blanchard, 1895.

Endo-ectothrix, megalosporon, downy-culture type. Mycelial spores found in the hairs are very large, 8 to 9 μ in diameter. On maltose agar the growth is at first white, with a velvety appearance; later, pinkish, or of a deep rose colour. Duvet becomes very abundant in old cultures. It is parasitic in fowls and pigeons: may infect man, causing a variety of tinea barbae without suppuration.

Ectotrichophyton vinosum Sabouraud, 1909.

Synonym.—*Trichophyton vinosum* Sabouraud, 1909.

Endo-ectothrix, megalosporon, of downy-culture type. Is very similar to *E. megnini*, but the colour of old cultures is of a deep wine red colour. Abundant duvet. Found by Sabouraud in a case of tinea circinata.

Ectotrichophyton equinum Gedoelst, 1902.

Synonym.—*Trichophyton equinum* Gedoelst, 1902.

Endo-ectothrix, megalosporon, downy-culture type. Mycelial spores of oval shape, 4 to 6 μ in length, 2 to 4 μ in breadth. On maltose agar the growth is orbicular, with abundant duvet; later on, the portion of the growth which is in contact with the medium becomes yellowish and afterwards dark red. It is parasitic in the horse, and may infect man.

Ectotrichophyton nodoformans Castellani, 1912.

Synonym.—*Trichophyton nodoformans* Castellani, 1912.

Found in Ceylon in cases of dhobi itch and tinea barbae: not very abundant in the lesions. On Sabouraud's agar the growth is white, with a powdery surface and a central small knob. The growth deepens in the medium, and the submerged portion has a characteristic brick-red colour, which generally disappears after repeated transplantations. The surface growth is whitish.

Glucose Agar.—Growth somewhat more abundant than in Sabouraud's agar. Colour of the surface and submerged growth white. Red pigment usually absent.

Maltose 4 per cent.—Scanty growth, no pigment.

Glycerine Agar.—Growth fairly abundant, no pigment.

Agar.—Scanty growth, whitish.

Saccharine.—Same as agar.

Adonite.—Same as agar.

Pathogenicity.—The fungus gives rise to a peculiar type of tinea cruris (p. 2042), with very thick, elevated margins and deep-seated nodules. It has pyogenic properties, and may spread to other parts of the body, in addition to the inguinal regions. It is capable of affecting the hair follicles. In one of our cases the fungus affected the hairs of the beard, producing a typical 'kerion barbæ.'

Genus Atrichophyton Castellani and Chalmers, 1918.

Definition.—Trichophytoneæ with mycelium and spores present in the lesions and conidia on short stalks, but they do not attack hairs.

Type Species.—*Atrichophyton albiscicans* Nieuwenhuis, 1907.

Classification.—The following table will indicate the characters of the species:—

A. *Has been cultivated*.—
  I. Culture whitish with powdery surface—*Albiscicans*.
  II. Culture brownish mass with deep furrows—*Macfadyeni*.
  III. Cultures pinkish with violet tinge—*Viannai*.

B. *Has not been cultivated*:—
  I. Spores are numerous and of various sizes—*Blanchardi*.
  II. Spores are few and about 4 microns in diameter—*Ceylonense*.

Atrichophyton albiscicans Nieuwenhuis, 1907.

Synonym.—*Trichophyton albiscicans* Nieuwenhuis, 1907.

Discovered by Nieuwenhuis in tinea albigena. In fresh preparations from scrapings spores are absent: the mycelial tubes are straight, occasionally showing a double contour; they are often dichotomous. On Sabouraud's agar the growth is very slow, whitish, with a powdery surface.

Atrichophyton blanchardi Castellani, 1905.

Synonym.—*Trichophyton sabouraudi* Castellani, 1905; *T. blanchardi* Castellani, 1905.

Temporary species, as the fungus has not been grown. In fresh preparations from the lesions the mycelial tubes are not, as a rule, quite straight; they are often banana-shaped; do not show a double contour; the mycelial segments are separated, the mycelial spores are shed without forming a filament by their union, and are of various sizes. All attempts at cultivation have failed. It is the cause of tinea Sabouraudi tropicalis.

Atrichophyton viannai de Mello, 1917.

Synonym.—*Trichophyton viannai* de Mello, 1917. Found by F. de Mello in a case of tinea corporis. Colonies on Sabouraud's maltose-agar pinkish with often a violet tinge.

Atrichophyton ceylonense Castellani, 1908.

Synonym.—*Trichophyton ceylonense* Castellani, 1908.
Found by Castellani in cases of tinea nigro circinata. Temporary species, cultivation having not been obtained; possibly a variety of *A. blanchardi*. In fresh preparations the spores are very few in number, roundish, rather large (4 μ), showing a double contour. The mycelial tubes are about 3½ μ in breadth, straight, or variously bent. It is found in tinea nigro circinata.

Atrichophyton macfadyeni Castellani, 1905.

Synonym. — *Trichophyton macfadyeni* Castellani, 1905.

Found by Castellani in some cases of tropical tinea corporis In fresh preparations mycelium and spores are rather of small dimensions. The mycelial tubes are regularly shaped, do not show swellings, and are about 2½ μ in breadth. The free spores are very numerous, and present a peculiar ovoid shape, the maximum diameter being 2½ to 3½ μ. In stained preparations the spores present a bipolar staining. The fungus grows with difficulty; on the rare occasions when the inoculations are successful, the growth is very slow, the colonies coalesce, forming a brownish mass, with deep furrows, and deeply rooted in the medium.

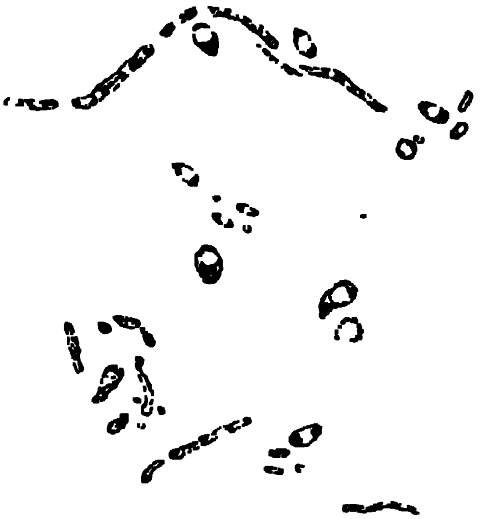


FIG. 508.—*Atrichophyton macfadyeni* CASTELLANI.
(Stained with fuchsin.)

INCERTÆ SEDIS.

Trichophyton balcaneum Castellani, 1916.

Found in cases of peculiar condition of the scalp in the Balkans, which clinically resembled more a diffuse type of severe *pityriasis sicca* than a trichophytic affection.

When grown on glucose agar from scales it slowly formed a somewhat crinkled growth of whitish colour. An interesting characteristic of this fungus is that apparently it does not become

TABLE SHOWING BIOCHEMICAL CHARACTERS OF *T. BALCANEUM.*

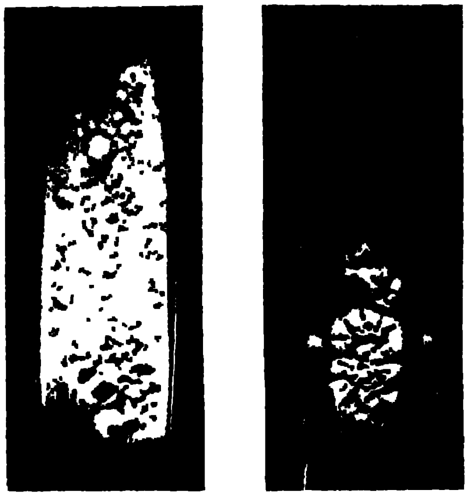
	Motility.	*Gram.*	*Gelatine.*			*Serum.*			*Litmus Milk.*			*Lactose.*			*Saccharose.*			*Dulcite.*			*Mannite.*			*Glucose.*			*Maltose.*		
			Day.			Day.			Day			Day.			Day.			Day.			Day.			Day.			Day.		
			4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12
Trichophyton balcaneum ..	O	O	+	+	−	O	O	O	O	AsC	A-C	O	O	O	O	O	O	O	O	O	O	O	O	Avs	Avs	Avs	O	O	O

	Dextrin.			*Raffinose.*			*Arabinose.*			*Adonite.*			*Inulin.*			*Starch.*			*Salicin.*			*Levulose.*			*Galactose.*			*Glycerine.*		
	Day.			Day.			Day			Day.			Day.			Day.			Day.			Day.			Day.			Day.		
	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12
Trichophyton balcaneum ..	O	O	O	O	O	O	A	As	As	O	O	O	O	O	O	O	O	O	O	O	O	Avs	Avs	O or Avs	O	O	O	O or Avs	O or Avs	O or Avs

Abbreviations used in the Table.—A = acid ; G = gas ; C = clot ; s = slight ; vs = very slight ; O = negative result—viz., non-production of acid or gas in sugar media, non-liquefaction of gelatine or serum, as the case may be ; + = positive result.

pleomorphic, even after very numerous transplantations. Gelatine is rapidly liquefied. It does not form gas in any carbohydrate medium.

Microscopically the fungus shows features intermediate between a trichophyton *sensŭ lato*, a microsporum and an achorion.



FIGS. 509 AND 510.—CULTURES OF *Trichophyton balcaneum* CASTELLANI: GLUCOSE AGAR.

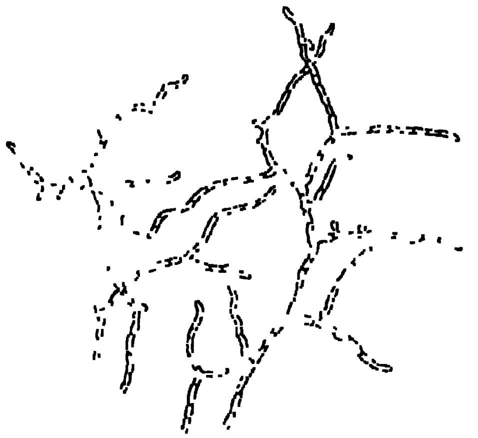


FIG. 511.—MICROSCOPICAL APPEARANCES OF *Trichophyton balcaneum* CASTELLANI: HANGING DROP CULTURE.

Genus Achorion Remak, 1845.

Definition.—Trichophytoneæ with mycelial filaments and spores in the lesions; in cultures conidial-bearing hyphæ present, with spores situate laterally and apically. Fusiform bodies in cultures in the form of swollen claviform ends of filaments. Yellow favic scutula present in lesions.

Type Species.—*Achorion schoenleini* Lebert, 1845.

Remarks.—The fungi belonging to this genus often show during parasitic life much longer mycelial segments than *Trichophytons* and *Microsporons*; masses of them, developing in hair follicles, form the well-known sulphur-coloured *scutula* which always develop round a hair. In the hairs the mycelial tubes are frequently trichotomous and tetrachotomous, forming structures which have been compared in appearance to the skeleton of the human foot, and called 'favus tarsi.'

Cultures.—Sabouraud has noted that in hanging-drop cultures the spores sometimes develop very slowly, sometimes rapidly. When the development is slow, there is formation of numerous chlamydospores of various sizes, with a double contour membrane. When the development is rapid, one notes that the mycelium ramifies quickly in every direction, with presence of very few or no chlamydospores. The following structures may be noted:

1. *Claviform Bodies.*—The terminal portion of some filaments becomes swollen and claviform. These claviform filaments have

been compared by some authorities to the 'spindles' of the *Trichophytons* and *Microsporons*, but they are slenderer, and not septate. The French authors call these formations 'chandeliers faviques,' on account of their shape somewhat resembling a candlestick.

2. *Favus Yellow Bodies.*—The protoplasm of some filaments collects itself at the terminal ends, the filaments becoming much thinner, and terminating in roundish or oval bodies, which must be considered to be terminal chlamydospores. It is to be noted that in the typical *Achorions* of human origin conidia-bearing hyphæ are not seen, while these are present in the *Achorions* of animal origin, in which separate spindles may be present.

Media.—*Achorions* grow well on all the usual sugar media, especially Sabouraud's agar and glucose agar. They generally liquefy gelatine fairly rapidly.

Pleomorphism.—Very common in all *Achorions*. If a culture becomes pleomorphic, it is impossible to make it revert to the original type.

Transmission.—In the case of *Achorions* of human origin infection takes place from man to man; in the case of *Achorions* of animal origin infection takes place from the lower animals. It is not impossible that *Achorions* may live saprophytically in nature.

TABLE OF ACHORIONS.

Genus.		Species.
Achorion Remak, 1815	Of human origin (typical)	A. schoenleini Lebert, 1845.
	Of animal origin (non-typical)	A. quinckeanum Zopf, 1890.
		A gypseum Bodin, 1907.
		A arloingi Blanchard, 1891.

These may be recognized as follows:—

A. Whitish-yellow cerebriform colonies—*Schoenleini*.
B. White downy colonies—*Quinckeanum*.
C. Yellowish colonies—*Gypseum*.

A. arloingi has not been properly described.

Achorion schoenleini Lebert, 1845.

Synonyms.—*Oidium schoenleini* Lebert, 1845; *O. porriginis* Montague; *Oöspora porriginis* Saccardo, 1886; *Oidium schoenleini* Zopf, 1890.

Causes the well-known affection called *favus*, which is characterized by the presence of peculiar disc-shaped crust formations, called *scutula*, of a sulphur-yellow colour, and emitting an offensive odour which has been compared to the smell of mice's urine.

The fungus may infect the hairs or glabrous parts of the body; it may attack the nails. In the hairs the mycelium is very abundant, the segments being comparatively long. Sometimes the mycelial threads divide into three or four branches, each of which terminates in a single row of roundish spores. This is known as *favic tarsus*.

Cultures.—The fungus is easily cultivated on various media. On Sabouraud's agar and on glucose agar the growth, when completely developed, is convoluted or cerebriform, and somewhat bulging. It has been compared by Sabouraud to the appearance of a sponge. The colour is white-yellowish, like that of old wax. After a time cultures become pleomorphic and abundant; white duvet is present. To prevent pleomorphism, media not containing sugars should be used (see p. 996).

A. schoenleini liquefies gelatine in between three to four days, while the *Trichophytons* take generally between fifteen to twenty days.

By inoculation of pure cultures of the fungus favus lesions are produced in man, dogs, mice, rabbits, and fowls. The inoculation in guinea-pigs does not give rise to typical favus lesions with scutula, but to circinate trichophytic-like lesions.

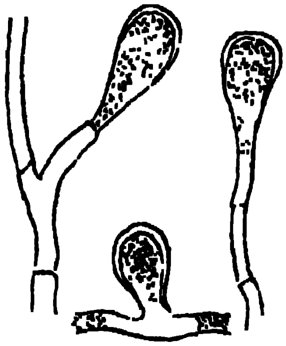


FIG. 512.—SO-CALLED YELLOW BODIES IN CULTURES OF *Achorion schoenleini* LEBERT.
(After Bodin.)

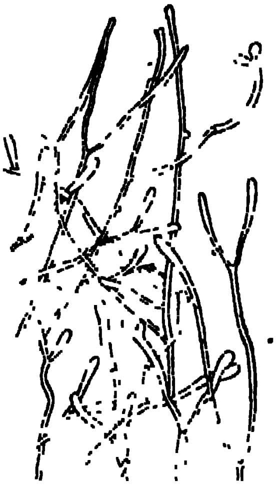


FIG. 513.—CLAVIFORM BODIES IN CULTURES OF *Achorion schoenleini* LEBERT.

Reproduction.—This takes place—

1. By sprouting.
2. By elongated fusiform structures analogous, according to some authorities, to the so-called 'spindles' of the *Trichophytons* and *Microsporons*, but they are slenderer and not septate. These formations are called by the French authors 'chandeliers faviques,' on account of their shape somewhat resembling a candlestick.
3. By so-called 'favus' or 'yellow bodies,' which are structures 8 to 15 μ in diameter, generally terminal, showing a double contour, and containing a granular substance. These structures should probably be considered to be chlamydospores (see also general remarks on the genus *Achorion*).

Sabouraud admits only one species of human *Achorion*, but Neeb and Unna have described as many as nine: *Achorion cysticum, A. tarsiferon, A. moniliforme, A. demergens, A. akromegalicum, A. dikroön, A. radians, A. euthythrix, A. atacton.* Sabouraud's opinion is the one generally accepted at the present time.

Achorion quinckeanum Zopf, 1890.

The fungus appears in the lesions in the shape of numerous mycelial filaments often dissociated in so many small segments constituting so-called spores. Grows readily on Sabouraud's agar, producing white, downy colonies.

This fungus botanically holds an intermediate position between the typical *Achorions* and the *Microsporons* and *Trichophytons*, conidia bearing hyphæ of the type *Acladium* being present. It produces, however, typical favus lesions with scutula.

Pathogenicity.—Is the cause of favus in mice, and may occasionally infect man, in whom, too, it induces typical favus. It can be inoculated into guinea-pigs.

Achorion gypseum Bodin, 1907.

Found by Bodin in 1907 in a typical case of favus. On Sabouraud's agar the growth, which is roundish, presents a little white duvet in the centre, while the rest has a glabrous surface of yellowish colour. Old cultures become pleomorphic, with presence of abundant white duvet all over the growth. Botanically the fungus is closely allied to the *Trichophytons* and *Microsporons*, but gives rise to typical favus, with scutula, when inoculated in mice and guinea-pigs. The inoculation of pleomorphic cultures does not cause any eruption.

Achorion arloingi R. Blanchard, 1891.

Synonym.—*Achorion arloingi* Busquet, 1891.

Incompletely known species. Was isolated from a human trichophytic-like eruption by Désir de Fortunet and Courmont. Is said to be inoculable into mice, rabbits, and man.

Genus Lophophyton Matruchot and Dassonville, 1899.

Mycelial filaments, either tortuous, very thin, or thick, with granular protoplasm. No spores present. One species only.

Lophophyton gallinæ Mégnin, 1881.

Synonyms.—*Epidermophyton gallinæ* Mégnin, 1881; *Lophophyton gallinæ* Matruchot and Dassonville, 1899; *Achorion gallinæ* Sabouraud, 910.

In the lesions mycelial filaments are seen, some thin and tortuous, without practically any protoplasm; others of much larger dimensions, with granular protoplasm. No spores observed. The fungus is easily cultivated, and is inoculable into rabbits, mice, and fowls, in which it gives rise to typical favus lesions. In man it does not produce favus, but merely trichophytic-like erythematous, squamous patches.

Genus Epidermophyton Lang, 1879, *emendavit* Sabouraud, 1907.

Definition.—Trichophytineæ with mycelial filaments and spores present in the lesions and with pluriseptate spindles present in the cultures. Does not attack the hairs or hair follicles, but grows in the superficial layers of the epidermis.

Type Species.—*Epidermophyton cruris* Castellani, 1905.

Remarks.—The fungi belonging to this genus, which has been investigated by Sabouraud and Castellani, grow superficially on the skin without invading the hairs and hair follicles; do not produce suppuration. Reproduction takes place principally by pluriseptate spindles, with, on the average, four to six cells. The septa, as noted by Pinoy, may not be complete, and the cavities may communicate. Spiral hyphæ, as found in most species of *Trichophyton*, absent; pectinate structures, as found in the *Microsporons*, absent; no spore-bearing hyphæ, with lateral conidia of type *Acladium*, as noted both in the *Trichophytons* and in the *Microsporons*. The cultures undergo rapid degenerative changes, losing their characteristics, and becoming covered with abundant uniform, long, whitish duvet (pleomorphism). They are not inoculable into guinea-pigs, except Pinoy's *Epidermophyton simii*. The species so far known have been isolated from human lesions, except the *Epidermophyton* discovered by Pinoy in monkeys.

TABLE OF EPIDERMOPHYTONS.

Epidermophyton Lang, 1879, *emendavit* Sabouraud, 1907	*E. cruris* Castellani 1905. *E. perneti* Castellani, 1907. *E. rubrum* Castellani, 1907.

These species may be recognized by their growths on Sabouraud's agar:—

A. Colour peculiar yellow—*Cruris*.
B. Colour pinkish—*Perneti*.
C. Colour deep red—*Rubrum*.

For *E. simii* Pinoy, 1911, we have created the genus *Pinoyella*.

Epidermophyton cruris Castellani, 1905.

Synonyms.—*Trichophyton cruris* Castellani, 1905; *Epidermophyton inguinalis* Sabouraud, 1907; *T. castellanii* Brooke, 1908.

Found in cases of tinea cruris in Ceylon by Castellani, and in France by Sabouraud. The fungus is very abundant in recent cases, extremely scarce in old ones. The mycelial tubes in recent cases are generally straight, have often a double contour, and the segments are somewhat rectangular, their breadth being $3\frac{1}{2}$ to $4\frac{1}{2}$ μ. Branching is not rare. The spores are rather large (4 to 7 μ), roundish, and have generally a double contour; they do not collect in clusters. In chronic cases degeneration forms of the fungus are met with; the mycelium may be banana-shaped, may show several constrictions, or long strings of ovoid elements may be seen.

This *Epidermophyton* grows well, but rather slowly, on Sabouraud's agar. The growth begins to be visible after four to eight days, the colonies being at first of a peculiar yellow colour, lemon-yellowish or orange-yellowish, occasionally with a greenish tinge. Later they become white, with pulverulent surface, and may be acuminate or crateriform. Pleomorphism, with abundant white duvet, develops quickly.

This fungus in Ceylon is the commonest species found in cases of tinea cruris. It is not inoculable into guinea-pigs. Attempts at reproducing the eruption in man by inoculating pure cultures have also failed.

Epidermophyton perneti Castellani, 1907.

This fungus has been described by Pernet. It differs from *E. cruris* by growing much more rapidly on Sabouraud's agar and by the cultures having a delicate pinkish colour, which is generally lost in subcultures. It is very rare in Ceylon.

Epidermophyton rubrum Castellani, 1909.

Synonym.—*Trichophyton purpureum* Bang, 1910.

This fungus was described by Castellani in Ceylon in 1909, and by Bang in France in 1910. On Sabouraud's agar the growth begins to appear four to six days after inoculation as a raised red spot, which gradually enlarges. At complete development the growth is of a deep red colour, either with a central knob or crateriform, and is partly covered with a white, delicate duvet. In old cultures the white duvet is much more abundant and thicker, and may hide the red pigmentation almost completely.

On *glucose agar* (4 per cent.), which is the best medium for this fungus, the growth is of a very deep blood-red colour, and the red pigmentation may spread to portions of the medium itself. In old cultures abundant white—occasionally white-greenish—duvet is present. This may hide the pigmentation, but, scraping out the duvet, the red pigmentation will be found to be still well marked. On ordinary agar and glycerine agar the fungus grows fairly well, but there is no red pigmentation.

Genus Endodermophyton Castellani, 1909.

Definition.—Trichophytoneæ with mycelial filaments and spores in the lesions, but no conidial filaments in cultures. Pluriseptate spindles unknown: grows between the superficial and deep layers of the epidermis, and does not attack the hairs or hair follicles.

Remarks.—The fungi belonging to this genus are characterized by their growth between the superficial and deep strata of the epidermis, forming an interlacing felt of mycelia, which detaches the horny and granular layers from the rete Malpighi. They do not invade the hair follicles, and do not cause suppuration. They have been cultivated by Castellani.

Cultures.—Botanically, these fungi are closely allied to the *Achorions*, as remarked by Sabouraud and Pinoy, who have examined Castellani's cultures. Attempts at cultivation failed for a long time, as they generally do not grow on solid media direct from the scales. These, after being treated with alcohol for five to ten minutes, must be placed in glucose-broth tubes, one scale in each tube. Most of the tubes become contaminated with bacteria, but in those which remain clear, after a time (five to ten days) a few delicate, short, white filaments will be seen originating from the scale. The growth slowly increases until, after three to four weeks, it takes the appearance of a small, white, fluffy mass, with a dark spot (the scale) in the centre. Portions of the broth cultures are sown on solid sugar media, on which growth takes place now quite easily. Fungi can then be indefinitely subcultured on solid media. The fungi grow much more abundantly on glucose agar, 4 per cent., than on Sabouraud or any other media.

Reproduction.—In hanging-drop cultures long mycelial filaments are seen; no conidia-bearing hyphæ are present; reproduction is apparently by sprouting, branching taking place; but further investigation is necessary on the subject.

Pleomorphism.—Pleomorphism is much less marked than in the *Trichophytons*, *Epidermophytons*, and *Achorions*, but old cultures may lose their characteristics, becoming covered with duvet.

TABLE SHOWING ENDODERMOPHYTONS FOUND IN MAN IN ORDER OF FREQUENCY.

E. tropicale Castellani.
E. indicum Castellani.
E. concentricum Blanchard.
E. mansoni Castellani.

These may be recognized as follows:—

A. Glucose agar cultures amber coloured, no duvet or only slight—*Tropicale*.
B. Glucose agar cultures deep red:—
  I. Causes *Tinea imbricata*—*Indicum*.
  II. Causes *Tinea intersecta*—*Castellanii*.
C. Glucose agar cultures after a time black:—
  I. Pigmentation fairly slow—*Concentricum*.
  II. Pigmentation very rapid—*Mansoni*.

Endodermophyton tropicale Castellani, 1914.

Remarks.—Manson, in 1872, described a trichophyton-like organism in the squamæ of *tinea imbricata;* with the laboratory techinque of that time attempts at cultivation did not succeed. Blanchard considered it non-cultivable, and called it *Trichophyton concentricum;* on the other hand, Nieuwenhuis stated that it was quite easily cultivable, and was characterized by the colonies being crateriform. His researches were not confirmed. In recent years the general opinion has been that aspergillus-like fungi were the real cause of the disease. Tribondeau described fructifications somewhat similar to those of an *Aspergillus*, and created for the fungus the genus *Lepidophyton*. Wehmer has described it as a true *Aspergillus*—*Aspergillus tokelau*. Castellani, from the investigations he has carried out in Ceylon, has come to the conclusion that *Aspergillus* and aspergillus-like fungi have nothing to do with the disease. When they are present in the squamæ, they are merely saprophytes or contaminations. By using a special technique he has succeeded in growing what he considers to be the true fungi causing the disease. He recognized at first two species, and more recently four, further investigation having shown that the term he used for one species (concentricum) covered more than one species.

Endodermophyton tropicale is very abundant in the lesions, forming a felting of interlacing mycelial threads with mycelial articles, regular in shape, rectangular or somewhat square-shaped, and usually straight. If the liquor potassæ be left to act some time, the mycelial articles, which are of very variable length, and 2½ to 3½ μ in breadth, will be seen to have a double contour. *Aspergillus* *fructifications*, described by so many authors, when present, are due to contaminations: they form no part of the fungus. Cultivation of this fungus has been obtained by Castellani, using the method mentioned in the paragraph above on the genus *Endodermophyton*.

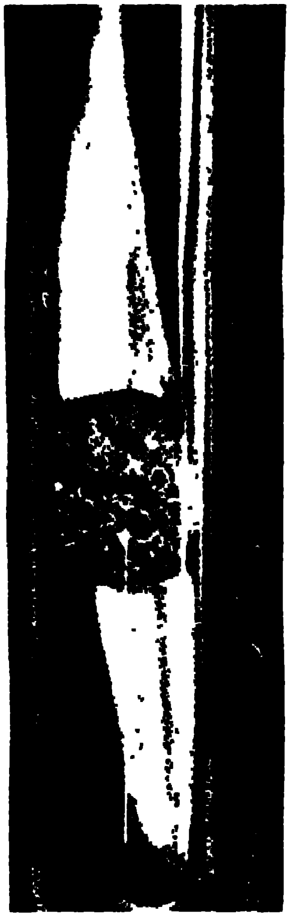


FIG. 514.—*Endodermophyton tropicale* CASTELLANI: GLUCOSE AGAR CULTURE.

FIG. 515.—*Endodermophyton tropicale* CASTELLANI: OLD GLUCOSE AGAR CULTURE.

The principal cultural characters on solid media, when the growth is fifteen to twenty-one days old, are as follows:—

Glucose Agar (4 *per cent.*).—Growth abundant; surface cerebriform or crinkled. The growth and the medium show a slight amber colour, which later on may become of much deeper hue. Duvet as a rule absent, but in old cultures which have been transplanted many times and are degenerating, some very scarce, short, whitish duvet may appear.

Sabouraud Agar.—Growth comparatively scanty, whitish-grey, mostly submerged. The colonies are whitish, have generally a small central knob and never show any duvet. The submerged portion is very firmly embedded, and often presents projections deepening in the medium. Colour of the medium unchanged.

Glycerine Agar.—Similar growth to Sabouraud's agar. When the colonies coalesce, the growth shows a knobby surface. No duvet.

Ordinary Agar.—Scanty growth, somewhat similar to Sabouraud. No duvet.

Mannite Agar (4 *per cent*).—Appearance somewhat similar to glucose, but growth less abundant. The medium may take a slight amber colour. No duvet.

Saccharose Agar (4 *per cent.*). Growth rather scanty, similar to Sabouraud. Duvet absent.

Nutrose Agar (4 *per cent.*). -Very slow growth. Separate young colonies have a central knob; they coalesce later into a knobby mass.

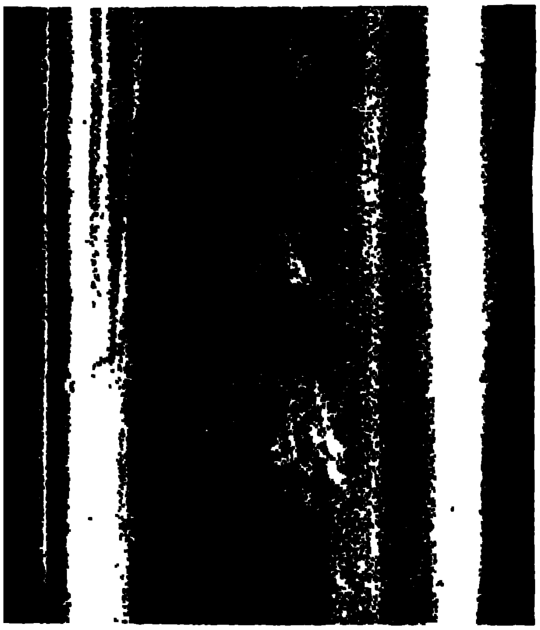


FIG. 516.—*Endodermophyton tropicale* CASTELLANI: AGAR CULTURE.

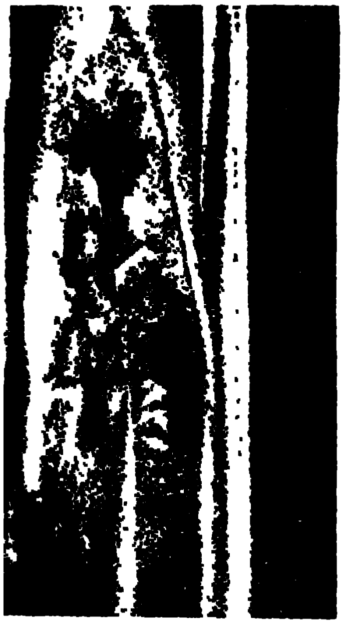


FIG. 517—*Endodermophyton tropicale* CASTELLANI: MALTOSE AGAR CULTURE.

Maltose Agar (*Acid*).—Similar to Sabouraud.

Maltose Agar (*Alkaline*).—Similar to Sabouraud.

Adonite Agar.—Not very abundant; cerebriform; duvet absent.

Galactose Agar.—Knobby or cerebriform.

Levulose Agar.—Knobby.

Raffinose Agar.—Cerebriform.

Inulin Agar.—Cerebriform.

Saccharine Agar (4 *per cent.*).—Somewhat knobby surface; duvet absent.

Lactose Agar.—Similar to Sabouraud, but surface growth more abundant.

Gelatine.—Very slow liquefaction of the medium.

Milk.—Very scanty growth. After a time the medium becomes separated

Sugar Broths (*Maltose, Lactose, etc.*).—Slight growth at the bottom of the tube; no production of acid or gas.

Hanging-Drop Cultures.—In hanging-drop cultures (Sabouraud's maltose broth) long mycelial threads are seen. Reproduction is apparently by sprouts from the mycelium, branching taking place.

Pathogenicity.—The fungus is the cause of a common type of tinea imbricata. Castellani has demonstrated that the inoculations into human beings of cultures of the fungus reproduce a typical form of tinea imbricata, and that from the scales of the eruption, experimentally induced, the same fungus is recoverable. For further details see Chapter XCII. on Tinea Imbricata (p. 2509).

Endodermophyton indicum Castellani, 1911.

This fungus was found by Castellani in some cases of *tinea imbricata.* The microscopical appearance of the fungus in the scales is identical with *E. tropicale.* The principal cultural characters on solid media, when the growth takes place in the dark, about 80° to 85° F., without rubber caps on the tubes, and is between fifteen and twenty-one days old, are as follows:—

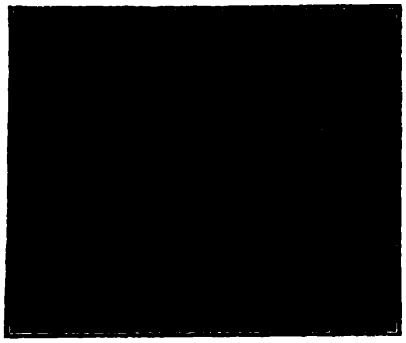


FIG. 518. — PATCH OF EXPERIMENTAL TINEA IMBRICATA IN A SINGHALESE BOY, OBTAINED BY INOCULATING A CULTURE OF *Endodermophyton indicum.*

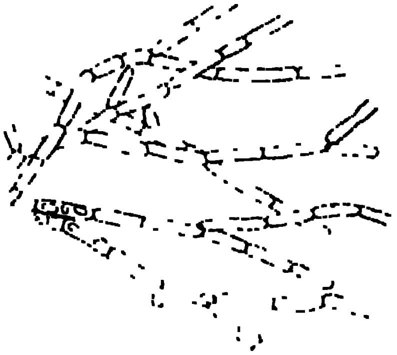


FIG. 519. — *Endodermophyton indicum* CASTELLANI: HANGING-DROP CULTURE.

Glucose Agar (4 *per cent.*).—Growth fairly abundant, with surface somewhat convoluted or furrowed. Portions of the growth, often the central, is of a deep orange, or pinkish-orange, or red-orange, occasionally of bright red colour. The surface of the rest of the growth often appears white and powdery, being covered by a very short delicate white duvet.

Sabouraud Agar.—Slow growth, with powdery surface, either with central knob or convoluted. The growth does not deepen in the medium so much as *E. concentricum.*

Glycerine Agar.—Growth abundant, white or amber colour; delicate white short duvet present on some portions of the growth.

Ordinary Agar.—Growth fairly abundant; knobby surface covered by snow-white very short delicate duvet.

Mannite Agar.—Growth knobby or convoluted, covered by short white duvet.

Saccharose Agar.—Cerebriform, covered by white duvet.

Saccharine.—Crinkled surface; delicate white duvet present.

Maltose Agar (*Acid*).—Somewhat similar to Sabouraud's, but the surface growth is more abundant.

Maltose Agar (*Alkaline*).—Similar to acid maltose, but the white duvet is more abundant.

Lactose Agar.—Knobby surface covered by snow-white duvet.

Nutrose Agar.—Yellowish crinkled surface; short white duvet present.

Levulose Agar.—Scanty growth, yellow or orange; scarce; very short white duvet present.

Galactose Agar.—Fairly abundant; surface convoluted with abundant, short snow-white duvet.

Raffinose Agar.—Same appearance as galactose.

Inulin Agar.—Same appearance as in galactose and raffinose agars.

Adonite Agar.—Cerebriform; surface covered with snow-white duvet.

Gelatine.—Very slow liquefaction.

Litmus Milk.—Very scanty growth. After a time the medium may become separated.

Various Sugar Broths (*Maltose, Lactose, etc.*).—Slight growth at the bottom of the tube. No production of acid or gas.

The annexed table shows at a glance the different cultural characteristics of the two fungi in the principal media.

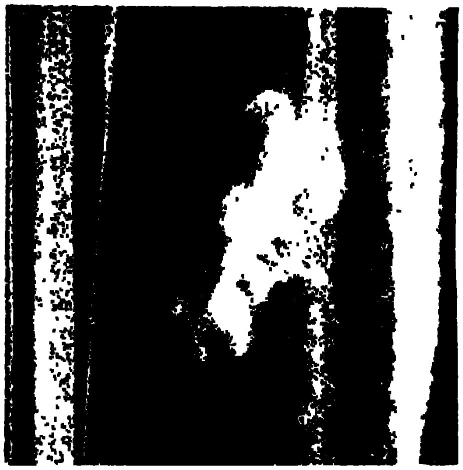


FIG. 520.—*Endodermophyton indicum* CASTELLANI: AGAR CULTURE.

FIG. 521.—*Endodermophyton indicum* CASTELLANI: GLUCOSE AGAR CULTURE.

COMPARISON BETWEEN THE CULTURAL CHARACTERS OF *Endodermophyton tropicale* AND OF *Endodermophyton indicum*.

Media.	*E. tropicale.*	*E. indicum.*
Glucose agar ..	Amber colour, duvet absent in young cultures.	Deep orange, at times, pinkish or red, very short white delicate duvet often present.
Sabouraud agar	Growth scanty, mostly submerged, grey-whitish duvet absent.	Surface growth more abundant, powdery white.
Agar	Scanty, mostly submerged; similar to Sabouraud agar; no duvet.	Fairly abundant, knobby well-marked snow-white duvet.
Glycerine agar ..	Growth mostly submerged; surface growth very scanty; similar to Sabouraud agar; no duvet.	Surface growth very abundant; crinkled appearance; white short duvet present.

The above characters are based upon the appearance of cultures kept in the dark at a temperature 80° to 90° F., and without rubber caps. If any of these conditions are altered, the cultural characters are changed. If rubber

caps are used, both *E. indicum* and *E. tropicale* may assume a bright red colour. If, however, subcultures are made from these, using tubes without rubber caps, the fungi again show the characters given above.

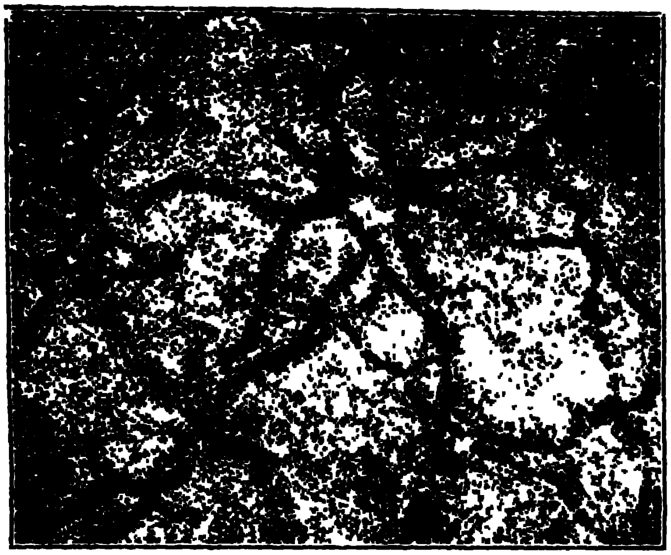


FIG. 522.—*Endodermophyton indicum* CASTELLANI IN THE SCALES.

Hanging-Drop Cultures.—Long mycelial filaments are present. No free spores are seen; reproduction is apparently by sprouts from the mycelium.

Pathogenicity.—The fungus is the cause of a certain number of cases of tinea imbricata. The type of the disease caused by this fungus seems to be more superficial than that caused by *E. tropicale*, but further researches are required on this subject. Castellani has succeeded in experimentally reproducing the disease by inoculating coolies, who had volunteered, with pure cultures of the fungus. The skin was first scarified with a sterile knife; then a certain amount of a pure agar culture of *E. indicum* was well rubbed in. After fifteen to twenty-one days the first signs of the eruption appeared, and the typical patches of tinea imbricata developed. From the scales of the experimental cases a fungus was grown absolutely identical with the strain of *E. indicum* with which the individuals had been inoculated.

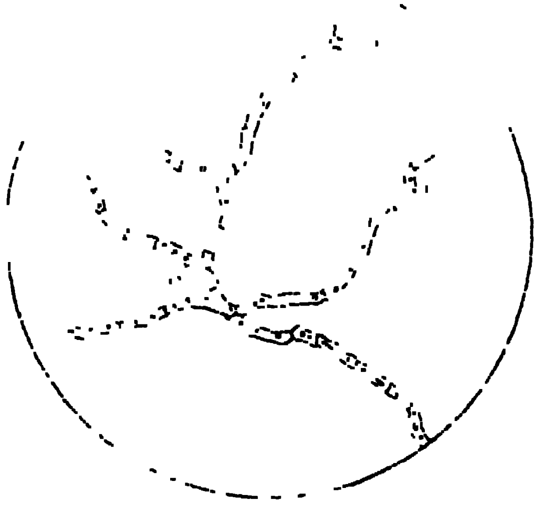


FIG. 523.—*Endodermophyton castellanii* PERRY.

Endodermophyton castellanii
Perry, 1907.

Found by Castellani in cases of *tinea intersecta*. In the scales the mycelium is fairly abundant; no free spores are seen. Mycelial segments uniform, rather straight, and, provided the liquor potassæ be left to act for sufficient time, they often show a double contour. Their breadth is $2\frac{1}{2}$ to $3\frac{1}{2}$ μ. Each mycelial segment has two roundish refringent dots, one at each extremity. Has been cultivated only on one occasion, the cultures being apparently similar to those of *E. indicum*. It is the cause of tinea intersecta.

Endodermophyton concentricum Blanchard, 1901.

Cultures on glucose agar are at first amber colour, but after four to eight weeks become jet-black and covered with abundant duvet.

Endodermophyton mansoni Castellani, 1914.

Portions of the growth are black from the very first, scanty duvet.

Genus Pinoyella Castellani and Chalmers, 1908.

Definition.—Trichophytoneæ with mycelial filaments and spores in the lesions, and in cultures conidial-bearing hyphæ, with the spores situate laterally only.

Type and only Species.—*Pinoyella simii* (Pinoy, 1911); *Epidermophyton simii* Pinoy, 1911.

Discovered by Pinoy in a trichophytic-like eruption observed in a monkey. On Sabouraud's agar the growth is at first yellowish-orange, somewhat similar to *Epidermophyton cruris*; later, the growth is whitish and covered with white duvet.

Pinoy's fungus has several interesting botanical features, some of which are those of the genera *Microsporon* and *Trichophyton*. In contrast to the typical *Epidermophytons*, it presents spore-bearing hyphæ with lateral conidia, and is inoculable into guinea-pigs, in which it produces a trichophytic-like eruption.

Genus Montoyella Castellani, 1907.

Definition.—Trichophytoneæ with mycelial filaments and spores in the lesions, in cultures conidial-bearing hyphæ with only terminal spores.

Remarks.—Temporary genus. Two kinds of mycelial threads: some slender, ramified, septate; others much thicker, having numerous intermediate chlamydospores. From the thicker filaments delicate hyphæ take origin, which terminate in large pear-shaped or globular conidia.

Type Species.—*Montoyella nigra* Castellani, 1907.

Classification.—There are two species, which may be differentiated as follows:—

A. **Cultures black—*Nigra*.**
B. **Cultures whitish or greenish—*Bodini*.**

Montoyella nigra Castellani, 1907.

Temporary species. Colonies on maltose agar are black. If glycerine agar is used, the medium takes a black colour. This species, discovered by Montoya, is common in black pinta.

Montoyella bodini Castellani, 1907.

Temporary species. Colonies whitish or greenish.

FAMILY ASPERGILLACEÆ.

Definition.—Aspergillales with compact peridium, small sessile closed perithecia.

Type Genus.—*Aspergillus* Micheli, 1729.

Classification.—The genera of the Aspergillaceæ can be recognized as follows:—

A. *Spores unicellular* :—
  I. Perithecium beaked—*Microascus*.
  II. Perithecium not beaked:—
    (*a*) Perithecia with appendages—*Cephalotheca*
    (*b*) Perithecia without appendages:—
      1. *Conidiophores* absent - *Thelavia*.
      2. *Conidiophores* present:—
        (A) Conidia solitary—*Aphanoascus*.
        (B) Conidia in chains:—
          (i.) Conidiophores simple—*Emericella*.
          (ii.) Conidiophores enlarged apically and bearing sterigmata:—
            (1) Sterigmata simple—*Aspergillus*.
            (2) Sterigmata branched—*Sterigmatocystis*.
          (iii.) Conidiophores branched:—
            (1) Sympodially branched—*Eurotiopsis*.
            (2) Bushy branched:—
              (*a*) In bundles, perithecia stalked—*Penicilliopsis*.
              (*b*) Not in bundles, perithecia sessile—*Penicillium*.
B. *Spores bicellular*—*Testudina*.

We are concerned with the genera *Penicillium*, *Aspergillus*, and *Sterigmatocystis*, of which the following species are parasitic in man:

Penicillium Link, 1809	*P. crustaceum* Linnæus, 1763.
	P. minimum Siebenmann, 1889.
	P. barbæ Castellani, 1907.
	P. montoyai Castellani, 1907.
	P. pruinosum Salisbury.
	P. brevicaule var. *hominis* Brumpt and Langeron, 1910.
Sterigmatocystis Cramer, 1869	*S. antacustica* Cramer, 1859.
	S. nidulans Eidam, 1883.
Aspergillus Micheli, 1725	*A. fumigatus* Fresenius, 1775.
	A. flavus Link, 1791.
	A. bronchialis Blumentritt, 1901.
	A. nigrescens Robin, 1851.
	A. repens De Bary, 1870.
	A. malignus Lindt, 1889.
	A. pictor R. Blanchard, 1895.
	A. barbæ Castellani, 1907.
	A. bouffardi Brumpt, 1905.
	A. herbariorum Wiggers, 1780.
	A. fontoynonti Guéguen, 1909.

Genus Penicillium Link, 1809.

The whole fruit-bearing hypha with its sterigmata and conidia resembles a hair-pencil, hence the name of the genus (*Penicillium*= hair-pencil). The conidiophore hypha shows verticillate branches, which give rise to slender fusiform formations (sterigmata) abstricting chains of conidia.

Penicillium crustaceum Linnæus, 1763.

Synonyms.—*Mucor crustaceus albus* Linnæus, 1763; *Monilia digitata* Persoon; *Penicillium glaucum* Linnæus, 1809: *P. expansum* Linnæus; *P. crustaceum* Fries, 1829.

An extremely common saprophyte found on bread, cheese, fruits, and various organic substances in a state of decomposition. The conidia are spherical or slightly elliptical, of bronze colour, with smooth surface; maximum diameter 4 µ. This fungus grows well at any temperature between 2° and 35° C., and is very resistant.

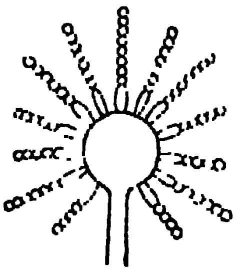


FIG. 524.—ASPERGILLUS FRUCTIFICATION.

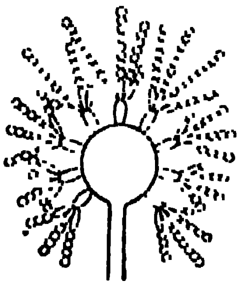


FIG. 525.—STERIGMATOCYSTIS FRUCTIFICATION.

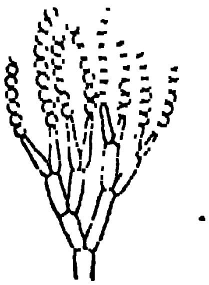


FIG. 526.—PENICILLIUM FRUCTIFICATION.

(After Brumpt.)

It has been found by Maggiora and Gradenigo in two cases of otitis media. Heinhorn has observed it in the vomiting of four cases of acid dyspepsia together with *Aspergillus herbariorum*.

Wertheim has observed that the intravenous inoculation of *P. crustaceum* is pathogenic to rabbits, dogs, and lambs.

Penicillium minimum Siebenmann, 1889.

Conidia are roundish, smooth, of a brownish-black colour: smaller than in *P. crustaceum*, being 2·5 to 3 µ in diameter. Was found in a case of acute otitis by Siebenmann.

Penicillium montoyai Castellani, 1907.

Synonym.—*P. pictor* Neveu-Lemaire, 1908.

Conidia roundish or slightly oval, smooth, 3 to 4½ µ in diameter. Grows well on maltose agar and ordinary agar; cultures of dark greyish colour. Discovered by Montoya in cases of pinta, of the greyish-violet variety. Similar species, not yet well defined, are found in other varieties of pinta.

Penicillium brevicaule var. hominis Brumpt and Langeron, 1910.

Found by Brumpt and Langeron in two cases of onychomycosis. In the lesions septate mycelial threads were seen, 2 to 10 μ in diameter, and large groups of chlamydospores, generally terminal, 10 to 30 μ in diameter. The fungus is easily cultivated on Sabouraud's agar and other sugar media, also on potatoes and carrots. Optimum temperature 25° C., but grows well also at 37° C. Conidia spherical or occasionally ovoid, of a chocolate colour.

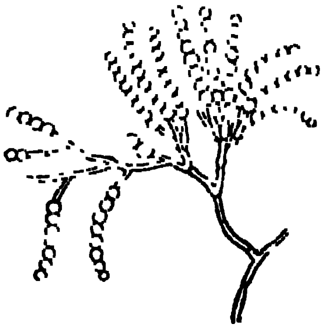


FIG. 527.—*Penicillium brevicaule* VAR. *hominis* BRUMPT AND LANGERON. (After Brumpt.)

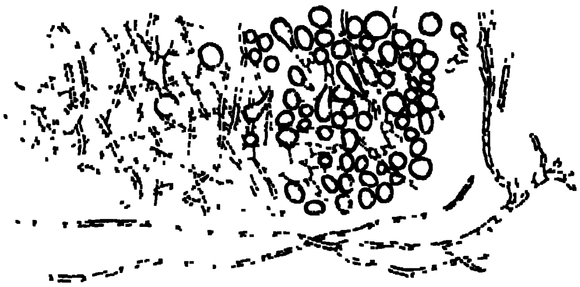


FIG. 528.—*Penicillium brevicaule* VAR. *hominis* BRUMPT AND LANGERON. (Preparation from the diseased nails, after Brumpt.)

Penicillium barbæ Castellani, 1907.

Found by us growing on the beard of natives of equatorial Africa, and in natives of Ceylon.

Penicillium pruriosum Salisbury.

Doubtful species found by Salisbury in the vaginal mucus of a woman suffering from intense vaginal pruritus.

Genus Aspergillus Micheli, 1725.

The conidiophore hypha are not ramified, and terminate into ovoid or roundish formations, which support numerous claviform elements (sterigmata), each of which supports a chain of roundish conidia.

Aspergilli are generally saprophytes, but they may become parasites. They are easily grown on acid media, liquid or solid, and also on alkaline media. Iron and manganese have a favourable influence on the growth and sporulation of these fungi.

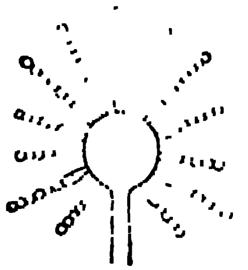


FIG. 529.—ASPERGILLUS FRUCTIFICATION. (After Brumpt.)

A medium much used is Raulin's liquid, the formula of which is: Cane-sugar, 70 grammes; tartaric acid, 4 grammes; ammonium nitrate, 4 grammes; ammonium phosphate, 0·60 gramme; potassium carbonate, 0·60 gramme; magnesium carbonate, 0·40 gramme; ammonium sulphate, 0·25 gramme; zinc sulphate, 0·07 gramme; ferrous sulphate, 0·07 gramme; potassium silicate, 0·07 gramme.

Fungi of the genus *Aspergillus*, when growing parasitically in the tissues, often lose their characteristics; the typical fructifications are absent, and only mycelial threads and roundish or oval yeast-like bodies are seen.

The various species may be differentiated with difficulty as follows, or cannot be differentiated :

- A. *Green species* :—
  - I. Spores 5 microns and more Can hardly be differentiated - *Repens, Flavus*
  - II Spores less than 5 microns:
    - (*a*) Lives saprophytically - *Fumigatus*.
    - (*b*) Not known to live saprophytically: -
      - 1. Very pathogenic for rabbits -*Malignus*.
      - 2. Found in bronchial sputum -*Bronchialis*.
- B. *Blackish-brown* species -*Nigrescens*.
- C. *Golden, brownish*, gold-brown, or reddish - -*Herbariorum*.

Aspergillus fumigatus Fresenius, 1775.

This is the commonest *Aspergillus*, and is very often found on various cereals, straw, hay, etc. On solid media it produces a brownish-black culture if the medium is alkaline or neutral, greenish if the medium is acid. The mycelial filaments are more or less ramified, the breadth varying between 2 and 3 μ. The conidiophore hyphae are much thicker than the mycelial tubes, being, on the average, about 5 μ in breadth. The sterigmata, which are situated very close together, are 6 μ long; the conidia are roundish, 2·5 to 3 μ in diameter, smooth, colourless. Optimum temperature, 37° C.; the growth stops below 20 or above 55°C.

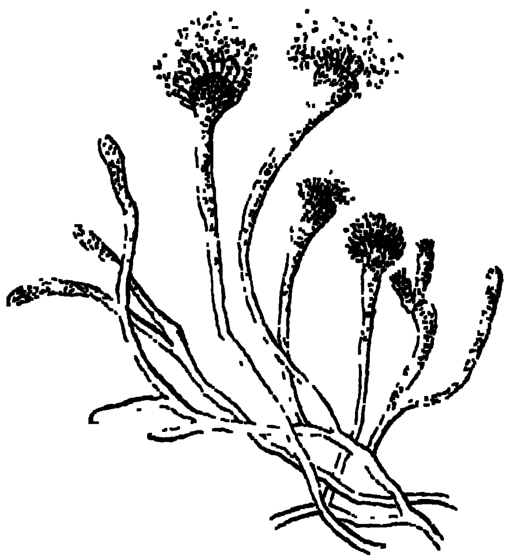


FIG. 530.—*Aspergillus fumigatus* FRESENIUS.

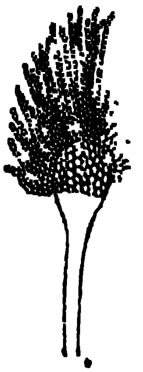


FIG. 531.—*Aspergillus bronchialis* BLUMENTRITT. (After Blumentritt.)

Pathogenicity.—This *Aspergillus* is the species most frequently found in man, giving rise to an aspergillosis of various organs. The spores are very resistant. Perchloride of mercury is the antiseptic which has the greatest destructive action on the spores. The effects on the human organism are due, in addition to mechanical action, to toxins secreted by the fungi. Lucet has found in cultures of *A. fumigatus* in Raulin's liquid a pyrogenic substance; Ceni and

Besta have isolated toxic products soluble in ether and alcohol, which act on the muscular and nervous system of dogs and rabbits. (See also remarks on Aspergillomycoses, p. 1031.)

Aspergillus flavus De Bary, 1870.

Synonyms.—*Monilia aurea* Gmelin, 1791; *Eurotium flavum* De Bary, 1870; *Aspergillus flavescens* Wreden, 1874.

Mycelium colourless; conidiophore hyphæ terminate in roundish formations of a gold-yellow colour. The conidia are dark yellow, roundish, 5 to 7 μ in diameter, with a surface showing numerous minute mammillar prominences. Found by several observers (Wreden, Siebenmann, etc.) in the ear. Optimum temperature, 37° C.

Aspergillus bronchialis Blumentritt, 1901.

Mycelium of a white colour, much ramified; conidiophore hyphæ are 6·2 to 12·6 μ in diameter, 280 to 300 μ in length. Conidia roundish, 3 to 4 μ in diameter, with a smooth surface, of a greyish-greenish colour. This *Aspergillus* was found by Chiari in the bronchi of a patient who had died from diabetes; it was investigated by Blumentritt. It has not yet been found as a saprophyte.

Aspergillus fontoynonti Guéguen, 1909.

Found by Fontoynont and Carougeau in a European living in Madagascar, who was suffering from multiple abscesses of the neck. In the pus and in the first cultures obtained the fungus had no true aspergillar appearance; it had to be subcultured several times before the typical aspergillar fructifications appeared. Conidia 4 to 5 μ in diameter, with surface finely verrucose. Optimum temperature, 22° to 25° C.

Aspergillus malignus Lindt, 1889.

Synonym.—*Eurotium malignum* Lindt, 1889.

Colourless mycelium, composed of short articles. Conidiophore hyphæ erected, terminating in pyriform formations, 22 to 24 μ in diameter, on which are situated the sterigmata, which are 10 μ long and 4 to 5 μ in breadth. Conidia roundish, of a greenish-bluish colour.

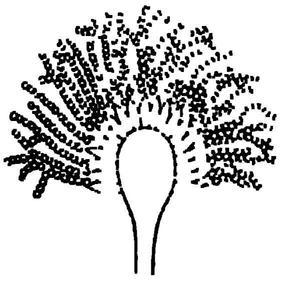


FIG. 532.—*Aspergillus malignus* LINDT.
(After Lindt.)

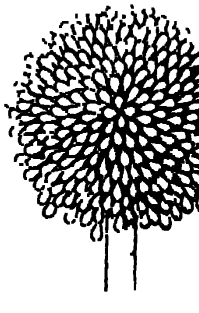


FIG. 533.—*Aspergillus repens* DE BARY.
(After Siebenmann.)

Pathogenicity.—This *Aspergillus* was found by Lindt in a case of otomycosis; according to this author, it is very pathogenic for rabbits.

Aspergillus herbariorum Wiggers, 1780.

Synonyms.—*Mucor herbariorum* Wiggers, 1780: *Aspergillus glaucus* De Bary, 1870.

Mycelium at first colourless, later yellow or reddish-yellow. This *Aspergillus* is characterized by the large size of the conidia, which are 9 to 15 μ in diameter. It is in nature a common saprophytic fungus. It has been found by Dunn in 1896 in the nasal cavities of a man, and by Einhorn in 1900 in the vomit of a case of hyperchloridia.

Aspergillus repens De Bary, 1870.

Synonym.– *Eurotium repens* De Bary, 1870.

This fungus is very similar to *A. herbariorum*, but for the smaller size of the conidia. Mycelium of a yellowish-green colour. Conidia large, 7 to 8·5 μ. Found by Siebenmann in the ear three times. Its pathogenic rôle is doubtful.

Quevedo has described an aspergillus very similar to *A. repens*, which he believes to be the cause of a type of encephalo-myelitis in horses in South America. He calls the organism *A. mayidis*.

Aspergillus pictor R. Blanchard, 1895.

Synonym. -- *Trichophyton pictor* R. Blanchard, 1895.

The term *Aspergillus* (*Trichophyton*) *pictor*, introduced by Blanchard in 1895, before the plurality of species of the fungi found in pinta was demonstrated, is now used to denote the species of *Aspergillus* which is found in the pure violet variety of pinta. This fungus shows the typical morphological characters of the genus *Aspergillus*. It grows easily on various sugar media. On maltose agar the growth has at first a whitish colour, which afterwards changes into greenish, to become violet or greenish with a violet tinge at a later period. The colour of the growth may vary according to the medium on which cultivation takes place. The conidiophores are comparatively thick; the conidia are globular, with a smooth surface.

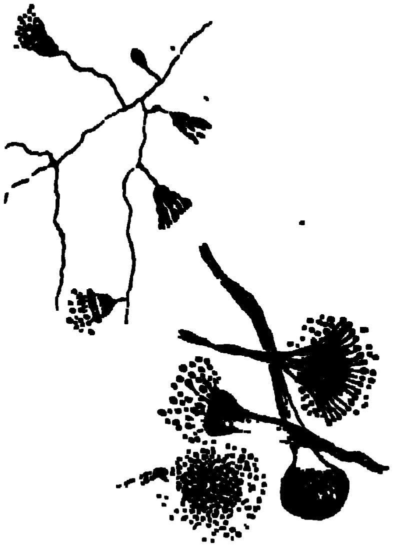


FIG. 534.—*Aspergillus pictor* R. BLANCHARD. (After Montoya y Florez.)

Several other species of aspergillar and aspergillar-like fungi are found in pinta, but their botanical position has not yet been defined with certainty.

Aspergillus bouffardi Brumpt, 1905.

Found by Bouffard in a case of black mycetoma, and completely described by Brumpt. Mycelium whitish in some zones, dark brown in others. Conidiophores erect, white, each terminating in a claviform structure, bearing some short chains of roundish conidia. Conidia 1·3 to 2 μ in diameter, roundish with a smooth surface, white. Chlamydospores present, 5 to 10 μ in diameter. Attempts at cultivation did not succeed.

Aspergillus barbæ Castellani, 1907.

Found by us in natives of Uganda, and in natives of Ceylon. Conidia spherical, 4 to 5 μ of a brownish colour.

Aspergillus nigrescens Robin, 1889.

Doubtful species, which, according to Wienfeld, causes a faviform eruption.

Genus Sterigmatocystis Cramer, 1859.

Definition.- Aspergillales with conidiophores terminating in roundish or ovoid formations, on which are situated short cylindrical structures *primary sterigmata* surmounted by similar elements—*secondary sterigmata*. Each of the secondary sterigmata supports a chain of roundish conidia.

Remarks. The genus was created by Cramer for a fungus found in a man's ear.

Type Species. *Sterigmatocystis antacustica* Cramer, 1859.

Classification. The two species of importance to us can be recognized as follows

A. Young conidial forms green; later strongly grey to brown. Conidia small 3 microns in diameter *Nidulans*

B Conidial forms blackish brown Conidia small, 2·5 microns in diameter—*Antacustica*.

Sterigmatocystis antacustica Cramer, 1859.

Synonyms. *Sterigmatocystis antacustica* Cramer, 1859; *Eurotium nigrum* De Bary, 1870; *Monilia pulla* Persoon; *Aspergillus nigricans* Wreden, 1874; *A. niger* von Tieghem, 1867.

Primary and secondary sterigmata: erected conidiophores: hyphæ more than 1 millimetre in length (3·5 to 4·5). Conidia globular, 2·5 μ in diameter, provided with a membrane of a brownish colour. Commonly found in decaying organic substances. It was first observed in man by Cramer, who observed it in the ear of a deaf patient. Later it was observed by Fürbringer and others in mycotic affections of the lungs.

Sterigmatocystis nidulans Eidam, 1883.

Synonym.—*Aspergillus nidulans* Eidam, 1883.

Mycelium of a greenish colour. Conidiophores are erect, 0·5 to 0·8 millimetre in length. Presence of primary sterigmata, supporting secondary sterigmata, each of which gives rise to a chain of conidia. Conidia small (2 to 3 μ in diameter), globular, of a greenish colour. The fungus has been completely investigated by Pinoy: grows badly in Raulin's liquid, better on Sabouraud's: is non-pathogenic for rabbits. This species is found living saprophytically in certain nests, hence the name *S. nidulans*. In man it has been found in several cases of otomycosis. Nicolle and Pinoy have found it, or a very similar species, in a case of mycetoma with white granules.

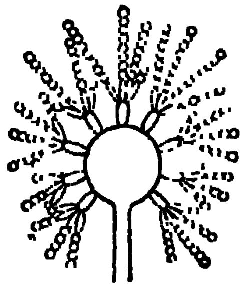


FIG. 535.—STERIGMATOCYSTIS FRUCTIFICATION.
(After Brumpt.)

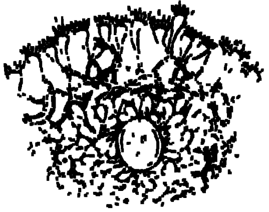


FIG. 536.—*Sterigmatocystis nidulans* EIDAM.
(After Eidam, from Brumpt.)

General Remarks on Mycoses due to Species of the Family Aspergillaceæ.

These mycoses are generally called aspergillomycoses. They have been recorded several times in man.

1. ASPERGILLOSIS OF THE LUNGS; ASPERGILLAR PSEUDO-TUBERCULOSIS; PNEUMOMYCOSIS OF ASPERGILLAR ORIGIN.—*Aspergilli* develop sometimes in the mucosa of the trachea, of the bronchi, and even in the pulmonary alveoli, without giving rise to any pathogenic effect. In other cases the fungi induce pseudo-membranous and ulcerative lesions. A very serious affection is a form of pseudo-tuberculosis (pseudo-tuberculosis aspergillina), characterized by the presence of mycotic nodules in the lungs, liver, kidneys, and other organs. This affection, due to *A. fumigatus*, is very common in some parts of France among pigeon-breeders (*gaveurs de pigeons*). The same affection attacks the pigeons. The infection is probably caused by spores of *A. fumigatus* being present in the grains used for feeding the pigeons.

2. ASPERGILLOSIS OF THE EYE.—*A. fumigatus* has been found several times in ulcers of the cornea (keratomycosis aspergillina).

3. ASPERGILLOSIS OF THE EAR (OTOMYCOSIS ASPERGILLINA).—Various species of *Aspergillus* have been found in the ear. In some cases they may give rise to a serious otitis, deafness, and tinnitus. Aspergillosis of the ear is not rare in the tropics. Syringing with hydrogen peroxide two parts and alcohol one part is useful.

4. ASPERGILLOSIS OF THE NOSE.—*A. glaucus* and *A. fumigatus* have been found in the nasal cavities; the first apparently does not

cause any disturbance. The second causes various inflammatory symptoms.

5. ASPERGILLOSIS OF WOUNDS AND ULCERS.—In wounds not properly treated, and in old ulcers, *Aspergilli* have been occasionally found.

6. ASPERGILLOSIS OF THE URETHRA.—In several cases a black urethral discharge has been observed, due to *Sterigmatocystis nigra.*

7. ASPERGILLOSIS OF THE SKIN.—Montoya's investigation has shown that several varieties of pinta are due to fungi of the genus *Aspergillus.* Another important tropical skin disease, tinea imbricata, was believed until recently to be due to an *Aspergillus*—*A. tokelau* Wehmer, 1903. In our experience the fungi of tinea imbricata never show aspergillar fructifications, and cannot be considered to be *Aspergilli.*

Aspergilli may also cause some varieties of mycetoma.

PYRENOMYCETES.

Ascomycetous fungi in which the asci are contained in a perithecium presenting an orifice at the apex for the escape of the spores. According to some authors, species of this family have been found parasitic in man. This is very doubtful, though Schubert states that he found in the nasal mucus of a patient an organism closely allied to *Botrytis bassiana,* which latter species, as is well known, causes the disease of silkworms called muscardin.

CLASS BASIDIOMYCETES.

Basidiomycetes have a septate mycelium, and are devoid of sexual reproduction. They reproduce by formation of basidia. Other accessory fructifications may be present—as, for example, chlamydospores. The basidia are of two principal types: (1) autobasidia; (2) protobasidia.

The autobasidia are large, unseptated cells, giving rise at their apices to four delicate sterigmata, each of which bears a spore.

The protobasidia are septated, and appear in two chief forms:—

A. Septated into four cells, each giving rise to a spore from a lateral inserted sterigma.

B. Septated by walls intersecting at right angles, each cell ending in an elongated tubular sterigma.

Of the Basidiomycetes, one species (*Ustilago phyodytes*) of the family Ustilagineæ is of special importance, while two others (*U. carbo* and *Tilletia lævis*) may produce otomycosis.

Ustilago hypodytes Schlecht.

Synonyms.—*Dendrodochium microsporus* Brigi; *Sporotrichum dermatodes* Kane.

The mycelium penetrates the stem and leaves of reeds (*Arundo donax*) in some parts of Provence, Italy, and Greece. After a time the mycelium produces innumerable so-called brand spores by a process of segmentation of its profusely branched hyphæ. In this way the mycelium is transformed into a brown dark mass of spores.

These brand spores, as regards the mode of their formation, may be considered chlamydospores. The brand spores are resting spores; they are scattered by the wind, and after an interval of rest they germinate, producing conidiospores of a basidium-like type.

The spores of *U. hypodytes* are the cause, according to most authors, of a peculiar affection found among workers who have to do with the cutting, etc., of reeds (*Arundo donax*). This affection is called 'frienite,' or 'frien disease.' The patient complains of symptoms somewhat resembling hay-fever—sneezing, headache, etc.—and, in addition, shows an erythematous erysipeloid eruption on the uncovered part of the body, and often also on the genital organs, which may become greatly œdematous. Desquamation follows.

According to other observers, the cause of this peculiar disease is to be found, not in the spores of *Ustilago*, but in an insect—*Aclerda berlesei*, discovered by Berlese—which often swarms on various reeds. The workers, in manipulating the canes, squash some of these insects, and the irritating juice exuding therefrom produces a dermatitis of an erythematous type.

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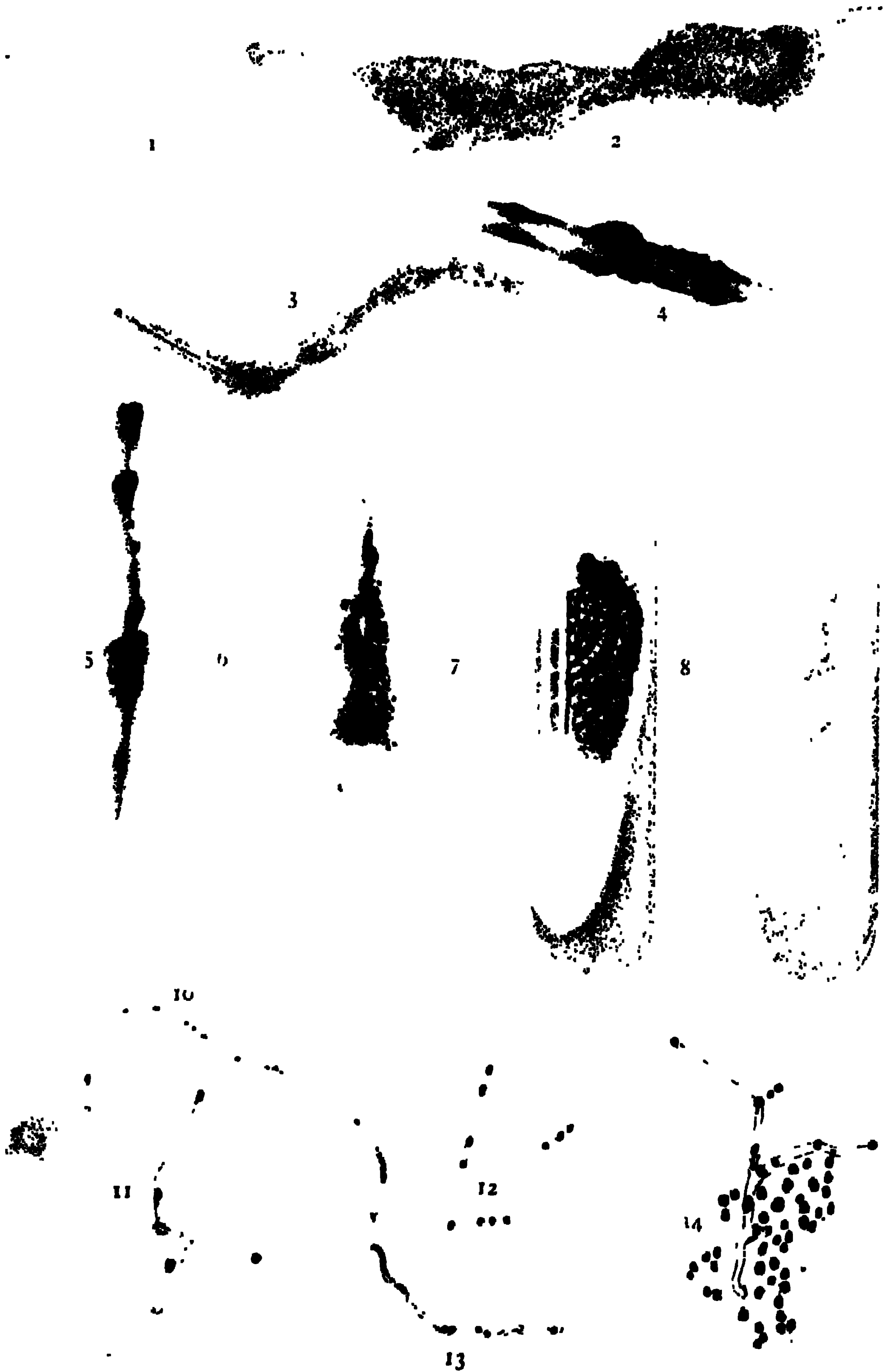
Thom and Currie (1916.) Journal of Agricultural Research, October (*Aspergillus niger* Group). Washington.

PLATE VI

NOCARDIAS AND ASSOCIATED ORGANISMS

1. Hair, natural size: Trichomycosis flava.
2. Trichomycosis flava.
3. Trichomycosis flava.
4. Trichomycosis nigra.
5. Trichomycosis rubra.
6. Hair, natural size: Trichomycosis rubra.
7. *Rhodococcus castellanii* (Chalmers and O'Farrell, 1913).
8. *Nocardia indica* (Kanthack, 1893).
9. *Nocardia convoluta* Chalmers and Christopherson, 1910.
10. Hair, natural size: Trichomycosis nigra.
11. *Cohnistreptothrix tenuis* (Castellani, 1911), branching.
12. *Cohnistreptothrix tenuis* (Castellani, 1911), bacillary forms.
13. *Cohnistreptothrix tenuis* (Castellani, 1911), long form.
14. *Cohnistreptothrix tenuis* (Castellani, 1911), branching forms and coccal forms from a culture.

PLATE VI.



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CHAPTER XXXIX

FUNGI IMPERFECTI

Preliminary—Fungi imperfecti—Hyphales—Vuillemin's classification—Microsiphonales — Thallosporales — Hemisporales — Conidiosporales — References.

PRELIMINARY.

We now come to the last class of Schroeter's Eumycetes—viz., the Fungi Imperfecti; that is to say, Eumycetes with a septate mycelium and with spores which are not contained in asci or basidia, but are carried on conidiospores, which may or may not be enclosed in pycnidia.

This class contains a large number of genera of importance in tropical medicine, but everyone who has studied these fungi must have felt, as we have, the great difficulty of determining to what genus the organism belonged at which he was working.

Various systems have been proposed, such as the mode of bearing spores and the colour of the fungus, matters which change with environment. Further septation of the spores often depends upon their age and other factors. Similarly new species have been made for a fungus, very like another fungus, but found on a new host. In this way the classification has become almost hopeless.

Vuillemin has, however, proposed a new classification, which prevents the same fungus being variously classified in different stages of its life-history. We adopt it for purposes of utility.

CLASS: FUNGI IMPERFECTI Fuckel, 1869.

Synonym.—*Deuteromycetaceæ* Saccardo ('Sylloge,' vol. xvi., p. 825).

Definition.—Fungi, almost invariably minute, in which asexual reproduction takes place by means of conidia produced on conidiophores, which are either enclosed in perithecia, placed on discs, or unprotected.

Remarks.—Fuckel gathered together under the above name all forms of fungi, the complete life-history of which was unknown, and made this class in contradistinction to his other class of Fungi Perfecti. Vuillemin, in 1910, suggested dividing the class into two subclasses, Deuteromycetes and Hyphales.

Classification.—The Class Fungi Imperfecti may be subdivided into two classes as follows:—

A. Accessory fructifications present in the form of closed or open receptacles—Subclass 1, *Deuteromycetes* Saccardo, 1886, ***emendavit*** Vuillemin, 1910.

B. No such accessory fructifications present. Reproduction by means of spores, isolated or in groups, situate on isolated or fasciculated hyphæ—Subclass 2: *Hyphales* Vuillemin, 1910.

SUBCLASS 1: DEUTEROMYCETES SACCARDO, 1886, *emendavit* VUILLEMIN, 1910.

Definition.—Fungi Imperfecti possessing accessory fructifications in the form of open or closed receptacles.

A. Conidiophores minute and enclosed in a perithecium—Order 1, *Sphæropsidales* Léveillé, ***emendavit*** Saccardo, 1882.

B. Conidiophores not enclosed in a perithecium, but crowded on a disc arising from a deeply embedded mycelium—Order 2, ***Melanconiales*** Corda, 1842, ***emendavit*** Saccardo, 1882.

SUBCLASS 2: HYPHALES VUILLEMIN, 1910.

Synonyms.—*Nematomyci* Nees, 1816; *Hyphomyceteæ* Martius, 1817, *pro parte*; *Hyphomycetes* Fries, 1833; *Moniliales* Clements, 1909.

Definition.—Fungi Imperfecti with hyphæ more or less developed, lax, or more or less compact, superficial or subsuperficial, or more rarely, as in man, vertebrates, and insects, endoparasitic. Conidiophores never situate in closed or on open receptacles. Reproduction by means of spores isolated or in groups, situate on isolated or fasciculated hyphæ.

Remarks.—The Hyphales of Vuillemin correspond to the Hyphomycetes of Fries, but the subdivision into families is so entirely different that it appears better to adopt a change of name in order to prevent confusion.

Vuillemin's classification appears to us to be more suitable from the point of view of tropical medicine, and therefore we adopt it in this chapter; but, in order to permit comparison, we give the outlines of the old division of the Hyphomycetes, which is as follows:—

ORDER HYPHOMYCETES Fries, 1833.

A. Hyphomycetes with hyaline or brightly coloured hyphæ which do not cohere in fascicles and with concolorous conidia—Family 1, *Mucidinaceæ* Link, 1809.

B. Hyphomycetes with dark-coloured or black hyphæ rarely hyaline, and then with dark-coloured conidia. The hyphæ do not cohere into fascicles—Family 2, ***Dematiaceæ*** Fries, 1832.

C. Hyphomycetes with hyaline or dark-coloured hyphæ of which the sterile are scanty and creeping, while the fertile are erect, cohering into elongated fascicles bearing conidia at the top or more rarely along the side—Family 3, ***Stilbellaceæ*** Vuillemin, 1910.

D. Hyphomycetes with hyaline or dark-coloured hyphæ compacted into a globose, discoid, or verruciform body called a sporodochium—Family 4, ***Tuberculariaceæ*** Ehrenberg, 1818.

With reference to the name of Family 3, this has been changed from *Stilbaceæ* Fries, 1825, to its present name, because Juel has demonstrated that some of the species of the genus Stilbum belong to the Basidiomycetes, and has given the name Stilbella to those left in Fungi Imperfecti.

The basis of reference with regard to fungi must for all time be Saccardo's 'Sylloge Fungorum,' because it details some 60,000 species of fungi, and this is based upon the colour of the hyphæ and conidia and the number of septa in the spore, as will be indicated when detailing the hyphales. Clements has published a most useful key in English to Saccardo's 'Sylloge.'

Leaving this form of classification, we will consider Vuillemin's new system.

Vuillemin's Classification.—Vuillemin has pointed out a difficulty which we have also experienced in classifying the fungi of the Hyphomycetes—viz., one and the same fungus may, under different conditions, show a mucedine type, a stilbelline type, and a tubercularine type, which makes its recognition most difficult. To obviate this difficulty he has concentrated his attention upon the 'spore,' in order to form the orders of the class Hyphales. and has given definitions of his terms so as to prevent confusion.

Terminology.—The following terms require to be carefully studied: Thallospore, Blastospore, Arthrospore, Chlamydospore, Hemispore, Protoconidium, Deuteroconidium, Conidium, Aleuriospore, Sporophore, Phialide, and Prophialide.

I. The *Thallospore* is a sporiform element which is really only a portion of the thallus secondarily adapted to the purposes of reproduction. The various forms of the Thallospore are named Blastospores, Arthrospores, and Chlamydospores.

> A blastospore (Fig. 537) is a thallospore, round or ovoidal in shape, developed by budding from the summit or sides of a hypha which may be the same size and appearance as the blastospore, as in Cryptococcus, or may be an elongated filament.
>
> An arthrospore is a thallospore developed by the disarticulation of hyphal elements at first with square cut ends, which subsequently become rounded off, and with thin walls which subsequently become thickened. A Chlamydospore (Fig. 538) is merely a variation of an arthrospore, and may be defined as an intermediate or terminal spore larger than the ordinary hypha, which, without becoming isolated, undergoes a kind of encystment, with the formation of a thick and sometimes coloured wall containing cytoplasm loaded with food material.

II. The *Hemispore* (Figs. 539 and 540) starts by a differentiation from the thallus, the 'Protoconidium,' but this remains where formed while the hypha continues to grow. Eventually the protoconidium forms secondary functional spores called 'Deuteroconidia,' which are the reproductive spores.

III. The *Conidia* (sing. *Conidium*) are spores which differ from the thallus in being incapable of forming new spores or hyphæ while still attached to the parent mycelium. They show great variety of form, being rounded, stellate simple or septate (staurospore); needle-shaped, simple or septate (scolecospore); or spirally twisted, simple or septate (helicospore), and of structure being simple (amerospore) or divided by septa (didymospores with two cells and one transverse septum; phragmospores with two or more transverse septa and three or many cells; dictyospores in which there are longitudinal septa as well as transverse septa). The variation of colour is also of importance as a means of classification. The colouring matter usually occurs in the membrane.

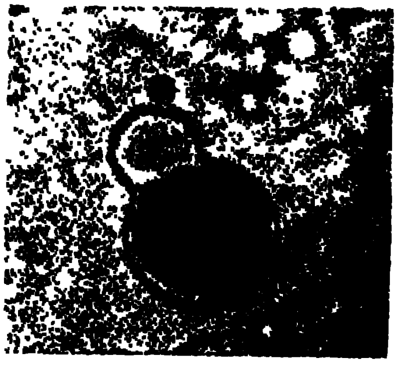


FIG. 537.—A BLASTOSPORE FROM *Cryptococcus myremeciæ* CHALMERS AND CHRISTOPHERSON.

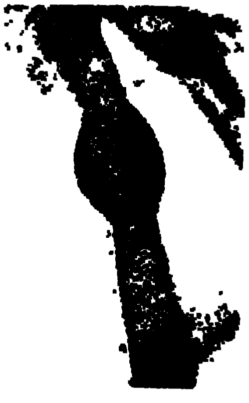


FIG. 538.—A CHLAMYDOSPORE FROM *Trichophyton currii* CHALMERS AND MARSHALL.

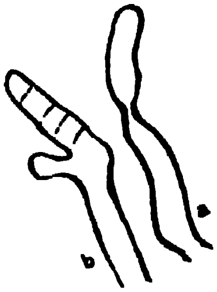


FIG. 539.—A HEMISPORE: DEVELOPMENT FROM *Hemispora stellata* VUILLEMIN.

(*a*) Protoconidia,
(*b*) Deuteroconidia.

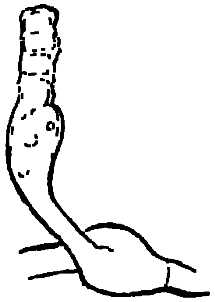


FIG. 540. A HEMISPORE FROM *Hemispora stellata* VUILLEMIN.

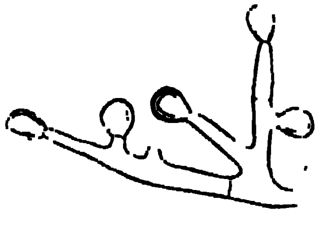


FIG. 541.—ALEURIOSPORES FROM *Aleurisma flavissimum* (LINK, 1816), EMENDAVIT CHEVALIER, 1836.

(After Vuillemin.)

Their number is also important, as they may be single, formed in basipetal chains which are more or less persistent, or they may be glued together into masses by agglutinating material.

The Conidia show two main types—viz., the Aleuriospore and the Conidium Verum.

An Aleuriospore (Fig. 541) is not a true conidium. It may be terminal, lateral, or intercalary, but in each case it is not originally distinct from the thallus, and is only set free by the death of the filament to which it is attached. It has the morphological significance of a chlamydospore.

FIG. 542.—SPOROPHORES AND CONIDIA FROM A CLADOSPORIUM.

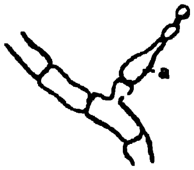


FIG. 543.—A PHIALIDE FROM *Spicaria aphodii* VUILLEMIN (*a*) PHIALIDE.

(After Vuillemin.)

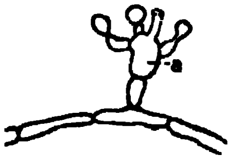


FIG. 544.—A PROPHIALIDE FROM *Urophial amycophiala* VUILLEMIN, 1910. (*a*) PROPHIALIDE.

(After Vuillemin.)

A Conidium Verum (Fig. 542) is quite distinct from the thallus, from which it is easily detachable. It may or may not be carried on a conidiophore, the varieties of which are as follows:—

A Sporophore (Fig. 542) is another name for a conidiophore—*i.e.*, for the hypha which carries the conidia.

A Phialide (Fig. 543) is a flask-shaped segment on the sporophore comparable to the sterigmata of the Basidiomycetes and interposed between the sporophore and the conidia.

A Prophialide (Fig. 544) is a special article on the sporophore from which phialides arise.

Having thus made clear Vuillemin's differentiation of the spores, it is possible to consider his classification of the Hyphales.

Classification.—Vuillemin divides the Hyphales as follows:—

A. Mycelium composed of fine bacilliform hyphæ in which the nuclei are usually indistinct—Order 1, *Microsiphonales* Vuillemin, 1912.

B. Mycelium not so composed:—
  1. Reproduction by thallospores—Order 2, *Thallosporales* Vuillemin, 1910.
  2. Reproduction by hemispores—Order 3, *Hemisporales* Vuillemin, 1910.
  3. Reproduction by conidia—Order 4, *Conidiosporales* Vuillemin, 1910.

ORDER I. MICROSIPHONALES Vuillemin, 1912.

Definition.—Hyphales with the mycelium composed of fine bacilliform hyphæ, usually 1 micron or less in diameter. Usually Gram-positive, when young, and without distinct nuclei. Parasitic on man, animals, and plants, or saprophytic.

Remarks.--This is a most interesting order, as its members (Fig. 545) are nearly always mistaken at first sight, by persons unaccustomed to them, for bacilli (Fig. 548). Hence the descriptions of bacilli as the cause of so many fungal diseases due to these organisms, among which could be classified the diphtheria organisms, the tubercular and leprotic bacilli.

Thus one form of division into families is as follows:—

A. **Nocardiaceæ** Castellani and Chalmers, 1918. **Synonyms.**—*Actinomycetes* Lachner-Sandoval, 1898; *Trichomycetes* Petrusky, 1903.
  Definition.- Microsiphonales with a mycelium.
  Type Genus.- -*Nocardia* Toni and Trevisan, 1889.

B. **Mycobacteriaceæ** Miehe, 1909. **Definition.**—Microsiphonales without a mycelium.
  GENUS 1.- -*Mycobacterium* Lehmann and Neumann, with the diphtheria bacillus as a type.
  GENUS 2.- -*Corynebacterium* Lehmann and Neumann, with the tubercle bacillus as a type.

We have, however, placed the *Mycobacteriaceæ* under the *Schizomycetes*, and therefore have only the *Nocardiaceæ* to consider.

FAMILY NOCARDIACEÆ.

Synonyms.—*Actinomycetes* Lachner-Sandoval, 1898; *Trichomycetes* Petrusky, 1903.

Definition.- -Microsiphonales with a mycelium.

Type Genus. *Nocardia* Toni and Trevisan, 1889.

Classification.- -Until quite recently all the species of this order were considered to belong to one genus- -*i.e.*, *Nocardia* Toni and Trevisan, 1889; but Pinoy has made an excellent subdivision, separating certain species into another genus, which he calls *Cohnistreptothrix* Pinoy, 1911. In doing this, he points out that the original discoverers of actinomycosis- -viz., Harz and Bollinger in 1877 and Rivolta in 1878- -thought that they were dealing with one organism, but when cultures were attempted it became apparent that more than one organism was implicated. Thus Bostrom isolated a parasite which grew well aerobically, producing a dry membrane on the surface of broth and capable of growth at 20° C. on gelatine, but growing better on potato at 37° C. and forming chains of arthrospores. Inoculation into animals was, however, negative. This form is commonly called *Nocardia bovis* (Harz, 1877).

Wolf and Israel, on the other hand, obtained a parasite which only grew anaerobically and was not capable of growth at ordinary European air temperatures. In broth it formed small granules or scales, which fell to the bottom of the tube. These cultures often contained club-like forms, and the branching filaments broke up into bacillary or coccal-like forms. Inoculations of gelatine cultures into the peritoneal cavities of guinea-pigs produced actinomycosis. This form is commonly called *Nocardia israeli* (Kruse, 1896). Wright maintains that this organism is the true cause of actinomycosis and that *N. bovis* is merely a contamination, but this cannot be accepted.

There are, therefore, two distinct organisms which can cause actinomycosis in man and oxen—viz., *N. bovis* (Harz 1877) and *N. israeli* (Kruse, 1896), but the difference between them is considerable; and therefore Pinoy has separated off the latter and its allies from the former and has founded the new genus *Cohnistreptothrix* Pinoy, 1911. The name is derived from the fact that in 1874 Cohn described a fungus in lachrymal concretions under the term *Streptothrix foersteri*, which was considered to be a Nocardia and is now one of the species of Pinoy's Cohnistreptothrix. These two genera are distinguished as follows:—

A. Grows aerobically, easy of cultivation, and producing arthrospores (Fig. 549)—Genus 1, *Nocardia* Toni and Trevisan, 1889.

B. Grows best anaerobically, but can often grow aerobically; difficult of culture, and not producing arthrospores—Genus 2, *Cohnistreptothrix* Pinoy, 1911.

Genus Nocardia Toni and Trevisan, 1889.

Synonyms.—*Actinomyces* Harz, 1877, *nec* Meyen, 1829; *Discomyces* Rivolta, 1878, *nec Discomycetaceæ* Fries, 1836; *Bacterium* Affanasieff, 1888, *nec* Ehrenberg, 1830, *emendavit* Cohn, Hüppe; *Streptothrix* Rossi-Doria, 1891, *nec* Cohn, 1875; *Oöspora* Sauvageau and Radais, 1892, *nec* Wallroth, 1833; *Cladothrix* Macé, 1897, *nec* Cohn, 1875.

Definition.—Nocardiaceæ growing aerobically, usually easy of culture, and producing arthrospores.

Type Species.—*Nocardia bovis* (Harz, 1877).

Nomenclature.—Bollinger's ray fungus (*Nocardia bovis*) belongs to a genus of which the correct name is *Nocardia* Toni and Trevisan, 1889, a term derived from Nocard, the celebrated French parasitologist, who was the first investigator to clearly recognize this fungus in France. We state that it is the correct name for the following reasons:—

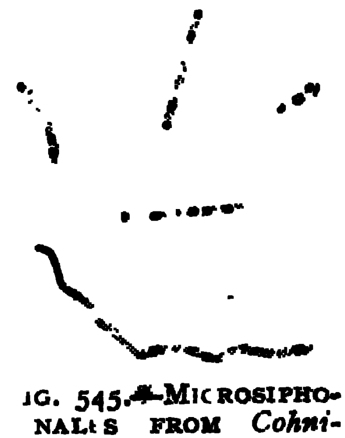


FIG. 545.—MICROSIPHONALES FROM *Cohnistreptothrix tenuis* CASTELLANI, 1911.

1. It is the oldest name, against which no objections can be raised.
2. It has been formally adopted by the Botanical Section of the First International Congress of Pathology.
3. The objections to the other names in use are as follows:—
    - (*a*) *Streptothrix*, as proposed by Rossi-Doria, cannot be used, as it was originally suggested by Corda in 1839 for *S. fusca*, which is quite a different fungus. It was also used in 1875 by Cohn for another organism closely allied to a 'Nocardia,' so that Cohn's and Rossi Doria's names can only be utilized as synonyms of the organisms to which they were wrongly applied because of the priority of Corda's name.
    - (*b*) *Discomyces* was used by Rivolta in 1878 merely as a trivial name, and though it has not been applied to any other genus, still the word *Discomycetaceæ* was introduced in 1836 by Fries for a large fungal family, and has come into general use, and therefore has the double claim of priority and general use; and as its type genus should bear the name *Discomyces*, confusion is bound to arise if the same term is retained as the generic name of Bollinger's organism.
    - (*c*) *Bacterium* was suggested by Affanasieff in 1888, but Ehrenberg had used this name in 1830 for the organisms popularly known as bacteria, and therefore Affanasieff's suggestion falls to the ground.
    - (*d*) *Oöspora*, as utilized by Sauvageau and Radais in 1892, is not available because it is younger than the name 'Nocardia,' and because it was previously used in 1833 by Wallroth for certain fungi previously classified as *Torula* Persoon, 1801.
    - (*e*) *Cladothrix*, as brought forward by Macé in 1897, cannot be used because the name 'Nocardia' has priority, and because it was originally used by Cohn in 1875 for the organism *Cladothrix dichotoma*, which is septate and is only falsely branched, and hence is quite different from Bollinger's fungus.

Remarks.—The genus *Nocardia* contains a large number of species which live saprophytically in soils, from whence their spores can be spread by the agency of air or water to sewage, sputum, etc. Some of them have acquired parasitic habits, living in plants in which they cause root tubercles, or, in other instances, tumours with ray fungi, thus somewhat resembling the actinomycosis of animals. They have also been found living in molluscs and in the alimentary canals of larval insects, as well as in the form of pathogenic fungi in reptilia, aves, and mammalia, in which they mostly occur in the

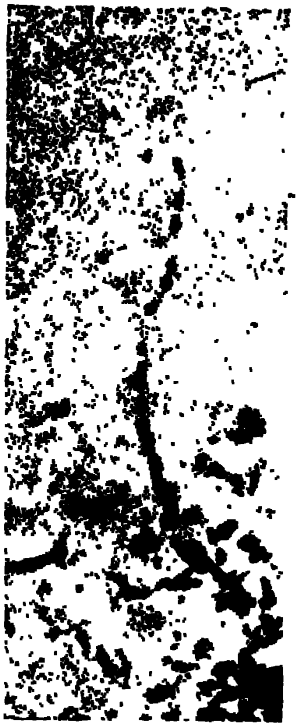


FIG. 546.—*Nocardia convoluta* CHALMERS AND CHRISTOPHERSON, 1916. HYPHA SHOWING BEADING AND ALSO COMMENCING SEPARATION INTO THREE PORTIONS. (× 1,500 DIAMETERS.)

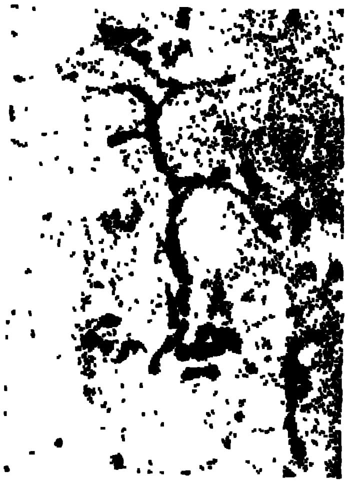


FIG. 547.—*Nocardia convoluta* TO SHOW BRANCHING.

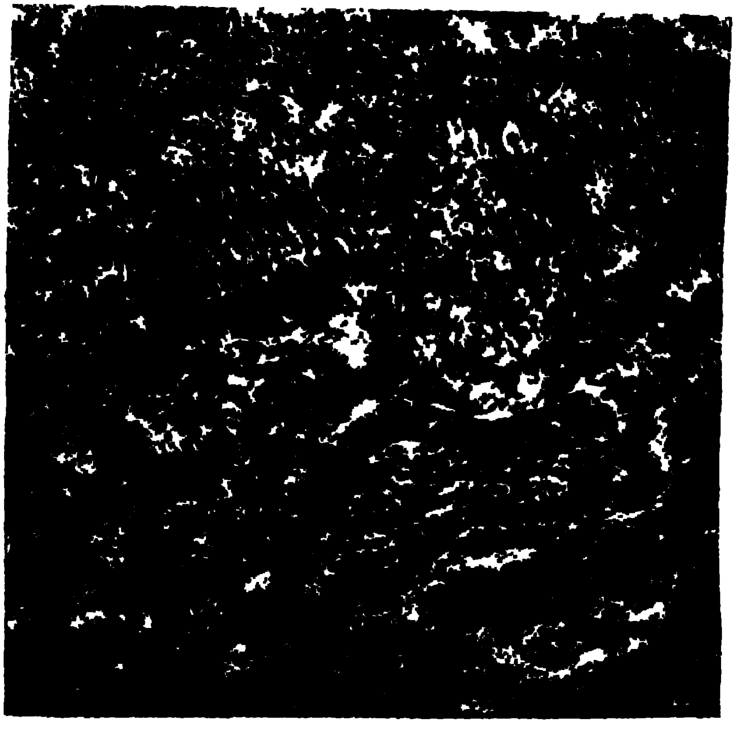


FIG. 548.—*Nocardia convoluta* IN SITU IN A GRAIN TO SHOW BACILLIFORM APPEARANCE.

herbivora or in omnivorous man, though they are known in the grass-eating dog, but are rare in other carnivora. Their geographical distribution appears to be world wide.

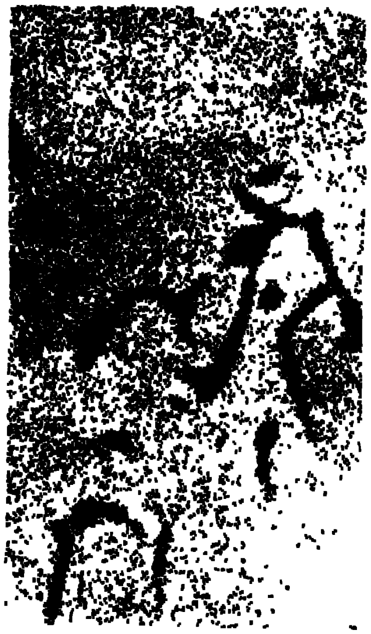


FIG. 549.—*Nocardia convoluta* TO SHOW ARTHROSPORES.

With reference to their method of entry into the human body, it appears to be often associated with some slight traumatism with some vegetal substance, such as a thorn, while the best treatment is undoubtedly complete removal wherever possible; still, partial extirpation, associated with treatment by iodide of potash, as first advocated for this purpose in 1885 by Tomassen, but in large doses such as 90 grains per diem, as used by Carroll with success in 1905, is sometimes also capable of effecting a cure.

Morphology.—Mycelial filaments of various sizes, but generally very thin (1 μ or less), often branching, non-septate, and without differentiated nuclei. In certain species during parasitic life some mycelial threads terminate in club-like formations and show a radial arrangement. It is doubtful whether these club-like formations are intrinsic parts of the fungus or partly products of reaction of the invaded tissues. Masses of mycelia may form in the

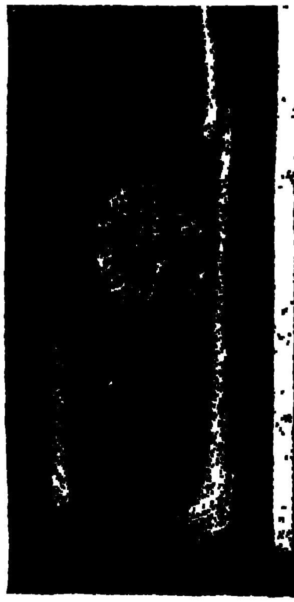


Fig. 550.

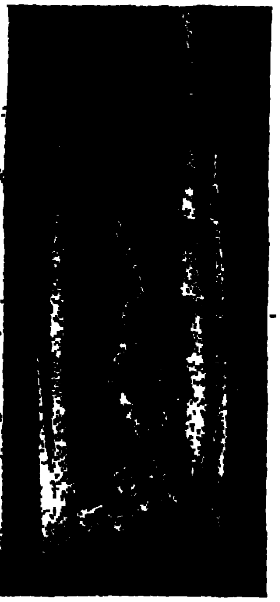


Fig. 551.

FIG. 550.—*Nocardia convoluta* TO SHOW EASY CULTURE AND LIMITED GROWTH ON SABOURAUD'S PRESERVATIVE MEDIUM.

FIG. 551.—*Nocardia convoluta* TO SHOW EASY CULTURE ON INSPISSATED BLOOD SERUM.

tissues peculiar grains (sclerotia) of various size, shape, colour, and consistency. Some species are facultative aerobes, others strictly anaerobic. All are Gram-positive, and several acid-fast. In cultures the mycelium very often undergoes fragmentation, and only bacillary and coccus-like bodies may be seen.

Classification.—The very large number of species in this genus can be classified as follows:—

A. Habitat, soil; can be found in air or water—Section 1, *Saprophytica* Foulerton, 1910.

B. Habitat, plants or animals—Section 2, *Parasitica* Foulerton, 1910.

C. Habitat, soils, plants, or animals, but imperfectly described —Section 3, *Incertæ sedis*.

Section 1: Saprophytica Foulerton, 1910.

This section can be divided into subsections as follows:—

SUBSECTION 1: *Majora*.	SUBSECTION 2: *Minora*.
1. Grow freely under artificial conditions at 22° C., and generally at 37° C., with a few exceptions.	1. Grow moderately under artificial conditions at 22° C. and 37° C.
2. Growth usually large and spreading.	2. Growth usually moderate and circumscribed.
3. Development of aerial hyphæ marked by a bright chalky efflorescence.	3. Development of aerial hyphæ marked by a dull dry powdery appearance.
4. Earthy or mouldy smell often present in the cultures.	4. Earthy or mouldy smell either faint or absent.
5. Generally peptonize gelatine and blood serum.	5. Rarely peptonize gelatine and blood serum.
6. Diastatic action often present.	6. Diastatic action usually absent.
7. Hyphal filaments usually coarser, and branching more marked than in next series.	7. Hyphal filaments usually finer, and branching rarer than in the preceding series.

SAPROPHYTICA SUBSECTION *Majora*.

This subsection contains the following species:—

1. *Nocardia saprophytica* (Foulerton, 1902):—
   Streptothrix leucea saprophytica Foulerton, 1902.
2. *Nocardia dichotoma* (Macé, 1888):—
   Cladothrix dichotoma Macé, 1888, *nec* Cohn, 1875.
   Streptothrix chromogena Gasperini, 1890.
   Streptothrix nigra Rossi-Doria, 1890.
   Oospora metschnikovi Sauvageau and Radais, 1892.
   Cladothrix brauner Hesse, 1892.
   Cladothrix odorifer Rullman, 1895, *nec C. odorifer* Rullman, 1898, parasitic in man.
   Streptothrix melanotica Price-Jones, 1900.
   Streptothrix humifica Beijernick, 1900.
   Streptothrix nigrescens Foulerton, 1902.

- *Actinomyces erythrochromogenes* Krainsky, 1914.
- *Actinomyces diastaticochromogenes* Krainsky, 1914.
- *Actinomyces viridochromogenes* Krainsky, 1914.
- *Actinomyces flavochromogenes* Krainsky, 1914.

3. *Nocardia violacea* (Rossi-Doria, 1891):—
   - *Streptothrix violacea* Rossi-Doria, 1891.
   - *Actinomyces violaceus* Berestneff, 1897.
   - ? *Actinomyces alni* Peklo, 1910.
   - ? *Actinomyces myricæ* Peklo, 1910.
4. *Nocardia beta* (Price-Jones, 1900):—
   - *Streptothrix beta* Price-Jones, 1900.
5. *Nocardia alba* (Rossi-Doria, 1891):—
   - *Streptothrix alba* Rossi-Doria, 1891.
   - *Actinomyces chromogenes* B Gasperini, 1890.
   - Streptothrix I., II., and III. Almquist.
   - *Actinomyces albus* Lehmann and Neumann.
   - *Oōspora guiguardi* Sauvageau and Radais, 1892.
   - *Actinomyces albus* Gasperini, 1890.
   - *Oōspora doriæ* Sauvageau and Radais, 1892.
   - *Streptothrix foersteri* Gasperini, 1890, *nec* Cohn.
   - *Streptothrix leucea* Foulerton, 1902.
   - *Streptothrix alpha* Price-Jones, 1900.
   - *Streptothrix pyogenes* Caminiti, 1907.
   - *Actinomyces grisea* Krainsky, 1914.
   - *Actinomyces diastatica* Krainsky, 1914.
   - *Actinomyces cellulosæ* Krainsky, 1914.
   - *Actinomyces nivea* Krainsky, 1914.
6. *Nocardia rosea* (Krainsky, 1914):—
   - *Actinomyces roseus* Krainsky, 1914.
7. *Nocardia citrea* (Krainsky, 1914):—
   - *Actinomyces griseoflavus* Krainsky, 1914.
   - *Actinomyces flavus* Krainsky, 1914.
   - *Streptothrix flava* Sanfelice, 1904.
   - *Streptothrix flava* Brins, 1899.
8. *Nocardia cinereonigra* (Berestneff, 1897):—
   - *Streptothrix cinereonigra aromatica* Berestneff, 1897.
9. *Nocardia orangica* (Berestneff, 1897):—
   - *Streptothrix orangica* Berestneff, 1897.
10. *Nocardia albida* (Rossi-Doria, 1891):—
    - *Streptothrix albido-flava* Rossi-Doria, 1891.
    - *Actinomyces farcinicus* Rossi-Doria, 1891.
    - *Nocardia farcinica* Rossi-Doria, 1891.
11. *Nocardia invulnerabilis* (Acosta and Grande Rossi, 1893):—
    - *Cladothrix invulnerabilis* Acosta and Grande Rossi, 1893.
12. *Nocardia rubea*, Chalmers and Christopherson, 1916.
    - *Actinomyces ruber* (no name).
    - *Nec Actinomyces ruber* Krainsky, 1914.

*Nec **Streptothrix rubra*** Casabó, 1894.
*Nec **Streptothrix rubra*** Kruse, 1896.

13. ***Nocardia cœlicolor*** (R. Müller, 1904):—
    Streptothrix cœlicolor R. Müller, 1904.
    Streptothrix cœlicolor Schurman, 1909.
14. ***Nocardia glauca*** (Lehmann and Schulze):—
    Actinomyces glaucus Lehmann and Schulze.
15. ***Nocardia thermophila*** (Gilbert, 1904):—
    Actinomyces thermophilus Gilbert, 1904.
    Cladothrix thermophilis Kedzior.
    Actinomyces thermophilus Berestneff, 1891.
16. ***Nocardia monospora*** (Schulze, 1908):—
    Actinomyces monosporus Schulze 1908.

These species may be recognized as given on p. 1048.

SUBSECTION *Minora*.

This subsection contains the following species:—

1. ***Nocardia pluricolor*** (Terni, 1894):—
    Streptothrix pluricolor Terni, 1894.
    Actinomyces gruberi Terni, 1894.
2. ***Nocardia carnea*** (Rossi-Doria, 1891):—
    Streptothrix carnea Rossi-Doria, 1891.
3. ***Nocardia aurantiaca*** (Rossi-Doria, 1891):—
    Streptothrix aurantiaca Rossi-Doria, 1891.
4. ***Nocardia melanosporea*** (Krainsky, 1914):—
    Actinomyces melanosporeus Krainsky, 1914.
5. ***Nocardia melanocycla*** (Krainsky, 1914):—
    Actinomyces melanocyclus Krainsky, 1914.
6. ***Nocardia albosporea*** (Krainsky, 1914):—
    Actinomyces albosporeus Krainsky, 1914.
7. ***Nocardia krainskii*** Chalmers, 1916.
    Actinomyces ruber Krainsky, 1914, ***nec*** Carabó, 1894, ***nec*** Kruse, 1896.
8. ***Nocardia parva*** (Krainsky, 1914):—
    Actinomyces parvus Krainsky, 1914.
9. ***Nocardia microparva*** (Krainsky, 1914):—
    Actinomyces microparvus Krainsky, 1914.
10. ***Nocardia chalcea*** (Foulerton, 1905):—
    Streptothrix chalcea Foulerton, 1905.
11. ***Nocardia erythrea*** (Foulerton, 1910):—
    Streptothrix erythrea Foulerton, 1910.
12. ***Nocardia hoffmanni*** (Gruber, 1891):—
    Micromyces hoffmanni Gruber, 1891.

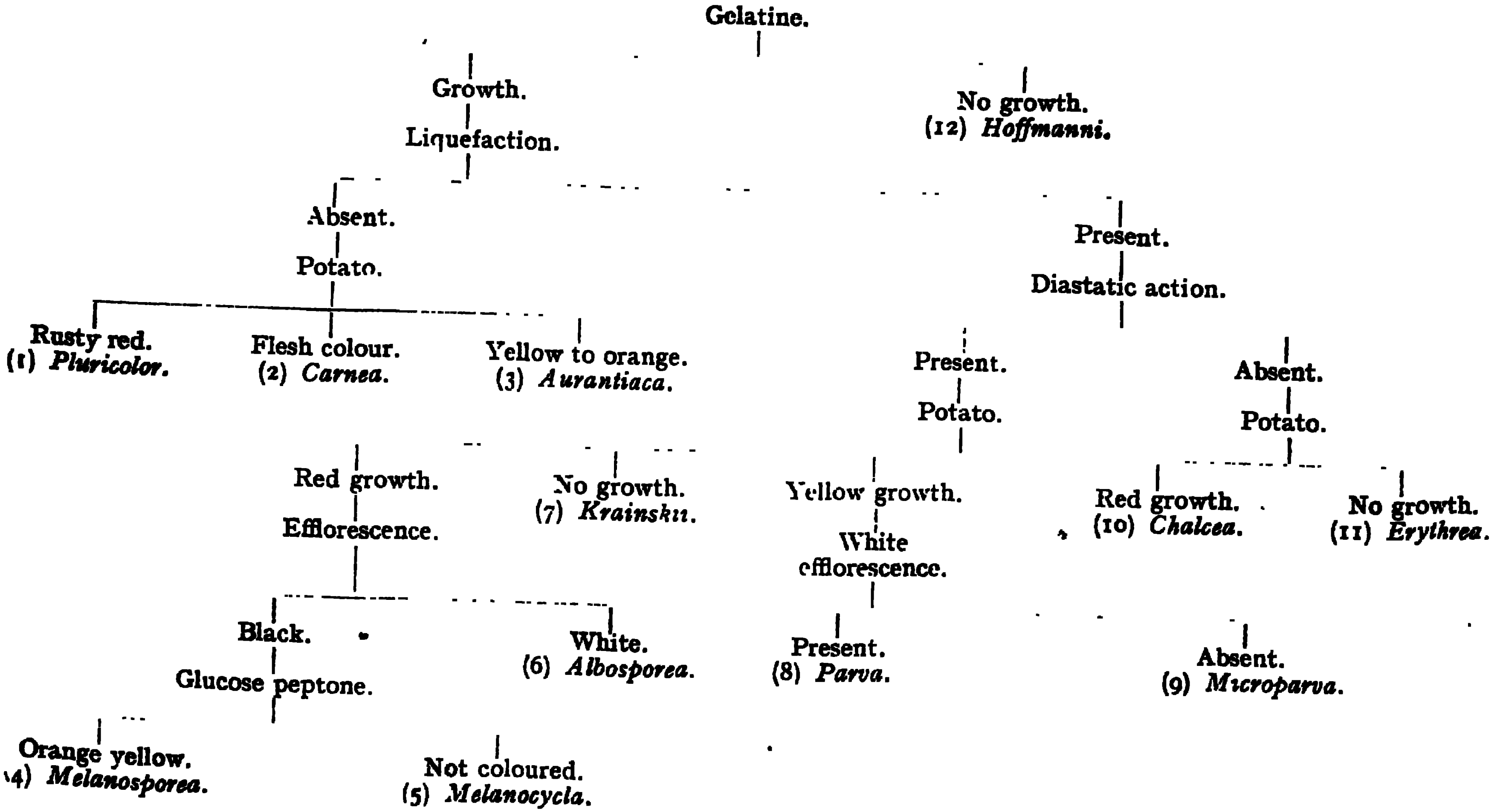
These species may be recognized as given on p. 1049.

DIAGNOSTIC TABLE OF THE SPECIES OF THE SECTION *SAPROPHYTICA*, SUBSECTION *MAJORA*.

Temperature Growth.

- Not at 37° C (1) ***Saprophytica.***
- At 22° C. and 37° C.
  - Gelatine liquefied.
    - Pigmentation.
      - Present.
        - Diastatic action.
          - Present. (2) ***Dichotoma.***
          - Absent.
            - Potato.
              - Violet. (3) ***Violacea.***
              - Buff. (4) *Beta.*
      - Absent.
        - Diastatic action.
          - Present.
            - Potato.
              - Grey to brown. (5) *Alba.*
              - Yellow.
                - Maltose agar.
                  - Rose. (6) ***Rosea.***
                  - Yellow. (7) ***Citrea.***
          - Absent.
            - Maltose agar.
              - Grey to yellow. (8) ***Cinereonigra.***
              - Transparent yellow.
                - No pigmentation of medium. (10) ***Albida.***
              - Orange red. (9) ***Orangica.***
          - Unknown.
            - Potato.
              - White.
                - Medium black. (11) ***Invulnerabilis.***
              - Red. (12) ***Rubea.***
              - Blue. (13) ***Cœlicolor.***
- Not below 35° C.
  - Spores.
    - In chains.
      - Coloration.
        - Green. (14) ***Glauca.***
        - White. (15) ***Thermophila.***
    - Single. (16) ***Monospora.***

DIAGNOSTIC TABLE OF THE SPECIES OF SECTION *SAPROPHYTICA*, SUBSECTION *MINORA*.



Section 2: Parasitica Foulerton, 1910.

The parasitic section can be classified into three subsections, as follows:—

No.	*Test.*	*Subsection* 1: *Majora.*	*Subsection* 2: *Minora.*	*Subsection* 3: *Brevis.*
1	Cultivation at 22° C. and 37° C.	Easy	Not difficult	Difficult at 37° C. Usually nil at 22° C.
2	Growth	Spreading	Circumscribed	Slight
3	Efflorescence	Bright chalky	Dull powdery	Usually absent
4	Hyphal branching	Well marked	Poorly marked	Rare, hypæ often bacilliform
5	Acid-fast species	Rare	Common	Rare
6	Odour of cultures	Earthy or mouldy	Absent or faintly as 1	Sometimes fæculent
7	Liquefaction of gelatine and blood serum	Often present	Rare, and usually only one liquefied	Often very slight indications
8	Potato	Growth	Usually growth	Often no growth
9	Diastatic action	Often present	Usually absent	Not known

SUBSECTION 1: *Majora*.

This subsection contains the following species:—

1. *Nocardia garteni* (Brumpt, 1910):—
   Cladothrix liquefaciens II. Garten, 1895.
   Discomyces garteni Brumpt, 1910.
2. *Nocardia liquefaciens* (Hesse, 1892):—
   Cladothrix liquefaciens Hesse, 1892.
   Streptothrix liquefaciens (Hesse, 1892).
   Streptothrix buccalis Goadby, 1903, *nec* Roger, Bory, and Sartory, 1909.
3. *Nocardia modoré* (Thiry, 1897):—
   Cladothrix modoré Thiry, 1897.
   Cladothrix polychromes Thiry, 1897.
   Actinomyces rubidaureus Lachner-Sandoval, 1898.
4. *Nocardia luteola* (Foulerton, 1910):—
   Streptothrix luteola Foulerton, 1910.
5. *Nocardia appendicis* Chalmers and Christopherson, 1916.
   Streptothrix hominis III. Foulerton, 1910.
   Streptothrix hominis IV. Foulerton, 1906.

6. ***Nocardia candida*** (Petruschky, 1898):—
 Streptothrix candida Petruschky, 1898.
 Streptothrix gedanensis II. Petruschky, 1898.
 Streptothrix lathridii Petruschky, 1898.

7. ***Nocardia bovis*** (Harz, 1877):—
 Actinomyces bovis Harz, 1877.
 Bacterium actino-cladothrix Affanasieff, 1888.
 Actinomyces hominis (Affanasieff, 1888).
 Nocardia actinomyces de Toni and Trevisan, 1889.
 Streptothrix actinomyces Rossi-Doria, 1891.
 Oöspora bovis Sauvageau and Radais, 1892.
 Actinomyces bovis sulphureus Gasperini, 1894.
 Cladothrix actinomyces Macé, 1897.
 Discomyces bovis Blanchard, 1900.
 Streptothrix hominis III. Foulerton, 1905, ***nec*** Foulerton, 1910.
 Streptothrix hominis IV. Foulerton, 1910, ***nec*** Foulerton, 1906.

8. *Nocardia graminarium* (Berestneff, 1891):—
 Streptothrix graminarium Berestneff, 1891.

9. *Nocardia rubra* (Carabò, 1894).
 Actinomyces rubra Carabò, 1894.
 Streptothrix rubra Kruse, 1896.
 Nec Actinomyces ruber Krainsky, 1914.

10. *Nocardia lingualis* (Weibel, 1888):—
 Vibrio lingualis Weibel, 1888.
 Spirosoma lingualis Migula, 1892.
 Streptothrix lingualis Bajardi, 1900.

11. *Nocardia odorifera* (Rullman, 1898):—
 Cladothrix odorifera Rullman, 1898, in sputum, not in air.

12. *Nocardia enteritidis* (Pottien, 1902):—
 Streptothrix enteritidis Pottien, 1902.

These species may be differentiated as given on p. 1052.

SUBSECTION 2: *Minora*.

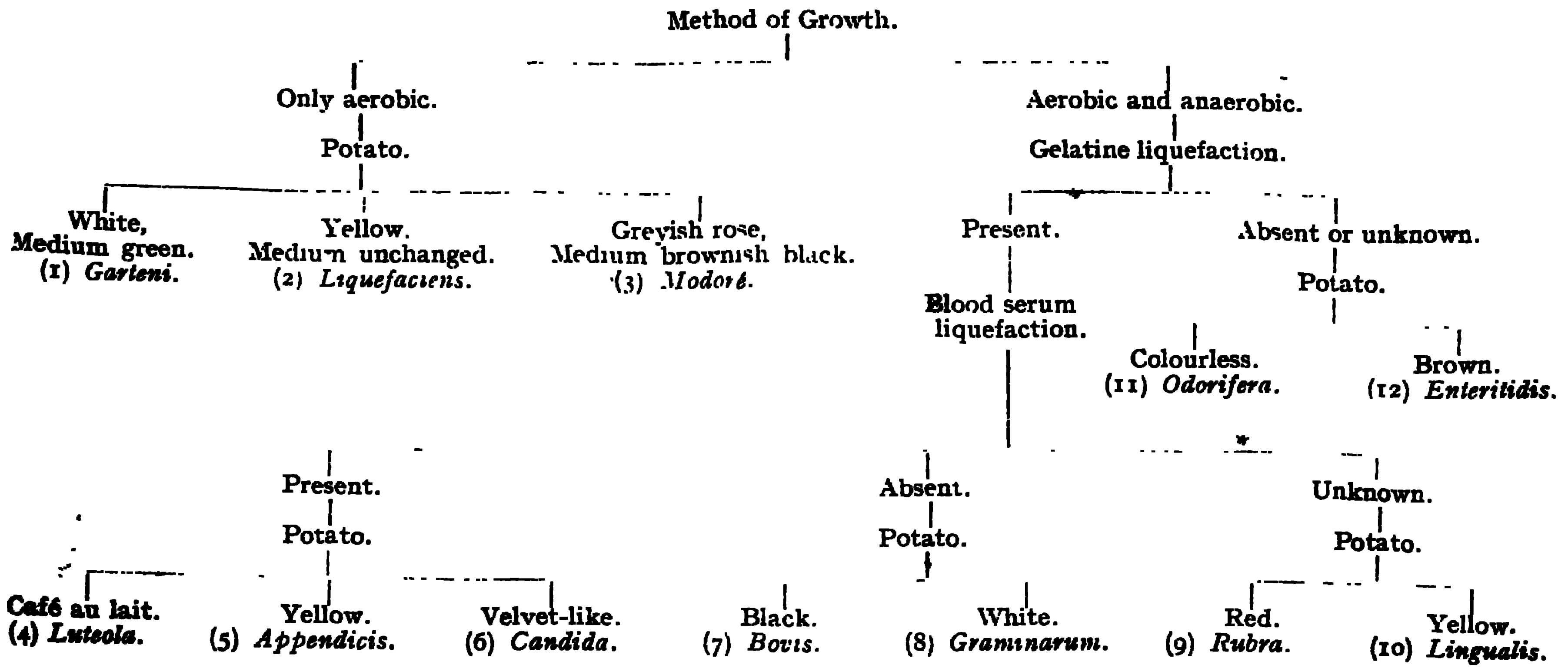
The species belonging to this section are:—

1. *Nocardia farcinica* Trevisan, 1889:—
 Bacillus du Farcin Nocard, 1888.
 Streptothrix farcinica Rossi-Doria, 1891.

2. ***Nocardia somaliensis*** (Brumpt, 1906):—
 Indiella somaliensis Brumpt, 1906.
 Indiellopsis somaliensis (Brumpt, 1913).
 Discomyces somaliensis Brumpt, 1913.

3. ***Nocardia indica*** (Kanthack, 1893):—
 Oöspora indica Kanthack, 1893.
 Streptothrix maduræ Vincent, 1894.
 Discomyces maduræ Vincent, 1895.

DIAGNOSTIC TABLE OF THE SPECIES OF THE SECTION *PARASITICA*, SUBSECTION *MAJORA*.


Method of Growth.
Only aerobic.
Potato.
White, Medium green. (1) *Garteni.*
Yellow. Medium unchanged. (2) *Liquefaciens.*
Greyish rose, Medium brownish black. (3) *Modoré.*
Present.
Potato.
Café au lait. (4) *Luteola.*
Yellow. (5) *Appendicis.*
Velvet-like. (6) *Candida.*
Black. (7) *Bovis.*
Aerobic and anaerobic.
Gelatine liquefaction.
Present.
Blood serum liquefaction.
Absent or unknown.
Potato.
Colourless. (11) *Odorifera.*
Brown. (12) *Enteritidis.*
Absent.
Potato.
White. (8) *Graminarum.*
Unknown.
Potato.
Red. (9) *Rubra.*
Yellow. (10) *Lingualis.*

Nocardia maduræ R. Blanchard, 1895.
Micrococcus pelletieri Laveran, 1906.
Oöspora pelletieri Thiroux and Pelletier, 1912.
Nocardia pelletieri Pinoy, 1912.
Nocardia rivierei Verdun, 1912 (?).

4. *Nocardia leishmani* Chalmers and Christopherson, 1916:—
New acid-fast streptothrix pathogenic to man and animals described by Birt and Leishman in 1902.

5. *Nocardia gedanensis* (Scheele and Petruschky, 1897):—
Streptothrix gedanensis I. Scheele and Petruschky, 1897.

6. *Nocardia convoluta* Chalmers and Christopherson, 1916.

7. *Nocardia minutissima* (Burchardt, 1859):—
Microsporum minutissimum Burchardt, 1859.
Trichothecium J. Neumann, 1868.
Microsporon gracile Balzer, 1883.
Sporotrichum minutissimum Saccardo, 1886.
Microsporoides minutissimus Neveu-Lemaire, 1908.
Discomyces minutissimus Brumpt, 1910.
Oöspora minutissima Ridet, 1911.
Nocardia minutissima Verdun, 1912.

8. *Nocardia rosenbachi* (Kruse, 1896):—
Streptothrix rosenbachi Kruse, 1896.

9. *Nocardia canis* (Rabe, 1888):—
Cladothrix canis Rabe, 1888.
Streptothrix capræ Silberschmidt, 1899.

10 *Nocardia asteroides* (Eppinger, 1890):—
Cladothrix asteroides Eppinger, 1890.
Streptothrix eppingeri Rossi-Doria, 1891.
Oöspora asteroides Sauvageau and Radais, 1892.
Nocardia asteroides R. Blanchard, 1895.
Streptothrix hominis Sabrazès and Rivière, 1895.
Actinomyces asteroides MacCallum, 1902.
Discomyces asteroides Brumpt, 1906.
Streptothrix freeri Musgrave and Clegg, 1907.
Discomyces brasiliensis Lindenberg, 1909.
The organisms described by Ferré and Faguet, by MacCallum, by Schabad, probably belong to this species.

11. *Nocardia hominis* (Berestneff, 1897):—
Nec Actinomyces hominis Bostroem, synonym of *N. bovis*.
Nec Actinomyces hominis Affanasieff=*N. bovis*.
Nec Actinomyces hominis Wolff and Israel=*N. israeli*.
Nec Streptothrix hominis Sabrazès and Rivière=*N asteroides*.
Nec Streptothrix hominis Hayo Bruns, 1899.
Nec Streptothrix hominis Foulerton, 1902.
Nec Streptothrix hominis II. Foulerton, 1910.

   Nec Streptothrix hominis III. Foulerton, 1905=*N. bovis*.
   Nec Streptothrix hominis IV. Foulerton, 1910=*N. bovis*.
   Nec Streptothrix hominis III. Foulerton, 1910.

12. *Nocardia nigra* (Castellani, 1913).
    Synonym, *Streptothrix nigra* Castellani, 1913.
13. *Nocardia pijperi* Castellani and Chalmers, 1918.

As there is so much confusion with regard to the specific name *hominis*, Chalmers and Christopherson proposed that—

S. hominis Bruns be changed to *Nocardia bruni*.
S. hominis Foulerton be changed to *Nocardia foulertoni*.
S. hominis II. Foulerton be changed to *Nocardia londinensis*.
S. hominis III. Foulerton be changed to *Nocardia appendicis*.

These species may be separated as given on p. 1055.

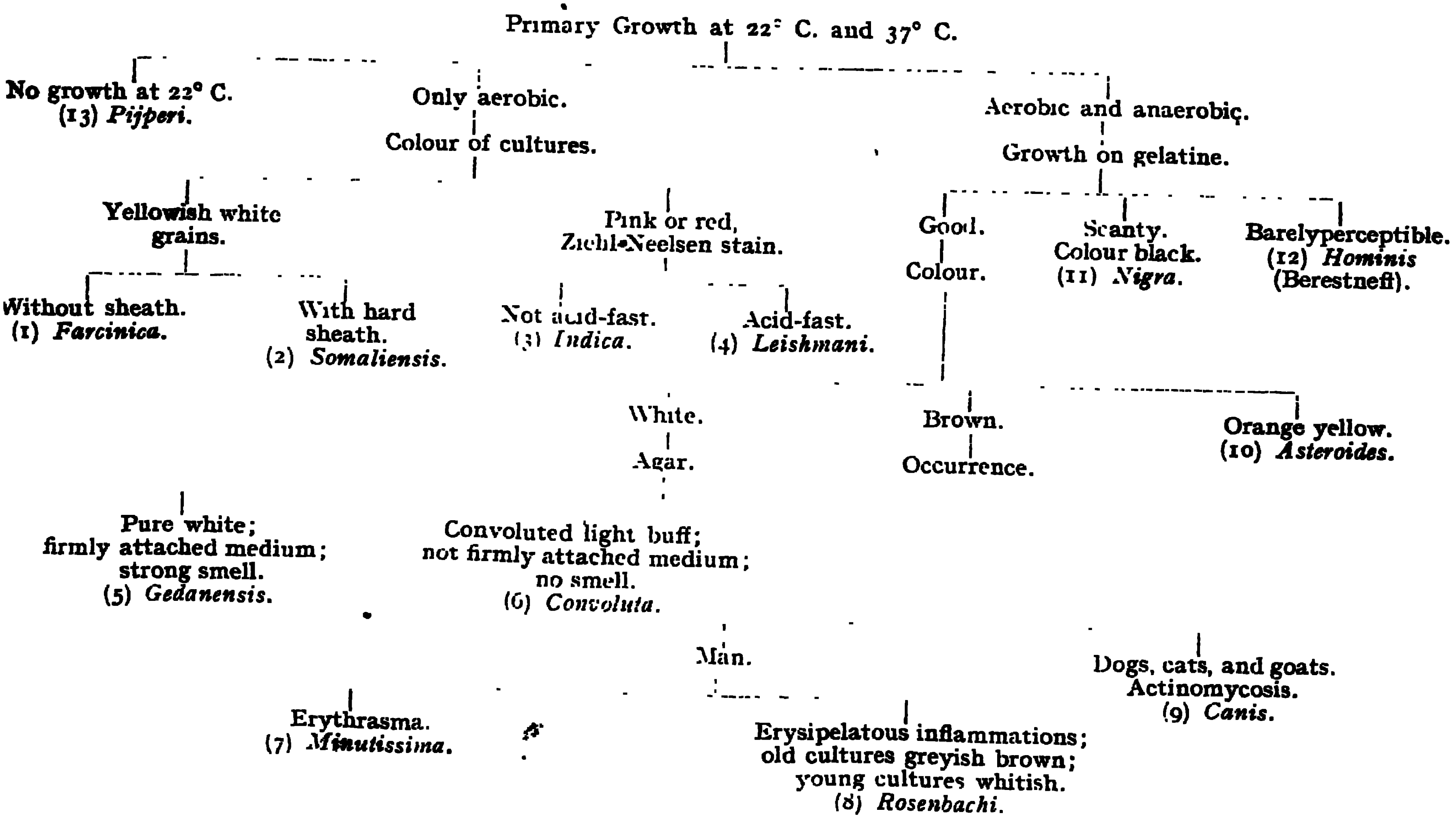
SUBSECTION 3: *Brevis*.

This subsection contains:-

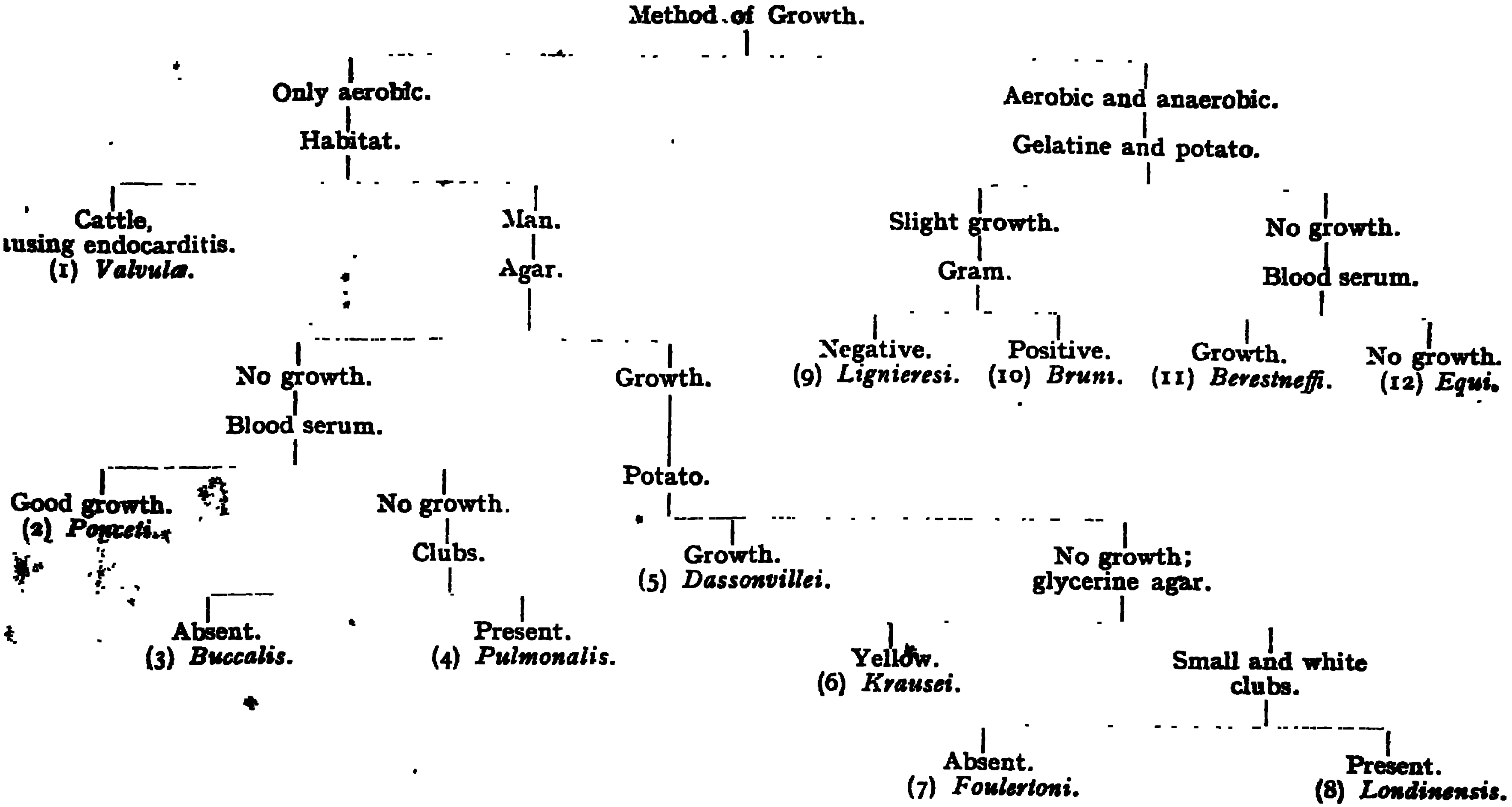
1. *Nocardia valvulæ* (Luginger, 1904):—
   Streptothrix valvulæ destruens bovis Luginger, 1904.
2. *Nocardia ponceti* Verdun, 1912.
3. *Nocardia buccalis* (Roger, Bory, and Sartory, 1909):—
   Oöspora buccalis Roger, Bory, and Sartory, 1909.
   Nec Streptothrix buccalis Goadby, 1903.
4. *Nocardia pulmonalis* (Roger, Bory, and Sartory, 1909):—
   Oöspora pulmonalis Roger, Bory, and Sartory, 1909.
5. *Nocardia dassonvillei* Brocq Rousseu, 1907:—
   Gasperini's Streptothrix, 1890.
6. *Nocardi krausei* (Chester, 1901):-
   Streptothrix krausei Chester, 1901.
7. *Nocardia foulertoni* Chalmers and Christopherson, 1916:—
   Streptothrix hominis Foulerton, 1902.
   Streptothrix hominis I. Foulerton, 1906.
8. *Nocardia londinensis*, new name:—
   Streptothrix hominis II. Foulerton, 1906.
9. *Nocardia lignieresi* (Brumpt, 1910):—
   Actinobacillus lignieresi Brumpt, 1910.
10. *Nocardia bruni* Chalmers and Christopherson, 1916:—
    Streptothrix hominis Hayo Bruns, 1899.
11. *Nocardia berestneffi*, new name:—
    Streptothrix cases 1 and 2 Berestneff, 1897.
12. *Nocardia equi* (Dean, 1900):—
    Streptothrix from a horse of Dean, 1900.
    Probably the organism described by Norris and Larkin should come here, but we have been unable to see a description.

These species may be differentiated as given on p. 1056.

DIAGNOSTIC TABLE OF THE SPECIES OF SECTION *PARASITICA*, SUBSECTION *MINORA*.



DIAGNOSTIC TABLE OF THE SPECIES OF THE SECTION *PARASITICA*, SUBSECTION *BREVIS*.



Section 8: Incertæ Sedis.

In this list we have included the forms concerning which we have been unable to obtain full information, and have, therefore, been unable to classify according to the above tables:—

1. *Actinomyces lacertæ* Terni, 1891.
2. *Streptothrix pseudotuberculosa* Flexner, 1898.
3. Streptothrix of Bonvicini, 1899.
4. *Streptothrix polychromogenes* Vallée, 1900.
5. *Actinomyces bicolor* Trollender, 1903.
6. *Nocardia liguire* Urizer, 1904.
7. *Actinomyces verrucosus* Adler, 1904.
8. *Nocardia lasserei* Verdun, 1912.
9. *Nocardia decussata* Langeron and Chevalier, 1912.
10. *Actinomyces musculorum suis* Duncker.
11. *Actinomyces pseudotuberculosis* Hamm and Keller.
12. *Discomyces holmesi* mentioned by Goedelst.
13. *Streptothrix gelatinosa*
14. *Streptothrix aquatilis*
15. *Streptothrix lehmann*
16. *Streptothrix chondri* Olsen, 1897 } mentioned by Peklo.
17. *Nocardia urinaria* Pijper, 1918.

Nocardia bovis Harz, 1877.

Synonyms.—*Actinomyces bovis* Harz, 1877; *Discomyces bovis* Rivolta, 1877; *Bacterium actino-cladothrix* Affanasieff, 1888; *Nocardia actinomyces* Toni and Trevisan, 1889; *Streptothrix actinomyces* Rossi-Doria, 1891; *Oöspora bovis* Sauvageau and Radais, 1892; *Actinomyces bovis sulphureus* Gasperini, 1894; *Nocardia bovis* R. Blanchard, 1895; *Actinomyces bovis sulphureus*, Gasperini, 1894; *Cladothrix actinomyces* Macé, 1897; *Discomyces bovis* R. Blanchard, 1900; *Streptothrix spitzi* Lignières and Spitz, 1903; *Nocardia bovis* Vuillemin, 1912.

This *Nocardia* is the cause of some cases of human and bovine actinomycosis, and of the actinomycotic mycetoma. The fungus lives parasitically in most tissues, in which it gives rise to degenerative and purulent changes. In the pus small, soft yellow granules—so-called 'sulphur grains'—are seen. These sulphur grains consist of masses of mycelium. At the periphery of the granule the threads are radially arranged, and their free extremities become club-like, 10 to 20 μ in length and 8 to 10 μ in breadth. These peculiar club-like formations have been considered by some authorities to be degeneration forms of the fungus, but Brumpt has demonstrated that they are young active forms, and disappear in old granules. Other writers consider that these club-like formations do not form an intrinsic part of the fungus, but are due to reactive changes in the tissues.

Cultures.—The fungus grows easily on agar, glycerinated agar, gelatine, broth, potato, and other media. Optimum temperature, 35° to 37° C. On glycerinated agar the fungus grows fairly rapidly, giving rise to small, dry, coarsely granular, brown-yellowish colonies, which latter coalesce together. The fungus is Gram-positive, but not acid-fast.

Saprophytic Life.—The fungus is found saprophytic on the spikelets of some cereals (*Phleum pratense* Linnæus, *Hordeum miurnum* Linnæus, etc.).

Pathogenicity.—The experimental reproduction of the disease by inoculating pure cultures has not so far succeeded. Wright therefore goes so far as to say that *Actinomyces bovis* is a contamination.

Varieties.—Gasperini describes three varieties: *N. bovis sulphurea, N. bovis sulphurea-alba, N. bovis luteo-rosea.* Caminiti has described a variety which he thinks may be a new species. *N. lanfranchii* Luigi Sani is also a variety of this Nocardia.

Nocardia rosenbachi Kruse, 1896.

Synonym.—*Streptothrix rosenbachi* Kruse, 1896.

Isolated by Rosenbach in a case of dermatitis, called by him 'erysipeloid.' Mycelial threads very slender; some terminate in club-like swellings. Can be cultivated on the usual laboratory media. Does not liquefy gelatine.

Nocardia asteroides Eppinger, 1890.

Synonyms.—*Cladothrix asteroides* Eppinger, 1890; *Streptothrix eppingeri* Rossi-Doria; 1891; *Oöspora asteroides* Sauvageau and Radais, 1892; *Nocardia asteroides* R. Blanchard, 1895; *Discomyces freeri* Musgrave and Clegg, 1907; *N. brasiliensis* Lindenberg, 1909.

Found in mycetoma and in cases of abscess of the brain. Mycelial threads very slender (0·2 μ wide); the mycelial articles become easily dissociated, when they look bacillus-like. This fungus is acid-fast and is very similar to *Bacillus tuberculosis*, but grows much more quickly on ordinary media: obligative aerobe. Inoculations in the rabbit and guinea-pig produce a form of pseudo-tuberculosis histologically indistinguishable from true tuberculosis.

McCallum has found a *Nocardia* very similar to *N. asteroides* in a case of peritonitis.

Nocardia indica Kanthack, 1893.

Synonyms.—*Streptothrix maduræ* H. Vincent, 1894; *Nocardia maduræ* R. Blanchard, 1895; *Micrococcus pelletieri* Laveran, 1906; *Oöspora pelletieri* Thiroux and Pelletier, 1912; *Nocardia pelletieri* Pinoy, 1912.

It causes Vincent's white mycetoma, very commonly found in Africa and Asia. The 'grains' which are found in the pus of such cases are soft, white, or slightly yellowish, and have a *mulberry-like* surface. At the periphery of the grains radiating filaments are found, but claviform swellings are usually absent; mycelial threads are always very slender (1 to 1½ μ). The fungus can be grown on the ordinary media: facultative aerobe. On glycerinated agar it forms discoid colonies, white in the centre and reddish at the periphery. In the cultures the mycelial threads are as slender as in the grains. Some of the mycelial threads have at their extremities short chains of small conidial elements. Gram-positive, but not acid-fast.

It is to be noted that this fungus very rarely produces bone lesions. Most strains are inoculable into monkeys.

Nocardia dassonvillei Brocq-Rousseu, 1907.

Synonym.—*Streptothrix foersteri* (Gasperini, 1890).

Very thin ramified, mycelial threads, which easily become fragmented and dissociated into bacillary-like bodies. Numerous spherical coccus-like bodies (spores) present. Gram-positive. The fungus grows fairly well on gelatine, giving rise to small white, roundish colonies. This fungus has been found by Landrieu and Liégard in a case of conjunctivitis in an old lady who powdered her face extensively several times daily with rice-powder. The authors suggest that the fungus may have been present in the rice-powder, as the same fungus is known to be found in several decaying cereals.

Gasperini isolated in 1890 from the air a *Nocardia* which he identified as *N. foersteri*. Further researches (Landrieu) have shown Gasperini's fungus to be *N. dassonvillei*.

Nocardia decussata Langeron and Chevalier, 1912.

Synonym.—*Discomyces decussatus* Langeron and Chevalier, 1912.

Found by Langeron and Chevalier in a patient presenting peculiar whitish, dry, squamous patches. The fungus grows on ordinary media extremely slowly. Colonies milk-white, the central portion of which is slightly elevated and flattened, but has a minute nodule in the middle; very often four furrows, forming a cross, are seen. The mycelial threads are thin, non-septate, and are easily dissociated into roundish bodies, 1 to 1·5 μ in diameter.

The pathogenic rôle of this fungus is doubtful.

Nocardia pulmonalis H. Roger, Bory, and Sartory, 1909.

In the parasitic stage may appear in the shape of bacillary-like bodies, about 0·5 μ in diameter. In cultures (maltose broth) thin mycelial filaments, 0·5 μ in diameter, are present, some branching, some terminating in club-like formations. Some mycelial threads are very fragile, and become fragmented into strings of bacillary or coccus-like bodies.

Pathogenicity.—Causes a type of pseudo-tuberculosis. In the expectoration occasionally small white granules, composed of masses of the fungus, are present. Sartory has found the fungus in a case of otitis

Nocardia pijperi Castellani and Chalmers, 1919.

Discovered and described by Pijper in a case of chronic bronchitis in South Africa. The fungus is non-motile, Gram-positive, not acid-fast. It grows on agar, giving rise to small whitish colonies, becoming visible after forty-eight to seventy-two hours. The colonies increase in size, slowly becoming hard like cartilage, and very adherent to the medium. The surface is crinkled. The fungus does not grow on gelatine nor on Sabouraud's maltose agar. Broth remains clear, growth taking place at the bottom.

The fungus can be grown also anaerobically. It is pathogenic to guinea-pigs by intraperitoneal injection. Nodules develop on the peritoneum, consisting of an outer wall of epithelioid cells and leucocytes surrounding a cavity filled with fluid, in which asteroid colonies of the fungus are found.

Nocardia candida Petruschky, 1901.

Found in sputum.

Nocardia aurea Du Bois St.-Sévérin, 1902.

Found in a case of ulcerative conjunctivitis.

Nocardia odorifera Rullman and Perutz, 1898.

Found by Rullmann in a case of chronic bronchitis. Merely a synonym of *N. chromogena* Gasperini.

Nocardia liquefaciens Hesse, 1892.

Synonym.—*Cladothrix liquefaciens* Hesse, 1892.

Gives rise to white colonies on *gelatine*, and later liquefies the medium. Was isolated from a case of actinomycosis. Liquefies serum.

Nocardia ponceti Verdun, 1912.

Not cultivable on agar or gelatine. Grows well on serum, where it takes a bacillary-like form. Found by Moorhof, Dor, and Poncet in a case of myomycosis resembling actinomycosis.

Nocardia fusca Karwacki, 1911.

Isolated by Karwacki from the sputum of a tubercular patient. Dark yellowish colour.

Nocardia luteola Foulerton and Jones.

Found in a case of purulent conjunctivitis.

Nocardia carnea Rossi-Doria, 1891.

Isolated by Baldoni from a case of chronic bronchitis. Red colonies.

Nocardia garteni Brumpt, 1910.

Synonyms.—*Cladothrix liquefaciens* No. 2 Garten, 1895; *Discomyces garteni* Brumpt, 1910.

Liquefies gelatine. On potatoes gives rise to white colonies, while the medium takes a greenish colour. Was isolated from a case of actinomycosis.

Nocardia enteritidis Pottien, 1902.

Found in cases of enteritis by Pottien.

Nocardia buccalis H. Roger, Bory, and Sartory, 1909.

Synonyms.—*Oöspora buccalis* H. Roger, Bory, and Sartory, 1909; *Discomyces buccalis* Brumpt, 1910.

Thin mycelial filaments (0·7 to 0·8 μ). Some ramified mycelial threads are very fragile, becoming fragmented into strings of bacillary-like or coccus-like bodies. Can be cultivated.

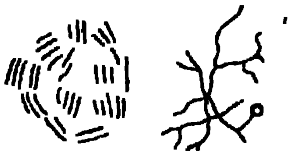


FIG. 552. - *Nocardia pulmonalis* H. ROGER, BORY, AND SARTORY.

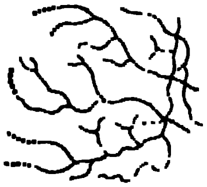


FIG. 553.—*Nocardia buccalis* ROGER, BORY, AND SARTORY.

(After Roger and Sartory.)

Pathogenicity.—May give rise to a form of stomatitis somewhat resembling thrush. It has been found also in tonsillar abscesses.

Nocardia lasserrei Verdun, 1912.

Synonym.—*Nocardia* sp. (?) Lassere, 1904.

Found by Lasserre in 1904 in an ulcerative lesion situated on the pharynx and upper lip. Mycelial filaments very thin (0·5 to 0·75 μ); fragile, club-like formations present. Can be cultivated. Pathogenic to rabbits and guinea-pigs, but only by intracerebral injection.

Nocardia lingualis Guéguen, 1908.

Synonyms.—*Oöspora lingualis* Guéguen, 1908; *Discomyces lingualis* (Brumpt, 1910).

In the parasitic stage the fungus appears in the shape of bacillary bodies, less than 0·3 μ in diameter. In cultures it shows a mycelial type with very thin filaments. It is probably non-pathogenic; it has been found in cases of lingua nigra in association with *Cryptococcus linguæ pilosæ*.

Nocardia rivierei Verdun, 1912.

Isolated by Rivière (1895) in a case of multiple abscesses. Is cultivable on ordinary media.

Nocardia appendicis Chalmers and Christopherson, 1916.

Synonyms.—*Streptothrix hominis* Foulerton, 1906; *Oöspora hominis* Ridet, 1911.

Discovered by Foulerton in a case of multiple abscesses; was present also in the expectoration of the same patient. Foulerton has found similar fungi (*N. hominis III.*) in cases of appendicitis.

Nocardia minutissima Burchardt, 1869.

Synonyms.—*Microsporum minutissimum* Burchardt, 1869; *M. gracile* Balzer, 1883; *Sporotrichum minutissimum* Saccardo, 1896; *Discomyces minutissimus* P. Verdun, 1907; *Microsporoides minutissimus* Neveu-Lemaire, 1906; *Oöspora minutissima* Ridet, 1911.

Mycelial threads extremely thin (0·6 μ); seldom ramified. The mycelial segments get easily dissociated, and have then the appearance of bacilli. Is the cause of erythrasma. Michele, Ducrey, and Reale claim to have cultivated it.

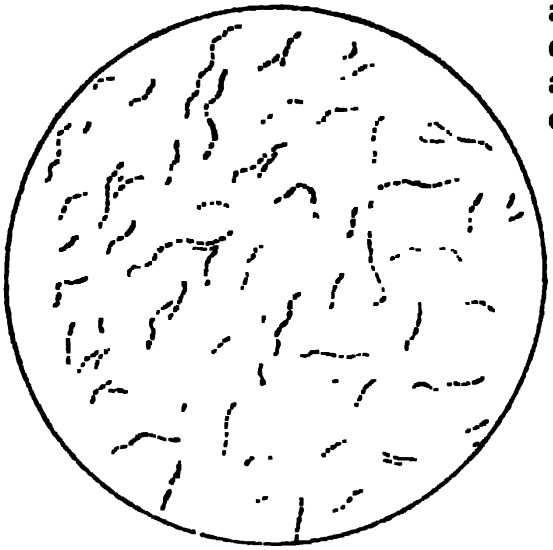


FIG. 554.—*Nocardia minutissima* BURCHARDT.

FIG. 555.—*Cohnistreptothrix tenuis* CASTELLANI.

Nocardia convoluta Chalmers and Christopherson, 1916.

NOCARDIA.—Gram-positive, but not acid-fast, without club formations; found parasitic in man; easy of cultivation, growing aerobically and anaerobically at 22° C. and 37° C., with a marked preference for alkaline media, and with the production of good but limited growths on the different agars, and the same at first on blood serum and potato, on which, however, it becomes more profuse later. Not liquefying gelatine, but causing liquefaction of inspissated ox-blood serum, without diastatic action. Colonies usually somewhat translucent when young, of a light to warm buff colour (Ridgway's Plate XV., 17, O-Y, f or d), and either convoluted or having the appearance of a jelly turned out of a mould, later developing a whitish powdery efflorescence, without distinct odour, never pigmenting the medium on which it is grown; not fermenting or peptonizing milk. Non-pathogenic for monkeys and other laboratory animals.

Remarks.—It is fairly frequently found in the actinomycotic type of Madura foot in Khartoum, Anglo-Egyptian Sudan.

Nocardia nigra Castellani, 1913.

Nocardia, Gram-positive, some strains acid-fast, no definite club formations. Grows aerobically and anaerobically at 22° C. and 35° C. Colonies on maltose agar and ordinary agar are black. Most strains liquefy gelatine.

Nocardia lutea was found by Christopherson and Archibald in 1918 in the lachrymal canal of a case in Khartoum.

Genus Cohnistreptothrix Pinoy, 1911.

Definition.—Nocardiaceæ growing best anaerobically, but can grow aerobically; usually difficult to cultivate and do not produce arthrospores.

Type Species.—*Cohnistreptothrix israeli* (Kruse, 1896).

Historical.—In 1891 Wolff and Israel published a beautifully illustrated account of a streptothrix, which they had isolated from two cases of actinomycosis in man—viz., from the lungs and from a retromaxillary growth. This organism was considered to differ from *N. bovis* in that it grew best anaerobically, that branching was absent, and that its injections into animals were regularly positive in their result. These three characteristics induced Kruse, in 1896, to make a new species for it under the name *Streptothrix israeli*. In 1911, for reasons already set forth, Pinoy founded a new genus, *Cohnistreptothrix*, with Israel's organism as the type species, and therefore its name becomes *Cohnistreptothrix israeli* (Kruse, 1896).

It appears to us to be of importance to give a brief history of the species.

Lachrymal concretions have been known since Césoin described them in 1670. In 1848, Gruby, examining one of these objects, found it to be composed of a fungus, which he believed to be the same as that causing favus, but Cohn, in 1875, examining another such concretion, also saw a fungus, for which he created a new genus streptothrix, calling the fungus in question *Streptothrix foersteri* Cohn, 1875, which may be the same organism as *S. aureus* Du Bois de Saint Sévérin, 1895, and must be closely related to *Nocardia tenuis* Castellani, 1911, which belongs to the same genus, and as its colonies on agar are 'cerebriform' it may possibly be the same as, or related to, *Streptothrix radiatus* and *S. cerebriformis* (both described from cases of keratitis by Namyslowski in 1909), as well as the more aerobic hyphal form of Silberschmidt's organism.

Unfortunately, a mistake was made, for Cohn was not aware that the name Streptothrix had already been given by Corda, in 1839, for another and quite different fungus, which is known as *Streptothrix fusca* Corda, 1839, and is to be found in all works of any importance on systemic mycology Therefore, as streptothrix is not available, after many changes, the generic name has become *Cohnistreptothrix* Pinoy, 1911, and to this genus Israel's human organism belongs. It differs from Bollinger's type of fungus in growing best anaerobically, in being difficult to cultivate, and in not producing arthrospores. Other allied organisms are *Cohnistreptothrix thibiergei* (Ravaut and Pinoy, 1909), also found in actinomycosis in man; *Streptothrix spitzi* Lignières, 1903, found in cattle, is probably identical with *C. israeli*, as may be Doyen's streptothrix; while *Nocardia carougeaui* Gougerot, 1909, in juxta-articular nodules, and *Streptothrix cuniculi* Schmorl, 1891, probably also belong to this genus, as well as the streptothrix recently discovered in a liver abscess in America by Bloomfield and Bayne-Jones (1915). Perhaps the bacillus described by Sawtschenko, in 1896, as the causal agent of a pseudo-mycetomatous condition may also belong to this genus, and it is also possible that the *Coccobacillus pseudo-actinomycosis polymorphus* Berestneff, 1898, may be the same as the chromogenic anaerobic streptothrix obtained from human pus by Neschezadimenko in 1908.

Classification.—The species included in this genus are:—

1. *Cohnistreptothrix silberschmidti* Chalmers and Christopherson, 1916:—

   This name is given to distinguish the obligatory anaerobic streptothrix found by Silberschmidt, in 1900, in dacryocystitis, and described in the *Centralblatt für Bakteriologie*, xxvii., and further cases in *Zeitschrift für Hygiene* (1901), xxxvii.

2. *Cohnistreptothrix cuniculi* (Schmorl, 1891):—
   Streptothrix cuniculi Schmorl, 1891.
   Actinomyces cuniculi Gasperini, 1894.
   Streptothrix necrophora Kitt, 1906.
   ? *Bacillus necroseos* Salmonsen.
   ? Necrosis bacillus of Bang.
   ? *Bacillus diphtheriæ vitulorum* Flügge.
   ? *Bacillus necrophorus* Flügge.

3. *Cohnistreptothrix neschezadimenki* Chalmers and Christopherson, 1916:—
   This name is given to distinguish the obligatory anaerobic streptothrix found by Neschezadimenko, in 1908, in human pus, and described in the *Centralblatt für Bakteriologie*, xlvi.
   ? *Coccobacillus pseudo-actinomycosis polymorphus* Berestneff, 1898.

4. *Cohnistreptothrix americana* Chalmers and Christopherson, 1916:—
   This name is given to distinguish the streptothrix which only grows under partial anaerobic and aerobic conditions, obtained from a liver abscess by Bloomfield and Bayne-Jones in 1915, and described in *Johns Hopkins Hospital Bulletin*, xxvi., No. 292.

5. *Cohnistreptothrix israeli* (Kruse, 1896):—
   Streptothrix israeli Kruse, 1896.
   Streptothrix spitzi Lignières, 1903.
   Possibly the streptothrices described by Doyen in 1891, by Jurinka in 1896, and some of those by Silberschmidt in 1901, by Schukewitsch in 1902, by Doepke in 1903, and by Wright in 1904.

6. *Cohnistreptothrix thibiergei* (Ravaut and Pinoy, 1909):—
   Discomyces thibiergei Ravaut and Pinoy, 1909.

DIAGNOSTIC TABLE OF THE SPECIES WHICH MAY POSSIBLY BELONG TO THE GENUS *COHNISTREPTOTHRIX* PINOY, 1911.

- Cultivation.
  - Cultures known.
    - Method of growth.
      - Obligatory anaerobes.
        - Bacillary forms in cultures.
          - Cultivation.
            - Easy.
              - Gelatine.
                - (1) *Silberschmidti.*
            - Very difficult.
              - No liquefaction of gelatine.
                - (2) *Cuniculi.*
        - Hyphæ in cultures; no growth gelatine or potato.
          - (3) *Neschezadimenki.*
      - Facultative anaerobes.
        - Grains.
          - Absent.
            - (4) *Americana.*
          - Present.
            - Laboratory animals.
              - Pathogenic.
                - Character of grains.
                  - Yellow.
                    - (5) *Israeli.*
                  - Very small and white.
                    - (6) *Thibiergei*
              - Non-pathogenic.
                - (7) *Foersteri.*
  - Cultures unknown.
    - Habitat.
      - Nodules on hair.
        - (8) *Tenuis.*
      - Juxta-articular nodules.
        - (9) *Carougeaui.*

7. *Cohnistreptothrix foersteri* (Cohn, 1874):—
    Streptothrix foersteri Cohn, 1874.
    Leptothrix oculorum Sorokin, 1881.
    Oöspora foersteri Sauvageau and Radais, 1892.
    Streptothrix aurea Du Bois de Saint Sévérin, 1895.
    Streptothrix foersteri Kruse, 1896.
    The aerobic streptothrix of Silberschmidt obtained from a case of dacryocystitis, 1901.
    ? *Streptothrix radiata* Namyslowski, 1909.
    ? *Streptothrix cerebriformis* Namyslowski, 1909.
8. *Cohnistreptothrix tenuis* (Castellani, 1911):—
    Nocardia tenuis Castellani, 1911.
9. *Cohnistreptothrix carougeaui* (Gougerot, 1909):—
    Discomyces carougeaui Gougerot, 1909.
    Nocardia carougeaui Castellani and Chalmers, 1913.

These species may be differentiated as given on p. 1065.

Cohnistreptothrix israeli Kruse, 1896.

Synonyms.—*Streptothrix israeli* Kruse, 1896; *Cohnistreptothrix israeli* Pinoy, 1911.

Found in some cases of human and bovine actinomycosis. It differs from *N. bovis* by being strictly anaerobic. Inoculations of pure cultures have reproduced actinomycotic lesions, while so far such experimental lesions have not been obtained by using cultures of *N. bovis*.

Wright states that *N. israeli* is the real cause of actinomycosis, while *N. bovis* would be only a contamination or a saprophytic agent. We agree, however, with Pinoy's opinion that the clinical features of actinomycosis may be due to several germs: in man Pinoy has found *N. bovis* and *N. israeli*; in oxen *N. israeli* in most cases, but also *N. bovis*, the actinobacillus, and mixed infections.

The actinobacillus of Lignières and Spitz, very common in South America, gives rise to a type of actinomycosis of cattle affecting generally the tongue and neck, in which no grains are found. The germ in the affected tissues appears in the shape of a club-like bacillus. Cultivation is difficult, the best medium being glucose serum agar. The colonies are minute, bluish, or translucid, with irregular edge. The germ generally dies out after two or three subcultures. Pinoy and Ravaut have described a case of meningitis in man due to this bacillus.

Cohnistreptothrix thibiergei Pinoy and Ravaut, 1909.

Synonym.—*Nocardia thibiergei* Pinoy and Ravaut, 1909.

Discovered by Pinoy and Ravaut in a case of peculiar nodular affection of the subcutaneous tissues and muscles. In the lesions very thin (0·2 μ) fragile mycelial threads are seen, often dissociated in bacillary-like bodies. Masses of mycelia embedded in amorphous cementing substance form minute grains or sclerotia, with a maximum diameter of about 80 μ. Some filaments terminate in club-like formations about 3 μ in breadth, which are acid-fast.

The fungus is easily cultivated, aerobically and anaerobically. On maltose agar it produces small white colonies; on broth it develops only at the bottom of the tube.

Cohnistreptothrix foersteri Cohn, 1874.

Synonyms.—*Streptothrix foersteri* Cohn, 1874; *Oöspora foersteri* Radais et Sauvageau, 1892; *Discomyces foersteri* Blanchard, 1895; *Cohnistreptothrix foersteri* Pinoy, 1911.

Mycelial threads very slender, seldom ramified, often terminating in a chain of rod-like or coccus-like elements. Masses of the fungus form some peculiar white bodies or concretions (Désmarres' dacryolithes), about 2 millimetres in diameter, which are occasionally found in the lachrymal canals of man.

The fungus has been cultivated with difficulty aerobically and anaerobically by several authors, among whom Kastalky, Axenfeld, Morax, and Landrieu. The last named has made a thorough investigation of the fungus, which, according to him, shows a slow growth and gives rise on maltose agar to small cerebriform colonies of a grey-stone colour.

The peculiar concretions found in the lachrymal canals were first studied by Césoin in 1670 and Sandifors in 1779. Désmarres, in 1842, considered them to be calculi composed of lime salts, and indicated them by the name of dacryolithes. Gruby believed they were induced by the fungus of Favus, but his observations remained unpublished. A. de Graefe, in 1854, first stated in a published work that these concretions were of mycotic origin. He thought they were due to *Achorion schoenleini*, while Conheim and others believed them to be caused by *Nocardia* (*Streptothrix*) *buccalis*. In 1875 Cohn described the fungus under the name of *Streptothrix foersteri*.

Cohnistreptothrix tenuis (Castellani, 1911).

Synonym.—*Nocardia tenuis* Castellani, 1910.

Found by Castellani in a nodular affection of the hair of the axillary regions. In the parasitic stage, the germ appears in the shape of bacillary-like bodies, varying in breadth (0·2 to 0·6 μ) and in length (2 to 10 μ), packed together and embedded into an amorphous cementing substance. The bacillary bodies are either straight or bent, seldom branching. Gram-positive, but not acid-fast. Masses of this fungus embedded in amorphous cementing substance form the nodules of trichomycosis flava of the axillary regions. (See Plate VI., p. 1034).

In the black variety of the affection *Nocardia tenuis* is associated with a black pigment-producing coccus—*Nigrococcus nigrescens* Castellani, 1911. In the red variety the same *Nocardia* is associated with a red pigment-producing coccus found by Castellani, and called by Chalmers and O'Farrell *Rhodococcus castellanii* Chalmers and O'Farrell, 1913.

For the growth of the black pigment-producing coccus, sugar media are more suitable than ordinary agar. On Sabouraud's agar the colonies of this coccus appear twenty-four to forty-eight hours after inoculation. They are roundish, at first white, but after a couple of days the centre of each colony turns black; at this pigmentation slowly spreads excentrically. After a time the colonies coalesce into a jet-black mass. On glucose agar the coccus presents the same characters. On ordinary agar the pigmentation is much less marked or almost absent.

The red pigment-producing coccus, on the other hand, grows better and shows more pigmentation on ordinary agar than on maltose or glucose agar.

ADDENDUM.

A few words may be inserted on certain filamentous vegetal organisms, on the classification of which there is much discussion—viz., organisms of the genus *Leptothrix*, of the genus *Cladothrix*, of the genus *Vibriothrix*.

Genus Leptothrix Kützing, 1843.

Definition.—Filamentous fungi with long, very thin mycelial threads, with no capsule or only a very delicate one; non-branching, non-septate, generally non-cultivable.

Type Species.—*Leptothrix maxima* Miller.

The following species concern us:—

Leptothrix maxima Miller, 1882.

Synonym.—*L. buccalis maxima* Miller.

Long thin filaments, unsegmented, or with very long segments. When treated with iodine and dilute sulphuric acid gives a blue granulose reaction. Has not been cultivated.

Leptothrix innominata Miller, 1882.

Morphologically identical with *L. maxima*, but when treated with iodine and dilute sulphuric acid does not give a blue reaction. Has not been cultivated.

Leptothrix racemosa Miller, 1882.

Filaments somewhat thicker than those found in the two preceding species. On staining shows a peculiar beaded appearance. Has not been cultivated.

Leptothrix placoides Dobrzyniecki.

Very long thin filaments, Gram-positive, non-motile. Gelatine liquefied. Growth on agar very slow; produces very hard granular colonies. Isolated from human mouth by Dobrzyniecki.

Leptothrix filiformis Flexner, 1896.

Synonym.—*Bacillus (Leptothrix ?) pyogenes filiformis* Flexner, 1896. Isolated by Flexner from a rabbit. Is non-motile, of difficult cultivation, pathogenic.

Leptothrix vaginalis Donné, 1885.

Found in vagina of women and mammals.

Genus Cladothrix Cohn, 1875.

Definition.—Filamentous fungi with mycelial threads very long, thin, showing pseudo-branching. The only species concerning us is *Cladothrix dichotoma* Cohn.

Cladothrix dichotoma Cohn, 1875.

Long thick mycelial threads straight or slightly undulating. They are not dichotomous, as the name would suggest; it is merely a case of pseudo-branching. The organism can be cultivated on ordinary laboratory media, forming on agar a brownish, wrinkled, tough, membranous layer, very adherent. The medium may become stained, slightly brownish. The organism is found often in waters. We have found it, or a very similar species, in an ulcer of the foot in association with many other organisms.

Genus Vibriothrix Castellani, 1917.

The mycelial articles are motile, of very different shape: bacillary, vibrio-like, spirillum-like, at times club-ended. Globular or pear-shaped bodies of very variable size may be present. Gram-negative, not acid-fast. Cultivable on ordinary media.

Type Species.—*Vibriothrix zeylanica* Castellani, 1910.

Synonyms.—*Spirillum zeylanicum* Castellani, 1910; *Vibrio zeylanicus* Castellani, 1913; *Bacillus zeylanicus* Castellani, 1913; *Vibriothrix zeylanica* Castellani, 1917; *Spirobacillus zeylanicus* Castellani, Spagnolo, and Russo, 1918.

Remarks.—Very polymorphic organism, vibrio-like, bacillus-like, and undulating forms being often found in the same preparation. Very small, medium size, and occasionally large roundish bodies are at times observed, and club-like forms may also be present (*vide* Figs. 764, 765, p. 1839).

The organism is motile, Gram-negative, not acid-fast. Easily grown on ordinary media. On potato the growth is often of a reddish colour. In broth there is often a pellicle; preparations from the fluid medium generally show a predominance of vibrio-like or bacillary forms, while in the pellicle long undulating forms are often found. On MacConkey's medium the colonies are white, and somewhat resemble those of the typhoid-dysentery group. The organism does not ferment any of the usual laboratory carbohydrates or alcohols: glucose, levulose, galactose, maltose, lactose, saccharose, mannitol, dulcite, raffinose. There is, in fact, frequently a production of alkalinity. Milk is not clotted and is rendered alkaline, and certain strains after several weeks may induce a certain degree of peptonization. The great majority of strains are non-pathogenic to rabbits and guinea-pigs.

The germ was first isolated by Castellani from cases of dysenteric enteritis in Ceylon, and has recently been observed by the same author and by Spagnolo, Russo, Taylor, Douglas, and Ghiron, in Europe (see p. 1839).

The germ is found in great abundance in a number of cases of dysentery, while it seems to be rare in other conditions; it is very doubtful, however, whether it can really become pathogenic, Castellani having found it also in cases in which the typical Shiga-Kruse bacillus was present. It may, perhaps, be considered to be a so-called 'nosoparasite' similarly to what is the case with certain species of proteus found in cholera, in typhus fever, and other conditions.

ORDER II. THALLOSPORALES Vuillemin, 1910.

Definition.—Hyphales with the mycelium composed of hyphæ more than one micron in diameter, and either short and resembling the conidia or longer and distinct therefrom. Reproduction by means of thallospores. Parasitic on man, animals, and plants, or saprophytic.

Classification.—This order may be divided as follows:—

Reproduction by means of the form of thallospore called blastospore—Suborder 1, *Blastosporineæ* Vuillemin, 1911.

Reproduction by means of the form of thallospore called arthrospore—Suborder 2, *Arthrosporineæ* Vuillemin, 1911.

SUBORDER 1. BLASTOSPORINEÆ Vuillemin, 1911.

Definition.—Thallosporales with hyphæ similar to or dissimilar from the spores, and reproducing by means of blastospores, which are in turn capable of immediately reproducing themselves.

Remarks.—This order includes *Cryptococcus*, which, in its old position among the Ascomycetes, was certainly an anomaly, being an Ascomycete without an ascus, and if an ascus was found in a species, then it at once became a saccharomyces. The researches of many observers, but particularly Busse, tend to show that the genus *Cryptococcus* Kützing, 1833, is good, and therefore should find a suitable place in a fungal classification.

Saccharomyces and its allies and cryptococcus and its allies are, however, so closely related that it is necessary to give some simple scheme whereby laboratory workers and clinicians may easily differentiate those found in pathological work; and such a scheme is as follows:—

I. In cultures budding forms present; mycelium absent, or only traces thereof present; asci present—*Saccharomyces*.
II. As I., but no asci present—*Cryptococcus*.
III. Budding forms present; mycelium well developed; septate or not, branched or not; asci present—*Endomyces*.
IV. As III., but asci not present—*Monilia*.
V. Budding forms absent; mycelium well developed, septate; oval or rectangular arthrospores (thallospores) present—*Oidium*.

Classification.—The various families of the Blastosporineæ with which we are concerned may be recognized as follows:—

A. *Hyphæ not manifestly different from the spores*:—
   I. Spores not in chains. Usually do not ferment carbohydrates with the production of gas—Family 1, *Cryptococcaceæ* Kützing, 1833.
   II. Spores in chains. Usually ferment carbohydrates with the production of gas—Family 2, *Oösporaceæ* Saccardo, 1886.

B. *Hyphæ manifestly different from the spores*:—
   I. Spores not in chains, but arranged verticillately—Family 3, *Enantiothamnaceæ* Chalmers and Archibald, 1915.
   II. Spores in chains—Family 4, *Haplographiaceæ* Saccardo, 1886.
   III. Spores in short chains or solitary—Family 5, *Cladosporiaceæ* Saccardo, 1886.

FAMILY 1: CRYPTOCOCCACEÆ Kützing, 1833.

Definition.—Blastosporineæ in which the hyphæ are little different from the conidia, both being yeast-like in form. The conidia are entirely formed by gemmation from the hyphæ and are never in chains.

Remarks.—This family, of which the type genus is Cryptococcus, is very commonly classified with the class Ascomycetes, which includes an order established by Brefeld and variously named hemiascomycetes, hemi-asci, proto-asci, and gymnascales. This order is looked upon by many authorities as a link between the Phycomycetes and the true Ascomycetes, and, indeed, its founder, Brefeld, believed that, in process of evolution, the sporangium of the Phycomycetes had been converted into the ascus of the Ascomycetes.

Classification.—The family contains the following genera:—*Torula* Persoon, 1801; *Cryptococcus* Kützing, 1833; *Pityrosporum* Sabouraud, 1895; and *Mycoderma* Persoon, 1822; which may be differentiated as follows:—

A. Vegetative elements not elongate:—
  I. *Non-pathogenic* :—
    Vegetative elements roundish or oval, containing a large globule of fat. Budding takes place, and often by several buds at one and the same time. Pigment is frequently present. In fluid sugar media a thick pellicle, without bubbles of air, is slowly produced—*Torula*.
  II. *Pathogenic* :—
    (*a*) Vegetative elements with well-developed double contour; no large globule of fat. Budding takes place with a single bud at a time. No thick pellicle on fluid sugar media. Cultivated—*Cryptococcus*.
    (*b*) Vegetative elements often without double contour. Not cultivated—*Pityrosporum*.
B. Vegetative elements elongate:—
  In fluid sugar media a thick pellicle containing bubbles of gas is quickly produced—*Mycoderma*.

The genera with which we are concerned are Cryptococcus and Pityrosporum.

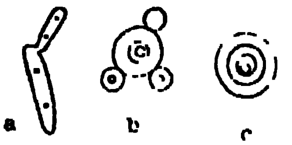


FIG. 556.—DIAGRAM SHOWING BUDDING CHARACTERISTIC OF *Mycoderma* (*a*) and *Torula* (*b*). (After Hansen.)

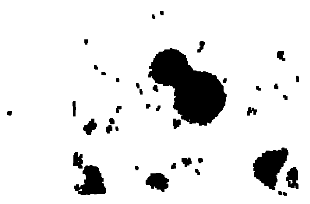


FIG. 557. *Cryptococcus myrmeciæ*.

Genus Cryptococcus Kützing, 1833.

Definition.—Cryptococcaceæ with vegetative elements not elongate; pathogenic, with well-developed double contour, but no globule of fat and only one bud at a time, and no formation of thick pellicle on fluid sugar media. Can be cultivated.

Type Species.—*Cryptococcus hominis* Vuillemin, 1901.

Remarks and Classification.—The name Cryptococcus was introduced by Kützing in 1833 as the generic name for certain forms of his algæ, which he classified as belonging to the subclass Malacophyceæ, tribe Gymnospermeæ, order Eremospermeæ, suborder Mycophyceæ, and family Cryptococcaceæ. This family he defined as: '*Globuli gonimici minutissimi mucosi in stratum indefinitum aggregati*,' and in this family he placed three genera, Cryptococcus, Ulvina, and Sphærotilus. The genus Cryptococcus was characterized as: '*Globuli gonimici in stratum amorphum diffusum aggregati.*' In this genus he gathered no less than thirteen species, all described by himself and mostly found in water or in pharmaceutical preparations.

His twelfth and thirteenth species were, however, more interesting, as they were called *Cryptococcus cerevisiæ* and *C. vini*.

In 1837 Meyen separated *C. cerevisiæ* from the genus Cryptococcus, because it reproduced by ascospores as well as by budding, and to this new genus he gave the name *Saccharomyces*, so that *Cryptococcus cerevisiæ* became *Saccharomyces cerevisiæ*.

Cryptococcus therefore remained for those yeast-like fungi which do not reproduce by ascospores, but only by budding.

The removal of the species *cerevisiæ* from *Cryptococcus* was not recognized by Charles Robin, and with it he grouped the fungus found by Remak in 1845 in the biliary passages and intestines of rabbits, to which in 1847 he gave the name *Cryptococcus guttulatus*. Later, however, it was also shown to belong to the genus Saccharomyces.

In 1873 Rivolta noticed peculiar bodies in a form of lymphangitis in horses, and in 1883 he and Micellone named this organism *Cryptococcus farciminosus*.

During this period one or two organisms had a temporary resting-place in this genus—*e.g.*, Fresenius's *Cryptococcus glutinus*.

The first case in which a cryptococcus was definitely proved to be the cause of disease was Busse's case of cystic swellings of the tibia in a woman, aged thirty-one. The bodies in question were first seen by Buschke, but it was Busse who first proved that they were the true cause of the disease, and showed that they were pathogenic to animals. These yeast-like organisms were found at the autopsy some thirteen months later to occur in sarcomatous-like growths consisting of young granulation tissue and giant cells, not merely in the cysts, but also in the lungs, kidneys, spleen, and in a vesicle on the cornea. The organism grew well on potato and in acid media. It fermented glucose and was specially pathogenic for rats. It only reproduced by budding, and no endospores or mycelium were ever seen. It was this that induced Vuillemin to give it the name *Cryptococcus hominis*, 1901.

Including *C. hominis*, and after excluding several wrongly classified forms, there are about fourteen species parasitic in man which can at present be referred to the genus Cryptococcus, *e.g.*:—

Cryptococcus breweri Verdun, 1912, described in an abscess of the vertebral column; *C. tonkini* Legendre, 1911, found in two cases of blastomycosis in Indo-China.

In addition a number of cryptococci have been found associated with cancers, sarcomata, and innocent tumours—*e.g.*, *C. plimmeri* Constantin, 1901; *C. degenerans* Vuillemin, 1896; *C. corsellii* Neveu-Lemaire, 1908; *C. hessleri* Rettger, 1904.

The following have been found in the mouth or throat:—*C. sulfureus* Beauverie and Lesieur, 1912; *C. lesieuri* Beauverie and Lesieur, 1912; *C. salmoneus* Sartory, 1911; *C. guillermondi* Beauverie and Lesieur, 1912; *C. rogeri* Sartory, 1911; and *C. linguæ-pilosæ* Lucet, 1901.

According to most authors, *Histoplasma capsulatum* Darling, 1906, is not an animal but a vegetal parasite, and should be classified as a cryptococcus.

The parasite found in cases of chronic ulcerative dermatitis in America, and named *Cryptococcus dermatitis* Gilchrist and Stokes, according to some authors, does not belong to the genus Cryptococcus of Kützing, but to the genus *Mycoderma* of Persoon, 1822; but we have retained it under Cryptococcus.

Recently Chalmers and Christopherson in the Anglo-Egyptian Sudan have found a cryptococcus in a peculiar disease consisting of spreading warts, to which they have given the name Murmekiasmosis amphilaphes. As the cryptococcus is closely associated with the condition, they have named it *C. myrmeciæ* Chalmers and Christopherson, 1914, but they were unable to prove conclusively that it was the ætiological factor, though they brought forward some facts to support such a contention.

Cryptococcus dermatitidis Gilchrist and Stokes, 1898.

Synonyms.- *Blastomyces dermatitis* Gilchrist and Stokes, 1898; *Cryptococcus gilchristi* Vuillemin; *Zymonema gilchristi* de Be and Gougerot.

Found by Gilchrist and Stokes in a case of chronic ulcerative dermatitis, and later in a case which had been diagnosed as a tuberculide of the skin. After Gilchrist and Stokes's cases, other cases of blastomycosis due to an identical or similar organism have been described by Hyde, Oppenheim, Ricketts, and others. Ricketts considered these fungi to be species of *Oidium*, and proposed the name '*oidiomycosis*' to indicate the disease produced by them.

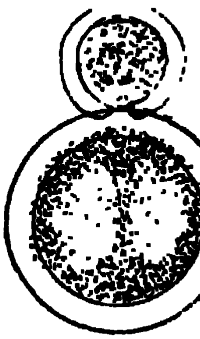


Fig. 558. *Cryptococcus dermatitis* Gilchrist and Stokes. (After Gilchrist.)

C. dermatitidis in the affected tissues has the appearance of a typical yeast- *i.e.*, large globular cells, 10 to 16 μ in diameter, reproducing by budding. In cultures, which are white, besides these globular elements, rudimentary mycelial tubes may occasionally be found, presenting lateral or terminal conidia; asci are absent. The fungus does not ferment sugars, and there is no formation of a pellicle. Gelatine not liquefied.

Cryptococcus hominis Vuillemin, 1901.

Synonyms.- *Saccharomyces* (sp. ?) Busse, 1894; *Atelosaccharomyces busse-buschki* de Beurmann and Gougerot, 1909; *Atelosaccharomyces rudeli* de Beurmann and Gougerot, 1911.

Found in abscesses in a woman by Busse. In the pus the fungus presented itself in the shape of oval bodies, with a membrane having a double contour. These elements were arranged in groups, each group embedded in an amorphous substance and surrounded by a capsule. Culturally the fungus showed only roundish budding forms, no mycelium, no asci. Growth on solid media generally white. Gelatine not liquefied. Glucose fermented. Pathogenic to rabbits, white mice, and dogs.

Cryptococcus linguæ-pilosæ Lucet, 1901.

Synonym.—*Saccharomyces linguæ-pilosæ* Lucet, 1901.

Found by Lucet and others in cases of so-called 'black tongue.' It appears on the surface of the hypertrophied lingual papillæ in the shape of roundish bodies, with double contour, 3 to 6 *μ* in diameter. Grows easily on sugar media. Often produces pellicle in sugar media. Glucose and levulose fermented. Attempts to reproduce the disease have failed. Guégen and Thaon believe that this fungus becomes pathogenic only when associated with *Nocardia lingualis*.

The condition known under the name of 'lingua nigra' is caused in addition to the above fungus, in some cases by *Rhizopus niger*, in other cases by *Nocardia lingualis*.

Fig. [illegible].—*Cryptococcus pilosæ* Lucet.
(After Lucet, from Brumpt.)

Cryptococcus plimmeri Constantin, 1901.

Found by Plimmer in many cases of cancer; is probably only a saprophyte. In the tissues roundish bodies of various sizes, 4 to 40 *μ* in diameter, are seen, occasionally budding, and either free or intracellular. Cultivation has succeeded only on one occasion, when it was found that it produced a white growth on agar and other media. Action on gelatine and other sugars have not been investigated. *Cryptococcus plimmeri*, according to some authors, has been applied to cellular changes.

Cryptococcus degenerans Vuillemin, 1896.

Synonym.—*Blastomyces vitro-simile degenerans* Roncali, 1896.

Found by Roncali and others in malignant tumours, sarcomata, and carcinomata. Easily grown; on potatoes it attains a much larger size than on any other medium; on gelatine growth greyish yellow. Sugar reactions scarcely known. Does not ferment saccharose, but nothing definite known about other sugars. Pathogenic for guinea-pigs.

Cryptococcus corsellii Neveu-Lemaire, 1908.

Found by Corselli and Frisco in a sarcoma of the mesenteric glands. The fungus appeared in the tumours under the shape of black masses. It was easily cultivated, and found pathogenic to guinea-pigs, rabbits, and dogs. Sugar reactions unknown.

Cryptococcus hessleri Rettger, 1904.

Synonym.—*Blastomyces hessleri* Rettger, 1904.

Isolated by Hessler from a small tumour which developed on a patient after a razor-cut. Easily cultivated, especially on alkaline media. Pathogenic for the rabbit and guinea-pig. Sugar reactions unknown.

Cryptococcus breweri Verdun, 1912.

Synonym. *Atelosaccharomyces breweri* Verdun, 1912.
Found by Brewer and Wood in an abscess of the vertebral column.

Cryptococcus tonkini Legendre, 1911.

Synonym.—*Blastomyces tonkini* Legendre, 1911.
Found by Legendre in two cases of blastomycosis in Indo-China. Pinoy considers that the characters given are not sufficient to create a new species for it.

Cryptococcus sulfureus Beauverie and Lesieur, 1912.

Found by Beauverie and Lesieur in certain pharyngeal lesions of a case of typhoid. Ferments slightly dextrose, saccharose, and lactose.

Cryptococcus lesieuri Beauverie and Lesieur, 1912.

Found in a case of stomatitis. Ferments dextrose only.

Cryptococcus salmoneus Sartory, 1911.

Described by Sartory. Found in human gastric juice. Growth on usual media of a pinkish or reddish colour. Does not ferment any sugar. Slowly coagulates milk.

Cryptococcus guillermondi Beauverie and Lesieur, 1912.

Found by Guillermond and Lesieur in cases of stomatitis.
Cellular elements *in situ* spherical, 10-25 microns, surrounded by large mucilaginous capsule. Growth on agar white or slightly yellowish. On potato scanty growth, white. Gelatine not liquefied. Does not ferment any sugar.

Cryptococcus harteri de Beurmann and Gougerot, 1913.

Synonym.—*Atelosaccharomyces harteri* de Beurmann and Gougerot, 1913.
Cells oval, 4-6 and 3-5 microns. Growth on sugar media and gelatine, which is not liquefied white. Does not ferment any sugar. Found by Harter in a case of systemic blastomycosis.

Cryptococcus hudelo de Beurmann and Gougerot, 1914.

Cellular elements *in situ* mostly spherical, 2-20 microns; at times oval, easily grown. Colonies white; gelatine not liquefied. Growth on potato at first white, later yellow, and finally reddish or blackish. Found by Hudelo, Duval, and Loederich in a case of periostitis.

Cryptococcus membranogenes Steinhouse, 1916.

Cellular elements roundish, 7-8 microns in diameter, with very distinct double contour. Surrounded by a thick capsule. Easily grown on all the usual culture media. Colonies white. Gelatine not liquefied. Ferments with gas production glucose but not maltose, lactose, or saccharose. Action on other sugars not known. Very pathogenic for rabbits.
Found by Steinhouse in 1916 in a case of scarlet fever showing symptoms of tracheal obstruction.

Cryptococcus epidermidis Castellani, 1914.

Found by Castellani in saccharomycosis epidermica. Cells of very variable size. Has not yet been cultivated.

Cryptococcus niger Vuillemin.

Found by Maffucci and Sirleo, in 1895, in a pulmonary myxoma of a guinea-pig. Cells *in situ* round or ovoid, with thick mucilaginous membrane. White on most media; on potato brown or black. Gelatine not liquefied. Said to ferment maltose. Nothing known about other sugars.

Cryptococcus lithogenes San Felice

Synonym. *Saccharomyces lithogenes* San Felice.

Found by San Felice in the lymphatic glands of an ox. Roundish cells with a membrane which is at times calcified. Growths whitish on most media, dark brownish after a time on potato. Gelatine not liquefied.

Cryptococcus granulomatogenes (San Felice).

Synonym.- *Saccharomyces granulomatogenes* San Felice.

Isolated from the lung of a hog by San Felice. It grows easily on ordinary laboratory media producing white colonies. It does not liquefy gelatine, but it produces slight rose-red pigment on slices of pear and on honey.

Cryptococcus farciminosus (Rivolta and Micellone, 1883).

Synonyms.- *Cryptococcus tokishigei* Vuillemin; *Lymphosporidium equi* Gasperini, 1908; *Leucocytozoön piroplasmoides* Ducloux, 1908.

Definition.- Vegetative cells *in situ*, oval or roundish, with well-marked double contour.

Remarks.—It is often included in hypertrophied endothelial cells and in leucocytes in the lesions in horses suffering from lymphangitis epizoötica in Europe, Africa, Asia, and America.

Cultivation.- It is of difficult cultivation. Nègre and Boquet have used with success a medium made of agar and dried horse-dung. Sugar reactions are unknown.

Cryptococcus capsulatus (Darling, 1906).

Synonym.- *Histoplasma capsulatum* Darling, 1906.

Definition.- In the affected tissue the parasite appears in round or oval form, measuring 1-4 microns in diameter, and enclosed in an achromatic refractile capsule. Cultivation so far negative.

Remarks.- It was found by Darling in the endothelial cells of capillaries and small bloodvessels in the lungs, spleen, liver, intestines, and lymph glands, as well as in the leucocytes. It was considered by Darling and others to be a protozoön, and for it the genus *Histoplasma* was created. At present there is a consensus of opinion that it is a *Cryptococcus*.

Pathogenicity. It is pathogenic for man, causing disseminated, hyaline, pseudogranulomata in the lungs, splenomegaly, necrotic areas in the liver, and ulceration of the small and large intestines.

Cryptococcus ruber Demme, 1889.

Synonym.- *Saccharomyces ruber* Demme, 1889.

This organism was found in the stools of children suffering from enteritis and also in certain specimens of milk.

It grows easily on ordinary laboratory media, producing red colonies. According to Casagrandi, it does not ferment any sugar.

Cryptococcus myrmeciæ Chalmers and Christopherson, 1914.

Cryptococcus measuring 1·4-2·1 microns in diameter, found in a case of murmekiasmosis amphilaphes in the Anglo-Egyptian Sudan. All attempts at cultivation on a large series of media under aerobic and anaerobic conditions at 20°, 37°, and 40° C. failed, as did inoculations into monkeys and dogs. It was named because of its association with the peculiar disease called murmekiasmosis, but evidence was wanting that it was the causal organism, although its association was intimate.

Genus Pityrosporum Sabouraud, 1895.

Synonym.—*Dermatophyton* Dodd, 1910.

Definition.—Cryptococcaceæ without well developed double contour.

Type Species.—*Pityrosporum ovale* (Bizzozzero, 1882).

Remarks and Classification.—This genus, which is difficult to classify, is allied in appearance in some forms, to a budding yeast, and as such comes close to Cryptococcus. No species has so far been cultivated (Dodd claims to have cultivated *P. malassezi*), but two are known—viz.: *P. ovale* Bizzozzero, 1882 (synonyms, *Saccharomyces capillitii* Oudemans and Pekelharing, 1885; *S. sphæricus* Bizzozzero, 1884; *S. ovalis* Bizzozzero, 1889; *Pityrosporum malassezi* Sabouraud, 1895, often called the bottle bacillus of Malassez, in cases of pityriasis simplex capitis and pityriasis alba in Europe) and *P. cantliei* (Castellani, 1908) in cases of seborrhœa capitis in children in Ceylon.

They may be distinguished as follows:—

A. Flask-shaped or oval, 3 to 15 microns, but usually small—*Ovale*.
B. Generally roundish, 5 to 16 microns, but usually large—*Cantliei*.

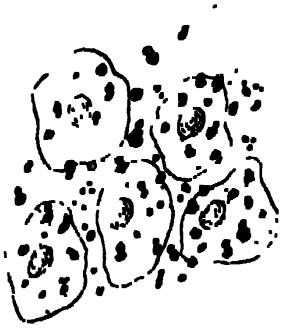


FIG. 500.—*Pityrosporum ovale* BIZZOZZERO.

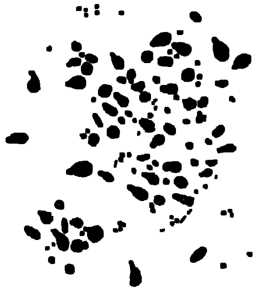


FIG. 501.—*Pityrosporum ovale* BIZZOZZERO.

(After Sabouraud.)

Pityrosporum ovale (Bizzozzero, 1882).

Synonyms.—*Saccharomyces ovalis* Bizzozzero, 1882; *Pityrosporum malassezi* Sabouraud, 1895. Usual term: bottle bacillus of Malassez.

This organism was first described by Bizzozzero, who considered it to be a *Saccharomyces*. Malassez and Sabouraud associated this organism with the ætiology of pityriasis simplex capitis and pityriasis alba.

Its shape somewhat resembles a budding yeast or a flask. The size varies greatly; the maximum diameter of some individuals may be as much as 10 to 15 μ, but much smaller forms (3 to 5 μ) are found.

Pityrosporum cantliei (Castellani, 1908).

Synonym.—*Saccharomyces cantliei* Castellani, 1908.

Somewhat similar to *Pityrosporum ovale*, but the cells are generally roundish and on the average larger (5 to 16 μ). Probably the cause of a variety of seborrhœa of the scalp occasionally met with in children in the tropics.

FAMILY 2: OÖSPORACEÆ Saccardo, 1886.

Definition.—Blastosporineæ in which the hyphæ may be long or little different from the spores, which are typically in chains.

Classification.—This family is divided into several genera—*e.g.* *Oospora* Wallroth, 1833; *Monilia* Persoon, 1797; and *Oidium* Link, 1809, which may be distinguished as follows:—

A. Hyphæ thin, short, simple, or nearly simple, terminating in chains of spores—*Oöspora*.

B. Hyphæ not thin, often long and branched:—

   I. Sporophores simple or subsimple, typically with disjunction apparatus. Glucose completely fermented, gas being produced. Numerous budding forms in cultures—*Monilia*.

   II. Sporophores simple, septate often with disjunction apparatus. Glucose not completely fermented, gas not being produced. Budding forms rare in cultures—*Oidium*.

These genera may now be briefly described.

Genus Oöspora Wallroth, 1833.

Definition.—Oösporaceæ with a lax or compact mycelium in which the hyphæ are slender, septate, and marked by differentiated nuclei. The fertile hyphæ are short, slender, and nearly simple. The conidia, which are globose or ovoidal, hyaline or brightly coloured, are arranged regularly in chains.

Remarks.—Saccardo in his 'Sylloge Fungorum' recognizes a large number of species as belonging to this genus, and these are grouped into sections by the varying colour of the conidia.

The only species known to cause disease in animals referable to this genus is *Oöspora canina* Sabrazès, 1893, which causes favus in dogs, and which can produce an eruption resembling ringworm when inoculated into man. According to Sabouraud, however, it has never been known to cause disease in man spontaneously (*i.e.*, without experimental inoculation), and is therefore of little importance at present.

Vuillemin considers that *Achorion schoenleini* Lebert, 1845, the fungus of favus of human origin, belongs to this genus.

Genus Monilia Persoon, 1797.

Definition.—Vague.

Original Definition.—*Stipitata aut effusa byssoidea, Fila moniliformis articulata.*

Botanical Definition.—Sporophores simple or subsimple, producing by constriction at their extremities a chain of large lemon-shaped conidia, often provided with a disjunction apparatus.

Usual Definition.—Oösporaceæ possessing *in situ* budding forms and mycelial threads, which latter are often long and branched; *in cultures* mostly budding forms, but sometimes filaments, in which thallospores of the blastospore type are formed. Glucose and often other carbohydrate media fermented with the production of gas.

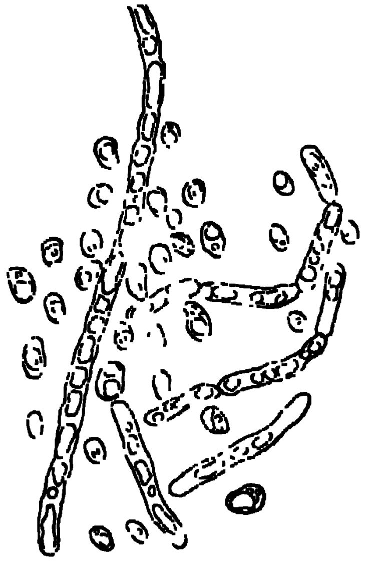


FIG. 502.—*Monilia tropicalis* CASTELLANI. FRESH PREPARATION FROM SPUTUM.

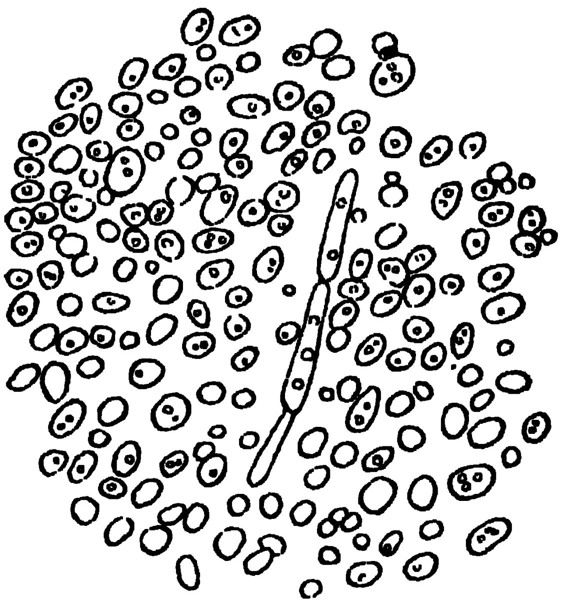


FIG. 503.—*Monilia intestinalis* CASTELLANI PREPARATION FROM GLUCOSE AGAR CULTURE.

Nomenclature.—A few words are necessary with regard to the nomenclature and the synonyms, as the greatest confusion has existed with regard to this genus. The first description of the genus Monilia, as we understand it, was given by Persoon as '*Stipitata, aut effusa byssoidea, Fila moniliformias articulata,*' and the first date given by Saccardo 1797, though the earliest we have found is in his book of 1801. The name is derived from *monile*, a necklace. Link's description in Gmelin's thirteenth edition (really the fourteenth edition) of Linnæus's 'Systema Naturæ,' 1791, refers, it is true, to *Monilia aurea* (Link, 1791), but it was described as *Oidium aureum* Link, 1791. The other synonyms do not require explanation.

We have not included the genus *Zymonema* de Beurmann and Gougerot, 1909, in the synonyms because *Z. gilchristi*, the cause of American blastomycosis, more usually called *Cryptococcus gilchristi*, is said to have lateral as well as terminal conidia, and is classified here as a cryptococcus.

The genus '*Parasaccharomyces*' de Beurmann and Gougerot, 1909, with its species *Parasaccharomyces harteri* Verdun, 1912, found in a case of enteritis with hepatic, bronchial, and cutaneous lesions, has not merely yeast-like forms, but septate hyphæ, but it is not known whether it develops terminal conidia in chains, and therefore it may, at present, correctly be placed in the genus Cryptococcus until more is known about it; and the same remarks apply, we think, to *Parendomyces* Querat and Laroche, 1909.

Fig. 564.

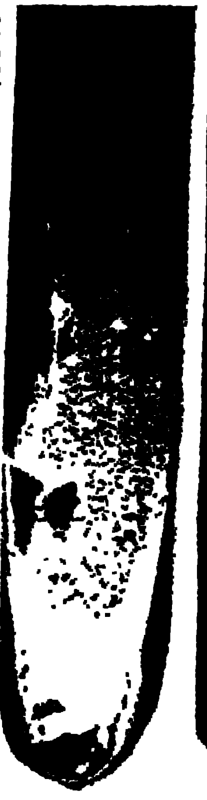


Fig. 565.

Fig. 566.

FIG. 564. *Monilia zeylanica* CASTELLANI. GLUCOSE AGAR CULTURE.
FIG. 565. —*Monilia bronchialis* CASTELLANI. GLUCOSE AGAR CULTURE.
FIG. 566. —*Monilia nivea* CASTELLANI. GLUCOSE AGAR CULTURE.

Remarks. —A number of species belonging to this genus are known to exist in nature growing on decomposing wood, dead leaves, and fruits.

The number of species known to infect man has been considerably extended during recent years by Castellani. The Monilias are of importance in that they are considered to be the ætiological agents of thrush, bronchomycosis (*pro parte*), some dermatomycoses, and, according to certain authors, of sprue.

Type Species.—It is difficult to know which is really the type species of this genus, but probably it is *Monilia aurea* (Link, 1791).

Geographical Distribution.—Possibly world-wide.

Biological Characters.—Some species clot milk, others have no action on this medium; some species liquefy gelatine and serum. Certain fungi of this genus, when growing on serum, produce a peculiar zone of brownish or black discoloration of the medium all round the growth using the serum of *Bos indicus*. The biochemical properties and sugar reactions vary from species to species. Rabbits can be immunized for these fungi, and attempts to use the immunization and agglutination reactions in the differentiation of the various species have been made with only partial success, as there is a large production of co-agglutinins in addition to the specific ones for very different fungi—*e.g.*, fungi of the genus *Sporotrichum*.

Pathogenicity.—Fungi of this genus are the ætiological agents of thrush, some types of bronchomycoses, and some dermatomycoses.

Classification.—There has been and there is still a great deal of confusion in the classification of such fungi. Many of the species of this genus can hardly be distinguished by purely morphological and botanical characters. We are of opinion that the classification should be based, not only on morphological data, but also on biochemical characters and immunization phenomena. Among the biochemical properties, the most important are the actions on milk, gelatine, serum, and on sugar broths. A large number of sugars should be used in the same manner as is done in the classification of the various species of intestinal bacteria. It is to be noted that the reactions with certain sugars are constant, while with others (for instance, mannite) these may vary; and the fermentative power on certain sugars—*e.g.*, galactose—may be rapidly lost. Hence species should be compared only in strains recently isolated. It is to be noted also that in analogy to intestinal bacteria, a species may be trained to ferment certain sugars on which it did not act when recently isolated.

While taking all this into account, we believe the investigation of the various biochemical reactions to be of great value for classifying these fungi, and for this purpose give the table on pp. 1082, 1083.

Determination of Species.—By means of the sugar reactions it is possible to divide the species of Monilia into groups by the use of the following carbohydrates—viz., glucose, levulose, maltose, galactose, saccharose, inulin, and dextrin. When the Monilia is classified into its group it is easy, by means of the table on pp. 1082, 1083, to make the specific determination:—

A. Gas produced in *glucose only*—Group I., *Balcanica* group:—*M. balcanica*, *M. parabalcanica*.

B. Gas produced in *glucose* and *levulose*—Group II., *Krusei* group:—*M. krusei*, *M. parakrusei*.

C. Gas produced in *glucose*, *levulose*, and *maltose*—Group III., *Pinoyi* group.—*M. pinoyi*, *M. nabarroi*.

D. Gas produced in *glucose*, *levulose*, *maltose*, and *galactose*—Group IV., *Metalondinensis* group—*M. metalondinensis*, *M. pseudometalondinensis*.

TABLE SHOWING PRINCIPAL BIOCHEMICAL AND CULTURAL REACTIONS OF THE FUNGI IN ALPHABETICAL ORDER:

Genus Monilia.	Litmus Milk.	Glucose.	Levulose.	Maltose.	Galactose.	Saccharose.	Lactose.	Mannite.	Dulcite.	Dextrin.
M. alba Castellani .. .	AC	AG	AG	AG	AG	A	O	O	O	O
M. albicans Robin, *emd.* Cast.	AC	AG	AGs	AGs	AG	Avs	O	O	O	O
M. balcanica Cast.	O	AG	As	O	O	O	O	O	O	O
M. blanchardi Cast. ..	Avs	AGs	A	A	A	A	O	O	O	O
M. bronchialis Cast. ..	Alk O	AG	AG	AG	O	AGs	O	O	O	A
M. burgessi Cast.	O	AGs	A	AGs	A	AGs	O	O	O	O
M. chalmersi Cast.	Alk As	AG	AG	As	AGs	AG	O	O	O	O
M. decolorans Cast. and Low	Alk DC	AG	AG	AG	A	A	O	O	O	A
M. enterica Cast. .. .	O	AG	AG	AG	AG	AG	O	As	O	As
M. fæcalis Cast.	Alk A	AG	AG	AG	AGs	AGs	O	O	O	O
M. guillermondi Cast. ..	DPs O	AG	AG	As	A	AG	O	O	O	O
M. insolita Cast.	AP As	AG	AG	AG	AG	AG	O	As	O	O
M. intestinalis Cast ..	Alk ADs	AG	AG	As	A	A	O	O	O	O
M. krusei Cast.	O	AG	AG	O	O	O	O	O	O	O
M. londinensis Cast ..	AC	AG	AG	A	A	A	A	O	O	O
M. lustigi Cast.	As	A	AGs	Avs	A	AGs	O	O	O	A
M. macedoniensis Cast. ..	D AC	AG	AG	AorO	AG	AG	O	O	O	O
M. metalondinensis Cast. ..	O	AG	AG	AG	AG	O	O	O	O	O
M. metatropicalis Cast ..	AC	AG	AG	AG	AG	AG	O	O	O	O
M. nabarroi Cast.	AC	AG	AG	AG	O	O	O	O	O	O
M. negrii Cast.	Avs	AG	AG	As	AGs	AG	O	O	O	O
M. nitida Cast.	Alk A	AG	AG	A	A	A	A	A	O	Avs
M. nivea Cast.	DC O	AG	AG	AG	AG	AGs	O	O	O	O
M. parabalcanica Cast. ..	Alk AC	AG	As	O	O	O	O	O	O	O
M. parachalmersi Cast. ..	AC	AG	AG	O	AG	AG	O	O	O	O
M. parakrusei Cast. ..	AC	AG	AG	O	O	O	O	O	O	O
M. paratropicalis Cast. ..	As	AG	AG	AG	AG	AG	O	O	O	Avs
M. perryi Cast.	Alk As	A	AGs	A	A	AGs	O	O	O	O
M. pinoyi Cast.	D Alk O	AG	AG	AG	O	O	O	O	O	O
M. pseudo-bronchialis Cast.	AC	AG	AG	AG	O	AG	O	O	O	O
M. pseudo-guillermondi Cast.	ACorP	AG	AG	O	O	AG	O	O	O	O
M. pseudo-londinensis Cast.	O	AG	AG	AG	AG	O	O	O	O	AG
M. pseudo-londinoides Cast. .	AC	AG	AG	AG	AG	O	O	O	O	AG
M. pseudo-metalondinensis	AC	AG	AG	AG	AG	O	O	O	O	O
M. pseudo-tropicalis Cast. ..	ACs	AG	AG	O	AGs	AG	AG	O	O	O
M. pulmonalis Cast. ..	O	AG	AG	AG	AGs	AG	O	Avs	O	O
M. rhoi Cast.	Alk D As Alk	AG	AG	Avs	AGs	AG	O	O	O	O
M. rosea Zenoni	—				....	...	..	--	-	—
M. tropicalis Cast.	A	AG	AG	AG	AGs	AGs	O	O	O	O
M. zeylanica Cast.	ACs	A	A	A	A	A	As	O	O	A

ABBREVIATIONS USED IN THE TABLE.—A = acid, G = gas; C = clot (milk), clear (broth and peptone water) CTP—clear at first, then thin pellicle present. D = decolourized. P = peptonized (milk), pellicle (broth).

Alk = alkaline. $\frac{A}{Alk}$ = acid, then alkaline. s = slight; vs = very slight.

CHARACTERS OF CERTAIN SPECIES OF MONILIA, WITH NAMES AFTER FIFTEEN DAYS' INCUBATION AT 35° C.

Raffinose.	Arabinose.	Adonite.	Inulin.	Sorbite.	Broth.	Peptone Water.	Indol.	Gram	Gelatine.	Serum	Neutral Red	Colour of Growth on Glucose Agar.
O	O	O	O	O	CTP	C	O	+	O	O	O	White
O	O	O	O	O	CTP	C	O	+	+	+s	O	White
O	OAs	O	O	O	CT	C	O	+	O	O	O	White
As	O	O	Avs	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
As	O	O	AGs	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
AGs	O	O	O	O	CTP	C	O		O	O	O	Yellowish or brownish
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O		White
AGs	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	AG	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
AGs	O	O	O	O	C	C	O	+	O	O	O	White
As or O	O	O	O	O	CTP	C	O	+	O	O	O	White
AG	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	AG	O	C	C	O	+		O	O	White
O	O	O	O	O	C or P	C	O	+	O	O	O	White
O	O	O	O	O	CTP	C	O	+	O	O	O	White
As	O	O	Avs	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	O	O	+	O	O	--	White
O	O	O	O	O	C	C	O	+	O	O	--	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
O	O	O	AG	O	C	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
A	AGs	O	O	O	CTP	C	O	+	O	O	O	White
O	O	O	O	O	C	C	O	+	O	O	O	White
—	--	—	--	—	---	--	--	—	O	O	---	Pink
O	O	O	O	O	C	C	O	+	O	O	O	White
Avs Gvs	O	O	Avs	O	C	C	O	+	O	O	O	Yellowish

O = negative result—viz., neither acid nor clot in milk; neither acid nor gas in sugar media; non-production of indol; non-liquefaction of gelatine or serum, as the case may be.

+ = positive result, liquefaction of medium.

E. Gas produced in ***glucose***, ***levulose***, ***maltose***, ***galactose***, and ***saccharose***—Group V., *Tropicalis* group:—***M. tropicalis***, ***M. paratropicalis***, ***M. pulmonalis***, ***M. nivea***, ***M. insolita***, ***M. enterica***.

F. Gas produced in ***glucose***, ***levulose***, and ***saccharose***—Group VI., *Guillermondi* group:—***M. guillermondi***, ***M. pseudoguillermondi***.

H. Gas produced in ***glucose***, ***levulose***, ***galactose***, ***saccharose***, and ***inulin***—Group VII., *Chalmersi* group:—***M. chalmersi***, ***M. parachalmersi***, ***M. macedoniensis***.

I. Gas produced in ***lactose and other carbohydrates***—Group VIII., *Pseudotropicalis* group:—***M. pseudotropicalis***.

K. Gas produced in ***dextrin*** in addition to other sugars—Group IX., *Pseudolondinensis* group:—***M. pseudolondinensis***.

A. *Species believed to be ætiological factors of disease in man*:—

- I. *Species found in thrush and allied infections*:—
  1. M. albicans (Robin, 1853).
  2. M. alba (Castellani, 1911).
  3. M. londinensis (Castellani, 1910).
  4. M. metalondinensis (Castellani, 1916).
  5. M. tropicalis (Castellani, 1910), and most of those found in bronchomycosis.
- II. *Species found in bronchomycosis*:
  6. M. tropicalis (Castellani, 1909).
- III. *Species found in otomycosis*:
  7. M. rhoi (Castellani, 1909).
- IV. *Species found in pinta*:
  8. M. montoyai Castellani, 1907.
- V. *Species found in cases of generalized moniliomycoses*:—
  9. M. rosea (Zenoni, 1912).

B. *Species associated with a disease in man*:

- I. *Associated with bronchomycosis*:—
  - (a) *By their presence in the sputum of cases of bronchomycosis (in alphabetical order)*:—
    1. M. guillermondi (Castellani, 1910).
    2. M. krusei (Castellani, 1909).
    3. M. negrii (Castellani, 1910).
    4. M. nitida (Castellani, 1910).
    5. M. parakrusei (Castellani, 1910).
    6. M. paratropicalis (Castellani, 1912).
    7. M. pinoyi (Castellani, 1910).
    8. M. pseudotropicalis (Castellani, 1910).
  - (b) *By their presence in bronchitis*:—
    1. M. chalmersi (Castellani, 1912).
    2. M. parachalmersi (Castellani, 1910).
    3. M. bethaliensis (Pijper, 1918).
  - (c) *By their presence in human sputum*:—
    1. M. balcanica (Castellani, 1910).
    2. M. bronchialis (Castellani, 1910).
    3. M. nabarroi Castellani, 1917.
    4. M. nivea (Castellani, 1910).
    5. M. parabalcanica (Castellani, 1916).
    6. M. pseudoguillermondi (Castellani, 1916).
    7. M. pseudolondinensis (Castellani, 1910).
    8. M. pulmonalis (Castellani, 1911).
    9. M. zeylanica (Castellani, 1910).
  - (d) ***By their presence in tea-dust***:—
    1. M. blanchardi (Castellani, 1912).
    2. M. lustigi (Castellani, 1912).
    3. M. perryi (Castellani, 1912).

II. *Associated with sprue :—*
1. M. decolorans Castellani and Low, 1913.
2. M. enterica Castellani, 1911.
3. M. fæcalis Castellani, 1911.
4. M. insolita Castellani, 1911.
5. M. intestinalis Castellani, 1911.

C. *Species found in vaginal discharge in the tropics and in Europe :—*
1. M. balanica (Castellani, 1910).
2. M. metalondinensis (Castellani, 1910).
3. M. naborroi (Castellani, 1917).
4. M. parabalcanica (Castellani, 1910).
5. M. pinoyi (Castellani, 1910).
6. M. tropicalis (Castellani, 1910).

D. *Species found in man, but not classified :—*
1. M. lactea Castellani, 1913.
2. M. lacticolor Castellani, 1913.

A brief description of these species may be given.

Monilia albicans Robin, 1853.

Synonyms. *Oidium albicans* Robin, 1853; *Syringospora robini* Quinquaud, 1868; *Saccharomyces albicans* Rees, 1877; *Monilia albicans* Zopf, 1890; *Endomyces albicans* Vuillemin, 1898.

One of the fungi giving rise to thrush. Widely different descriptions have been given of the so-called thrush-fungus. Some authorities (Hewett) state that the organism liquefies gelatine; others affirm the reverse. Several writers give it as clotting milk, others as having no action on this medium. Castellani has demonstrated that man can be affected by numerous different species of *Monilia*, and that the term thrush-fungus (*Oidium albicans*, *Endomyces albicans*, *Monilia albicans*) has been in the past used to cover a number of different species, in the same manner that the term *B. coli* was for years applied to a multitude of different intestinal bacteria, when a few fermentation tests only were carried out. As the species *M. albicans* has to be split into many species, we keep the term *M. albicans* for the species which we are now describing, and which clots milk and liquefies gelatine.

FIG. 567 *Monilia albicans* ROBIN.

Parasitic Life.—This fungus forms white patches on the tongue and oral mucosa. The patches are easily detached. A particle of the patch examined microscopically shows septate mycelial threads, occasionally ramified, with segments straight or somewhat bent, and easily dissociated. Each segment is about 20 μ in length and 3 to 5 μ in breadth. At the terminal end of each mycelial thread three or four shorter ovoid elements are found, which reproduce by budding. Some similar ovoid or roundish globular refringent cells may be observed originating laterally at the septations of the mycelium. These globular elements (conidia) become detached, and reproduce by budding.

Cultures.—The fungus grows best of all on slightly acid Sabouraud's maltose agar or on glucose agar, but grows fairly well also on all alkaline media. In cultures the fungus appears under two forms—a globular form morphologically similar to a typical yeast, and reproducing by budding; a filamentous form, showing mycelial threads, simple or ramified. *Asci* and *internal spores*, as in the genus *Endomyces*, are absent. On Sabouraud's and glucose agar the growth is abundant, smooth, of a creamy-white colour; on ordinary agar the growth is less abundant. Gelatine and serum are very slowly liquefied. Milk is rendered acid, and after a time it clots. The sugar reactions are given in the table.

Pathogenicity.—*M. albicans* is one of the fungi which gives rise to *thrush*. This condition may be due to several different fungi—*M. albicans*, *Endomyces vuillemini*, *M. tropicalis*, etc. (p. 1741). *Thrush* is generally restricted to the oral mucosa, but in certain cases it may spread to the œsophagus, stomach, intestine. *M. albicans* has been found also in a few cases of bronchomycosis.

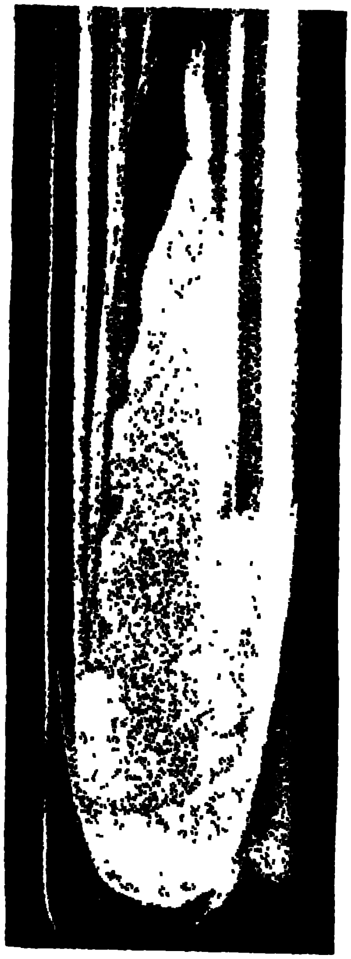


FIG. 568.—*Monilia tropicalis*—CASTELLANI

Monilia tropicalis (Castellani, 1909).

Synonym.—*Endomyces tropicalis* Castellani, 1909.

Found by Castellani in Ceylon in many cases of bronchomycosis. In the expectoration round or oval shape yeast-like cells are seen, and at times segments of mycelium. Cultures are easily obtained on Sabouraud's or glucose agar, and even on ordinary agar. It grows more abundantly on slightly acid than on alkaline media. On Sabouraud's and glucose agar the growth is abundant, creamy white, with a smooth surface when young; often slightly crinkled when old. The growth is composed practically of only globular yeast-like cells, while in the water of condensation globular cells and mycelium may be found together. A little mycelium may be found, however, occasionally in the growth on the slope. Ascus formations are absent. Gelatine and serum are not liquefied; there is no brownish discoloration of the serum, as is the case with some other species of *Monilia* (*M. insolita*, etc.). Litmus milk is generally rendered acid, but is not clotted. The sugar reactions will be found in the table on pp. 1082, 1083. It produces acid and gas in glucose, levulose, maltose, and also, in less amount, in galactose and saccharose. After some transplantations it often loses its fermentative power on galactose and saccharose.

Pathogenicity.—Is the commonest cause of a type of bronchomycosis (see Bronchomoniliasis, p. 1886). In Ceylon it has been found by Castellani also in a few cases of *thrush*, and in a case of *pseudo-diphtheria* which terminated fatally. This case was a little native girl, who developed white patches on the tonsils, uvula, and soft palate. The microscopical examination revealed absence of *B. diphtheriæ* and presence of *M. tropicalis*. Symptoms of broncho-pneumonia soon developed, and the child died. At the autopsy the fungus was found in enormous amount in the bronchi; it was pathogenic for guinea-pigs.

Monilia paratropicalis (Castellani, 1909).

Synonym.—*Endomyces paratropicalis* Castellani, 1910.

Found in some cases of bronchomycosis by Castellani. Microscopically and on Sabouraud's and glucose agars identical with *M. tropicalis*. Does not coagulate milk. Differs from the typical *M. tropicalis* by producing acid and gas in very large amount in saccharose and in rendering dextrin acid (see table).

The same fungus, or a very similar one, was found in two cases of blastomycosis of the skin in Ceylon.

Monilia pseudo-tropicalis (Castellani, 1910).

Synonym. —*Endomyces pseudo-tropicalis* Castellani, 1910.

Found by Castellani in a few cases of bronchomycosis. Differs from *M. tropicalis* and *M. paratropicalis* by clotting milk and fermenting lactose with the production of gas. For the sugar reactions see table.

Monilia metatropicalis Castellani, 1916.

Differs from *M. tropicalis* in clotting milk

Monilia bronchialis (Castellani, 1910).

Synonym.—*Endomyces bronchialis* Castellani, 1910.

Found in sputum. Colonies white. Has no action on milk, gelatine, serum. Sugar reactions are found in the table.

Monilia chalmersi Castellani, 1912.

Found by Castellani in a case of bronchitis. Colonies of white colour. Renders the milk first slightly acid, then alkaline. Does not liquefy either gelatine or serum. Sugar reactions are collected in the table.

Monilia parachalmersi (Castellani, 1917).

Differs from *M. chalmersi* in slowly liquefying gelatine and in other minor characters. Found in sputum.

Monilia macedoniensis Castellani, 1917.

Found in sputum. Clots milk. Belongs to the Chalmersi group.

Monilia guillermondi (Castellani, 1910).

Synonym.—*Endomyces guillermondi* Castellani, 1910.

Observed in sputum once by Castellani. Milk is rendered alkaline. Serum and gelatine are not liquefied. For sugar reactions see table.

Monilia pseudo-guillermondi Castellani, 1916.

Clots milk.

Monilia nivea (Castellani, 1910).

Synonym.—*Endomyces niveus* Castellani.

Found in a sample of sputum which had not been collected in a sterile vessel. Of doubtful pathogenicity. For cultural and biochemical characters see table.

Monilia nitida (Castellani, 1910).

Synonym.—*Endomyces nitidus* Castellani, 1910.

Observed in a sample of sputum by Castellani. Of doubtful pathogenicity. Milk is rendered first acid, then decolourized and clotted. Other cultural characters are found in the table.

Monilia zeylanica (Castellani, 1910).

Synonym.—*Endomyces zeylanicus* Castellani, 1910.

Found in sputum by Castellani. Growth on glucose agar of a yellowish colour. Milk is rendered very acid and is slowly clotted. Gelatine and serum are not liquefied. Does not produce gas in any carbohydrate, with the doubtful exception of raffinose.

Monilia krusei (Castellani, 1909).

Synonyms.—*Saccharomyces krusei* Castellani, *Endomyces krusei* Castellani.

Found in sputum by Castellani. In sputum it appeared as a saccharomyces, and in cultures had all the characters of a saccharomyces at first, except that no asci were observed; after several generations a little mycelium was present on Sabouraud's agar. The sugar reactions are found in the table. It produces acid and gas in glucose and levulose. Its reactions remain constant after ten years.

Monilia pinoyi (Castellani, 1910).

Synonym.—*Endomyces pinoyi* Castellani, 1910.

Found in sputum. Grows well on Sabouraud's and glucose agar, and other sugar media; also on ordinary agar, though less abundantly. Does not clot milk; does not liquefy either gelatine or serum. Produces acid and gas in glucose, levulose, maltose.

Monilia enterica (Castellani, 1911).

Synonyms.—*Endomyces entericus* Castellani: *Monilia psilosis* Ashford: *Parasaccharomyces ashfordi* Anderson, 1916.

Found in stools by Castellani. Milk is rendered alkaline. Gelatine and serum are not liquefied. For sugar reactions see table.

Monilia fæcalis (Castellani, 1911).

Synonym.—*Endomyces fæcalis* Castellani, 1911.

Found in intestinal contents by Castellani. Milk is rendered first acid, then decolourized, and, later, slightly peptonized. Gelatine is not liquefied; serum is not liquefied, but a brownish pigmentation develops on the medium all round the growth. For sugar reactions see the table (p. 1082).

Monilia insolita (Castellani, 1911).

Synonym.—*Endomyces insolitus* Castellani, 1911.

Found in stools and in the saliva. The milk is rendered first slightly acid, then alkaline. On serum a zone of dark pigmentation develops on the surface of the medium round the growth. The medium is not liquefied. For other cultural characters see the table.

Monilia intestinalis (Castellani, 1911).

Synonym.—*Endomyces intestinalis* Castellani, 1911.

Found in stools and saliva by Castellani. Colonies on solid media white. Milk first rendered acid, then slowly decolourized. The growth on serum is not surrounded by a zone of dark pigmentation. Further cultural characters are found in the table (p. 1082).

Monilia alba (Castellani, 1911).

Clots milk. Produces acid and gas in glucose, levulose, maltose, galactose, and acid only in saccharose. Does not liquefy gelatine or serum.

Monilia rhoi (Castellani, 1909).

Synonym.—*Endomyces rhoi* Castellani, 1909.

Found by Castellani in Ceylon in several cases of otomycosis, and once in a sample of tea. In the ear the fungus forms a whitish

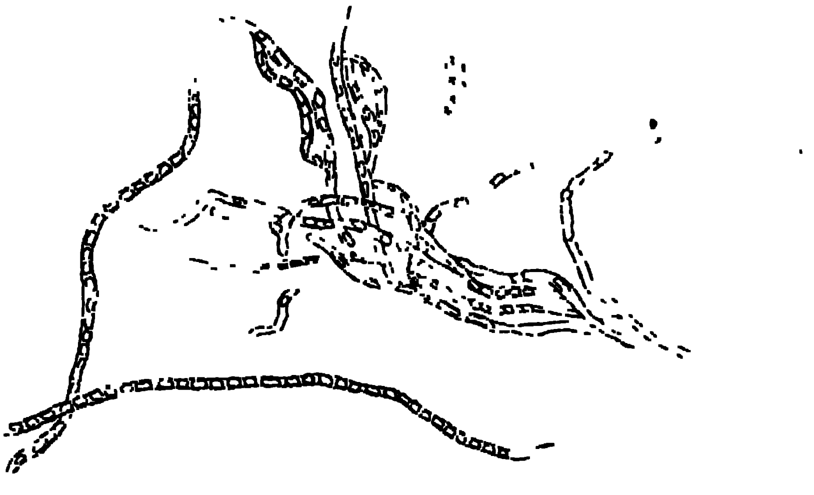


FIG. 569.—*Monilia rhoi* CASTELLANI.

(From a fresh preparation. The free spores are not shown.)

mass (generally embedded in wax), in which numerous long, septate mycelial threads, 2 to 3·5 μ in breadth, and numerous roundish free spores, 3·5 to 5 μ in diameter, are seen. On laboratory media it generally grows, showing a yeast-like type. Does not clot milk; does not liquefy gelatine and serum. The sugar reactions are quoted in the table (p. 1082).

In the cases of otomycosis the mycelium was abundant, the mycelial threads being very long and septate, 3 to 4 μ in breadth; very numerous free, round spores, 4 to 5 μ in diameter, were present For cultural characters see table.

Monilia burgessi (Castellani, 1912).

Synonym.—*Endomyces burgessi* Castellani, 1911.

Isolated from the air Grows abundantly on the usual sugar media, the growth being of a white creamy appearance. Does not render acid or coagulate milk. Does not liquefy serum or gelatine. On serum it produces a zone of peculiar brownish or black discoloration in the medium all round the growth. The sugar reactions are found in the table.

Monilia pulmonalis Castellani, 1911

Found by Castellani in sputum and also in samples of tea. For cultural characters see table (p. 1082).

Monilia lustigi Castellani, 1912

Found in samples of tea. Grows well on all sugar media and also on ordinary agar, the growth being of a snow white colour. Renders litmus milk slightly acid, and then decolourizes it completely. Does not liquefy serum or gelatine. On serum it induces a narrow zone of black discoloration all round the growth. The sugar reactions are found in the table (p. 1082).

Monilia balcanica Castellani, 1916.

Found in sputum and also in a case of dermatitis, of which it was not the cause. Produces gas in glucose only. Levulose often rendered acid (see table).

Monilia parabalcanica Castellani, 1916.

Differs from *M. balcanica* in clotting milk.

Monilia perryi Castellani, 1912.

Found by Castellani in samples of tea-dust. The cultural characters and chemical properties are seen in the table.

Monilia nabarroi Castellani, 1917.

Clots milk and produces gas in glucose, levulose, and maltose. Found in sputum. An identical or very similar variety has been found in vaginal mucus by Castellani and Taylor.

Monilia blanchardi (Castellani, 1912).

Synonym.—*Endomyces blanchardi* Castellani, 1912.

Isolated from tea-dust by Castellani. Grows abundantly on maltose, glucose, and other sugar media; also on ordinary agar, though less vigorously. The growth is of a white colour and smooth surface. Milk rendered at first very slightly acid, and then alkaline. No liquefaction of gelatine or serum. Does not produce gas in any sugar except, in small quantity, in glucose.

Monilia bethaliensis Pijper, 1918.

Found by Pijper in a case of bronchitis. Ferments glucose and maltose with production of gas. Action on levulose not known. Gelatine not liquefied, milk not clotted

Monilia rosea (Zenoni, 1912).

Synonym.—*Oidium roseum non liquefaciens* Zenoni, 1912.

The cultures on Sabouraud's and other sugar media are of a pinkish colour. Neither serum nor gelatine are liquefied

Pathogenicity.—Was isolated by Zenoni in a peculiar case of hepatitis with fever and jaundice which ended fatally. Microscopically conidia and mycelial filaments could be seen very abundant in and about the smaller hepatic bloodvessels and the bile-ducts. The fungus is pathogenic to rabbits, guinea-pigs, and white rats

Monilia subtilis (Blanchard, 1895)

Synonyms.—*Oidium subtile cutis* Babès, 1895; *Mycoderma subtile* Verdun, 1912.

Found by Babès in some ulcers on which the fungus produced white membranes. The mycelial threads were thinner than in most species of *Monilia* There was dichotomous branching, and at the extremities of the mycelial threads ovoid conidia were present. Biochemical properties of the fungus not known Pathogenic for the rabbit.

The same, or a very similar, fungus was later found by Clozel, de Boyer and d'Antin in a peculiar pustular affection observed in cachectic children

Monilia pulmonea (Bennett, 1842).

Synonyms.—*Oidium pulmoneum* Bennett, 1842; *Oöspora pulmonea* Saccardo, 1886; *Mycoderma pulmoneum* Vuillemin, 1891.

The organism was found in a case of pneumothorax by Bennett in 1842, it was observed again by Vuillemin in the sputum of a tubercular patient in 1891, and in an ulcerative dermatitis by Balzer, Burnier, and Gougerot in 1910. It grows under two types—a saccharomyces-like and a filamentous type. Colonies on glucose agar white. Biochemical reactions not given.

Monilia candida (Bonorden, 1851).

Synonym.—*M. bonordeni* Vuillemin.

Commonly found vegetating in decomposing vegetable matter; occasionally seen parasitic in Mammalia, giving rise to white patches on the tongue and buccal mucosa, somewhat similar to human *thrush*. Once found in a child in some white patches present on the tongue. Mycelium elements easily dissociated. Yeast-like conidial elements. Pellicles in fluid sugar media. Ferments glucose and saccharose, and, according to Bau, dextrin. Its action on other carbohydrates and gelatine has not been recorded. Mycelial tubes thinner than in most *Monilias* (1 to 1½ μ in breadth); conidia roundish, smooth, 7 to 8 μ in diameter. Biochemical actions of the fungus have not yet been investigated completely. Found in cow-dung, on which it forms white membranes.

Monilia kochi (von Wettstein, 1885).

Synonym.—*Rhodomyces erubescens* Aster, 1900.

Morphologically similar to *M. candida*; grows well on sugar media, where it produces pinkish colonies; was observed by Wettstein in a case of chronic acid dyspepsia. Biochemical properties not studied.

Monilia montoyai (Castellani, 1907).

Synonym.—*Monilia pictor* Neveu-Lemaire, 1908.

Discovered by Montoya in cases of white pinta. Some fertile hyphæ are much thicker than others; the spores are large, globular (5 to 7 μ), and contain a large nucleus. Grows well on sugar media, giving rise to white creamy colonies which rapidly fuse together. Biochemical properties of the fungus not known.

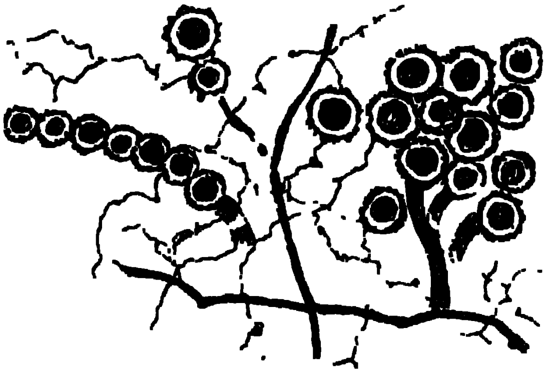


FIG. 570. *Monilia montoyai* (After Montoya y Florez.)

Monilia cutanea (de Beurmann, Gougerot, and Vaucher, 1909).

Synonyms.—*Oidium cutaneum* de Beurmann, Gougerot, and Vaucher, 1909; *Mycoderma cutaneum* Verdun.

Isolated by de Beurmann, Gougerot, and Vaucher from a case showing a peculiar gummatous condition clinically resembling sporotrichosis or syphilis. The fungus, on certain media (glycerine agar), vegetates as a saccharomyces and ferments glucose; on other media (agar) mycelium and yeast-like cells are present, and the fungus does not ferment glucose any longer. On glucose agar the growth is white-yellowish, mammillary, with a radiating aureola. The fungus, unless injected in massive doses, is not very pathogenic to the rabbit, guinea-pig, and rat. Intraperitoneal injections of rather large doses induce in these animals a nodular peritonitis.

Monilia caoi Verdun, 1912.

Found by Cao in the sputum of a tubercular patient in association with the tubercular bacillus. Yellowish colonies on ordinary agar. Pathogenic to rabbits. Biochemical reactions not given.

Monilia harteri Verdun, 1912.

Synonym. *Parasaccharomyces* sp. (?) de Beurmann and Gougerot.

Found by Harter in a case of enteritis which later developed hepatic, bronchial, and cutaneous lesions, due to the same fungus. On maltose agar and carrots the colonies are cream-white, and yeast-like cells only are generally found. In Raulin's liquid mycelial threads are present, septated, 2 μ in breadth. The fungus does not liquefy gelatine, does not coagulate milk; produces slight acidity, but not gas, in saccharose.

Monilia perieri Matruchot and Antoine, 1917.

Synonym.—*Oöspora perieri* Matruchot and Antoine.

Found in a case of thrush of a wound. Biochemical reactions not given.

Monilia parakrusei Castellani, 1912.

Differs from *M. krusei* in clotting milk. Found by Castellani in sputum.

Genus Oidium Link, 1809, *emendavit* Pinoy.

Definition.—Oösporaceæ with hyphæ terminating in chains of spores. Hyphæ long and branched. Sporophores simple, septate, often without disjunction apparatus. Do not produce gas in carbohydrates.

Type Species.—*Oidium lactis* Link, 1809.

Remarks.—Pinoy has adjusted this genus, so that now it contains human parasites, which are:—

Oidium lactis Link, 1809.
Oidium rotundatum Castellani, 1911.
Oidium asteroides Castellani, 1914.
Oidium matalense Castellani, 1915.

These fungi may be differentiated as follows:—

A. Only produces slight acidity, and only at times, in glucose; cultures white—*Lactis*

B. Produce acidity in several carbohydrates:—
  I. No acidity in glucose, culture white and hairy—*Matalense*
  II. Acidity in glucose:—
    (*a*) No acidity in mannitol:—
      Mycelial spores, roundish or oval. Typical colonies convoluted—*Rotundatum*.
    (*b*) Acidity in mannitol:—
      Mycelial spores, quadrangular. Typical colonies asteroid—*Asteroides*.

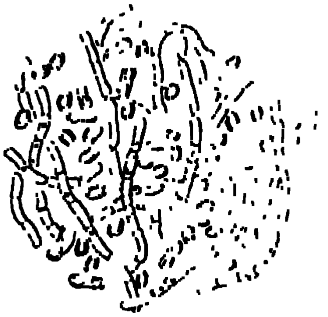


FIG. 571.—*Oidium rotundatum* CASTELLANI. FRESH PREPARATION.

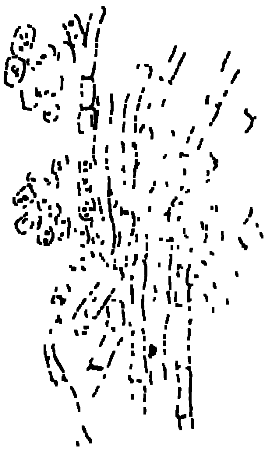


FIG. 572.—*Oidium asteroides* CASTELLANI. FRESH PREPARATION.

Oidium lactis Link, 1809.

Definition.—Oidium found in milk, in which it produces acid and clot. Grows easily on ordinary culture media, producing white colonies. It does not form gas in carbohydrate media, and only slight acidity at times in glucose.

Name of Fungus	*Litmus Milk.*	*Glucose.*	*Levulose*	*Maltose*	*Galactose*	*Saccharose*	*Lactose*	*Mannite*	*Dulcite*	*Dextrin*	*Colour of Growth.*	*Remarks.*
Oidium asteroides Cast., 1914 ..	AC	A	A	A	A	A	A	O or Avs	O	O	Whitish yellowish and amber colour	Isolated colonies have often a radiating appearance. Liquefaction of gelatine may be extremely slow.
Oidium lactis Link, 1809 ..	AC	O or As	O	O	O	O	O	O	O	O	White	—
Oidium matalense Cast., 1915	O or As	O or A	O or A	As	O or Avs	O or As	O	O	O or As		White	--
Oidium rotundatum Cast., 1911	A or AC	As	A	O or As	As	O	O or Avs	O or As	O		Yellowish	Surface of cultures often has a crinkled appearance. Liquefaction of gelatine may be extremely slow.

Name of Fungus	*Raffinose*	*Arabinose.*	*Adonite.*	*Inulin.*	*Sorbite.*	*Indol.*	*Gram*	*Gelatin.*	*Serum*	*Colour of Growth.*	*Remarks*
Oidium asteroides Cast., 1914	O or Avs	O or As	O	O		O	-	—	O	Whitish-yellowish and amber colour	Isolated colonies have often a radiating appearance. Liquefaction of gelatine may be extremely slow.
Oidium lactis Link 1809 ..	O	O	O	O	-	O	+	O	O	White	—
Oidium matalense Cast., 1915	O	O or A	O or As	O or Avs	-	O	—	O	O	White	--
Oidium rotundatum Cast., 1911	O	O or A	--	O	---	O	+	+	O	Yellowish	Surface of cultures often has a crinkled appearance. Liquefaction of gelatine may be extremely slow or absent.

Abbreviations used in the Tables.—A = acid; G = gas; C = clot (in milk); [illegible] P = [illegible] pellicle present. D = decolourized. P = peptonized (milk); p = pellicle (broth). Alk = alkaline. $\frac{A}{Alk}$ = acid, then alkaline. s = slight; vs = very slight. O = negative result—viz., neither acid nor clot in milk; neither acid nor gas in sugar media; non-production of indol; non-liquefaction of gelatine or serum as the case may be. + = positive result, liquefaction of medium. f = fine.

Remarks.—It was found by Link in milk and recently by Linossier in cases of bronchitis. The latter was considered to be slightly different and to form a pathogenic race, *Oidium lactis* var. A.

Oidium rotundatum Castellani, 1911.

Definition.—Oidium growing on glucose agar and producing crinkled or vermiform yellowish growths. It gives rise to acidity in milk, and after a variable time may form a clot. Gelatine is liquefied, but liquefaction may be extremely slow or absent with certain strains. For the sugar reactions see the table (p. 1094). It forms acid in glucose, levulose, galactose, maltose, and lactose.

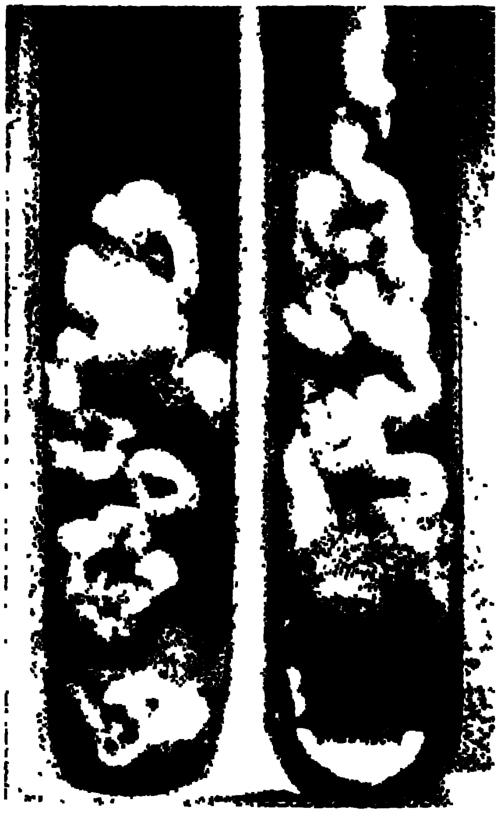


Fig 573 Fig. 574.

Figs. 573 and 574.—*Oidium rotundatum* Castellani. Culture.

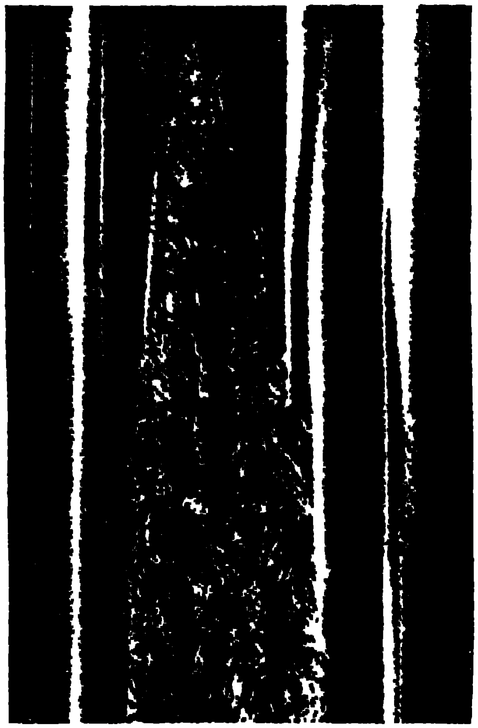


Fig. 575.—*Oidium asteroides* Castellani. Culture.

Remarks.—Found in cases of bronchitis and a very similar or identical form in the fæces of cases of sprue and of enteritis.

Oidium asteroides Castellani, 1914.

Definition.—Oidium producing colonies with a characteristic radiating appearance on glucose agar, from which it derives its name. It grows badly or not at all upon inspissated blood serum, which it does not liquefy. It turns milk acid and clots it in a variable time. No gas is formed in any carbohydrate medium.

Remarks.—This fungus was isolated from stools in cases of sprue and from the sputum in cases of chronic bronchitis.

FIG. 576.—*Oidium matalense* CASTELLANI. CULTURE.

Oidium matalense Castellani, 1915.

Definition.—Oidium producing a white growth on glucose agar. It turns milk sometimes slightly acid, without the formation of a clot, or it may have no effect. Gelatine is not liquefied, nor is any gas produced in carbohydrate media.

FAMILY 3: ENANTIOTHAMNACEÆ Chalmers and Archibald, 1915.

Definition.—Blastosporineæ with a thallus composed of ramifying hyphæ, with regular septa, which easily disappear, thus dissociating the segments, which are 2-2·5 microns broad. The conidia are arranged verticillately around the septa.

Remarks.—This family contains only one genus, *Enantiothamnus* Pinoy, 1911. The name is derived from ἐναντίος, 'opposite,' and θάμνος, 'a shrub.'

Genus Enantiothamnus Pinoy, 1911.

Definition.—Enantiothamnaceæ with the characters of the family.

Remarks.—There is only one species so far known, *Enantiothamnus braulti* Pinoy, 1911.

Enantiothamnus braulti Pinoy, 1911.

Definition.—Enantiothamnus with oval conidia 2-2·5 by 1-1·5 microns.

Habitat.—Parasitic in man.

Remarks.—This fungus was discovered by Brault in umbilicated tumours containing pus, in the gluteal region of an Arab in Algiers.

On Sabouraud's agar the colonies are white, with a yellowish central portion.

Pathogenicity.—Produces tumours and pus in man, and is pathogenic for guinea-pigs.

FIG. 577.—*Enantiothamnus braulti* PINOY. (After Brault and Pinoy.)

FAMILY 4: HAPLOGRAPHIACEÆ Saccardo, 1896.

Definition.—Blastosporineæ with hyphæ manifest and distinct from the conidia, which are usually arranged in chains, or, in parasitic condition in man, in grape-like masses.

Remarks.—This family contains the genera *Hormodendrum* Bonorden, 1851, and *Malassezia* Baillon, 1889, which are recognizable as follows:—

All sterile hyphæ creeping. Conidia all alike and produced on the hyphæ. Conidiophores not spirally twisted; hyphæ dendroid:—

A. Conidia in cultures in chains, in parasitic form in masses—Genus *Hormodendrum* Bonorden, 1851.

B. Conidia in parasitic form in masses. Cultural form unknown—Genus *Malassezia* Baillon, 1889.

Genus Hormodendrum Bonorden, 1851.

Definition.—Haplographiaceæ with creeping dendroid sterile hyphæ and branched conidiophores, bearing conidia all of one kind.

Remarks.—The genus Hormodendrum contains about ten species, which are generally parasitic on plants or saprophytic, but one is known to occur in man—viz., *H. fontoynonti*.

Type Species.—*Hormodendrum olivaceum* (Corda, 1838). The name is derived from *ὅρμος*, 'a chain,' and *δένδρος* (or *δένδρον*), 'a

Hormodendrum fontoynonti Langeron, 1913.

Definition.—Hormodendrum in cultures with sterile hyphæ 3 to 8 microns in diameter, greenish brown in colour, septate with thick walls. Sporophores well defined, not swollen at the extremity, carrying chains of very caducous spores. In man mycelium broken in segments, long and undulating; spores, which are capable of budding, arranged in masses.

Remarks.—Found by Fontoynont and Carougeau in the scales of a dermatosis, called 'hodi-potsy' in Madagascar, which is comparable to that termed 'tinea flava' in other tropical countries. It is doubtful whether the fungus is the ætiological agent of the condition.

Genus Malassezia Baillon, 1889.

Definition.—In man mycelium broken into septate segments, with T-shaped or budding extremities. The hyphæ carry round or oval conidia, which may be solitary or in grape-like masses, and may be smooth or with longitudinal, radial, or spiral marks. In culture unknown.

Remarks.—This genus is only known to contain parasites of man The two species may be recognized as follows:—

I. Causing a brown eruption on the white skin—*i.e.*, tinea versicolor. Lesions very superficial—Species *Malassezia furfur* Charles Robin, 1853.

II. Causing a red eruption on the white skin and a yellow eruption on the dark skin—*i.e.*, tinea flava. Deeper lesions—Species *Malassezia tropica* (Castellani, 1905).

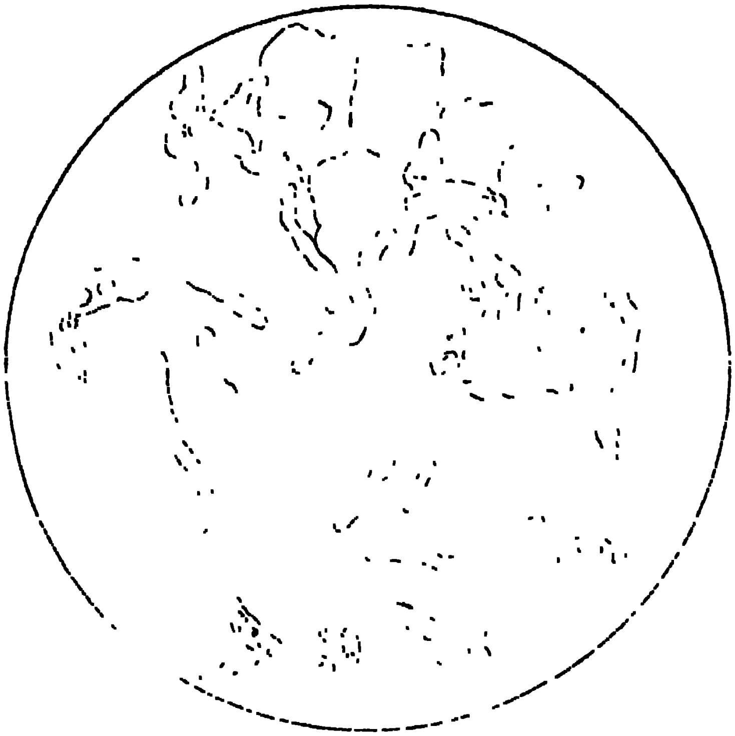


FIG. 578.—*Malassezia tropica* CASTELLANI.

From a fresh preparation in liquor potassæ. Old case.)

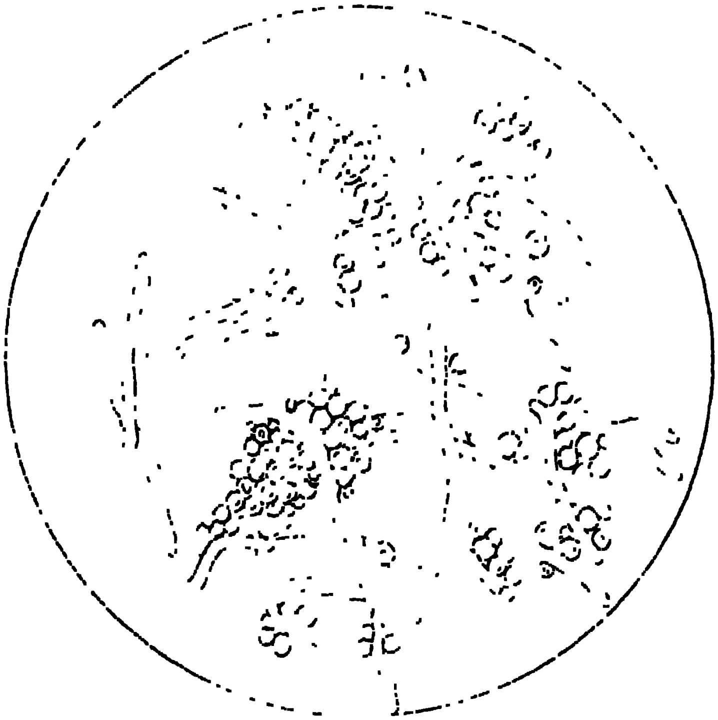


FIG. 579.—*Cladosporium mansoni* CASTELLANI.

(From a fresh preparation in liquor potassæ. The mycelial tubes are in reality not so regular in outline as in this drawing.)

Malassezia furfur Ch. Robin, 1853.

Synonyms.—*Microsporon furfur* Ch. Robin, 1853; *Sporotrichum furfur* Saccardo, 1886; *Malassezia furfur* Baillon, 1889; *Oidium furfur* Zopf, 1890; *O. subtile* Kotliar, 1892.

Mycelium abundant, septate, non-ramified; some mycelial threads are much larger than others; the breadth varies between 3 and 4 μ. The spores are roundish (3 to 5 μ in diameter), and run into clusters. Attempts at cultivation have failed. It is the cause of pityriasis versicolor.

Malassezia tropica Castellani, 1905.

Synonym. *Microsporon tropicum* Castellani, 1905.

Mycelial threads generally thick (3 to 5 μ wide), with numerous swellings, constrictions, and other irregularities of shape; spores roundish (4 to 5 μ), with a double contour; are often collected in clusters. The fungus does not grow on artificial media. It is the cause of tinea flava or pityriasis flava of tropical climates.

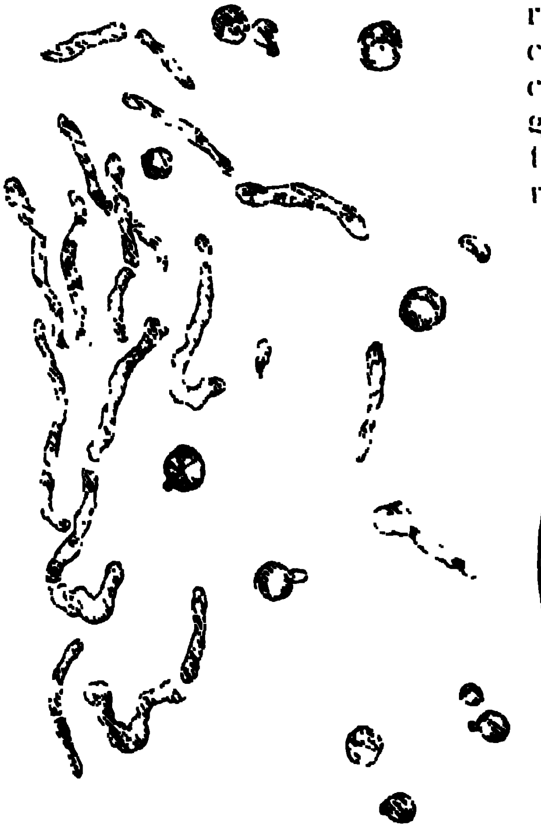


FIG. 580.—*Cladosporium mansoni* CASTELLANI.

(From a preparation stained by fuchsin.)

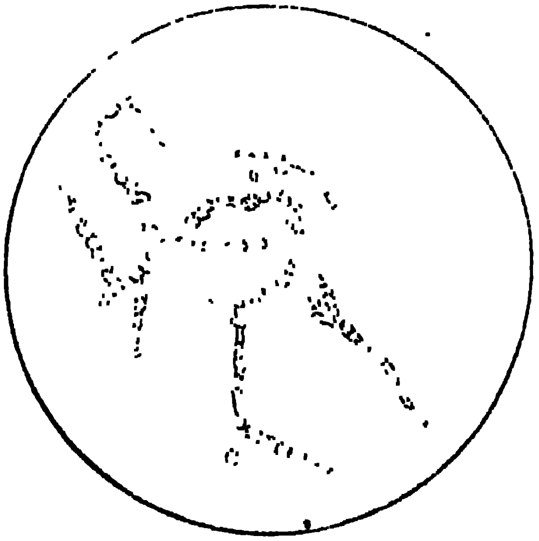


FIG. 581.—*Cladosporium mansoni* CASTELLANI. HANGING-DROP CULTURE.

FAMILY 5: CLADOSPORIACEÆ Saccardo, 1886.

Definition.—Blastosporales with hyphæ manifest and distinct from the conidia, which are either solitary or arranged in short chains.

Remarks.—We are only concerned with the type genus *Cladosporium* Link, which may be recognized as follows:—

Conidia smooth, not capitate, more or less in chains at first. Hyphæ and conidia uniform. Hyphæ not inflated, but decumbent; conidia in short chains and finally solitary—Genus *Cladosporium* Link, 1809.

Genus Cladosporium Link, 1816.

Definition.—Cladosporiaceæ with decumbent hyphæ. Conidiophores bearing smooth, uniform conidia arranged in short chains or solitary.

Etymology.—The name is derived from κλάδος, 'a young shoot.'

Remarks.—The type species is *Cladosporium herbarium* Persoon, 1801, and there are a very large number of species scattered all over the world, and commonly found on plants in tropical gardens, from whence the spores can easily be conveyed to the human skin, and either grow there, causing a lesion, or simply remain sheltered among the scales of other lesions, from which they may be grown in pure culture, thus giving rise to the impression that they may be causal organisms, but they do not agglutinate with the patient's serum.

They may also grow as contaminations of laboratory media, so commonly may their spores be found in the air. The two species known in man may be recognized as follows:-

Habitat, tinea nigra—Species *Cladosporium mansoni* (Castellani, 1908).

Habitat, ulcerating nodules—Species *Cladosporium penicilloides* Gueguen, 1911.

Fig. 582.—*Cladosporium mansoni* Castellani. Young Agar Culture.

Cladosporium mansoni Castellani, 1905.

Synonyms.—*Microsporon mansoni* Castellani, 1905; *Foxia mansoni* Castellani, 1908; *Cladosporium mansoni* Pinoy, 1912.

The fungus is found very abundantly in the lesions of tinea nigra; the mycelial articles are rather short—18 to 20 μ in length and 2½ to 3½ μ in breadth; non-ramified. Sometimes they may be irregular in outline, bent, banana-shaped. The spores are globular, and most of them very large—5 to 10 μ. They are frequently arranged in clusters.

The fungus is easily cultivated by inoculating scrapings of the affected patches on maltose agar. After two to four days roundish hemispheric colonies appear, which are black, but at first have usually a greenish tinge, and may present at the periphery some radiating, delicate, pale greenish hyphæ. These colonies may remain separate or more often gradually coalesce into a jet-black knobby mass, deeply rooted into the medium. The fungus grows well, though less abundantly, on the other sugar agars, and also on ordinary agar. In *broth* and *peptone-water* the growth is very slow, and takes place at the botton of the tubes, with formation of a black or greenish-black sediment. Gelatine is very slowly liquefied.

The *optimum temperature* for the growth of the fungus is between 30° C. and 32° C.; above 35° C. and under 25° C. the growth is much slower, and may be nil under 20° C.

This fungus is the cause of tinea nigra (p. 2078).

Cladosporium penicilloides Gueguen, 1911.

Synonym.—*C. Madagascariense* Verdun, 1913.

Found by Fontoynont in a patient with some ulcerated nodules of the leg in Madagascar. The fungus grows easily on Sabouraud's and other media, giving rise to black cerebriform colonies. In hanging-drop cultures shows the typical features of the genus.

Cladosporium herbarium Persoon has been demonstrated by Nassee to be the cause of the black spots so often found on imported frozen meat.

SUBORDER 2. ARTHROSPORINEÆ VUILLEMIN, 1910.

Definition.—Thallosporales with yeast-like forms, associated in cultures with hyphæ and other forms with longer hyphæ. Reproduction by means of arthrospores parasitic on man.

Remarks.—Vuillemin includes in this suborder the genera Trichophyton, Microsporon, Achorion, and their allies, although it is more usual to consider these to be allied to the Gymnoascaceæ, because *Ctenomyces serrata* Eidam, 1880, when injected into animals, develops a trichophyton-like mycelium and eruption, which classification has recently been supported by the work of Marshall and one of us on *T. currii*. However, for the present, we propose to leave these genera and their allies out of consideration.

Classification.—This suborder contains the following genera:—

A. Producing *Piedra* on hairs—Genus *Trichosporum* Behrend, 1890.

B. Producing *Black Maduromycosis*—Genus *Madurella* Brumpt, 1905.

C. Producing *White Maduromycosis*—Genus *Indiella* Brumpt, 1906.

Genus Trichosporum Behrend, 1890.

Definition.—Arthrosporales living parasitically on the hairs of man in the form of large, oval, or roundish bodies embedded in a ground substance. In cultures elongated hyphæ and spores are formed.

Remarks.—Care must be taken not to confuse *Trichosporum* Behrend, 1890, with *Trichosporium* Fries, 1849, a very different genus with over forty species, mostly saprophytic.

The species of this genus give rise to nodosities on hairs. They are:—

T. giganteum Behrend, 1890, the cause of piedra in Columbia, in hairs of the head.

T. beigeli (Rabenhorst, 1867), the cause of piedra in Europe, in hairs of the beard.

T. ovoides (Behrend, 1890), the cause of piedra, in hairs of the moustache.

T. ovale Unna, 1896, on the hairs of the moustache in Europe.
T. glycophile du Bois, 1910, on the pubic hairs of a diabetic.
The various species may be differentiated as follows:-

A. *Bodies around hair polyhedral* :—
  I. Diameter of bodies 12-15 microns—*Giganteum*
  II. Diameter of bodies 3-4 microns—*Beigeli*.

B. *Bodies around hair oval and small, 3-4 microns by* 1·5-2·5 *microns*:—
  I. In cultures hyphæ often twisted like a corkscrew—*Ovale*.
  II. In cultures hyphæ not so twisted—*Ovoides*.

C. *Bodies around hair roundish*, 3-4 *microns in diameter* :—
  Fungus associated with a coccus, with which it grows well on sugar media—*Glycophile*.

These fungi live parasitic on the surface of the hairs, but do not penetrate into their interior g their parasitic life they vegetate in the shape of large oval or roundish elements, embedded in an amorphous substance. Saprophytically (cultures) they vegetate, forming mycelial threads and spores.

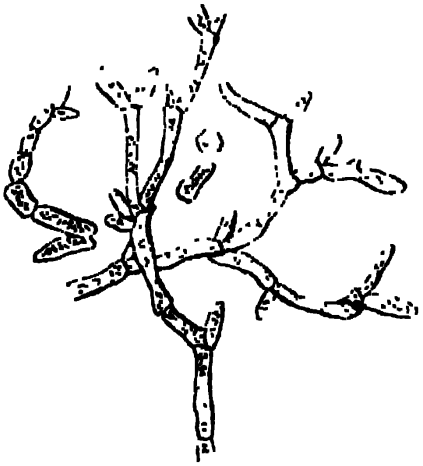


FIG. 583.—TRICHOSPORUM (After Vuillemin

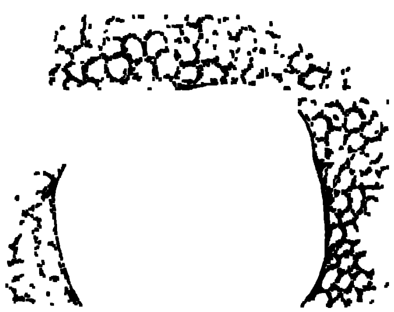


FIG. — TRANSVERSE SECTION OF A PIEDRA NODULE.

Trichosporum giganteum Behrend, 1890.

This is the cause of *piedra* of Columbia; develops on the surface of the hair in the shape of large polyhedric cells 12 to 15 μ in diameter. Masses of the fungus form hard nodules along the hair. The fungus is easily grown on various media. In cultures the mycelial threads are septated, cylindrical, between 1 and 4 μ wide. The spores are of various dimensions, between 2 and 12 μ. The colour of the colonies is light brownish. Horta describes in the nodules of a variety of piedra certain large cyst-like bodies containing generally eight fusiform bodies. When the membrane bursts, these bodies escape, being provided with one flagellum at each end. Pinoy is inclined to consider these formations to be asci containing ciliated ascospores.

Trichosporum beigeli Rabenhorst, 1867.

Synonyms.—*Pleurococcus beigeli* Rabenhorst, 1867; *Sclerotium beigelianum* Hallier, 1868; *Hyalococcus beigeli* Schroeter, 1886; *Chlamydotomus beigeli* Trevisan, 1889; *Micrococcus beigeli* Migula, 1900; *Trichosporum beigeli* Vuillemin, 1901.

This fungus has been found in Europe several times in nodosities of the hairs of the moustache. It lives parasitically under the form of ovoid or polyhedral elements massed together on the surface of the hair. These ovoid or polyhedral elements are much smaller than those of the preceding species, their maximum diameter varying between 3 and 4 μ. It is easily cultivated on ordinary media. In cultures mycelial threads are found, septate, slender (1·57 to 2 μ). In old cultures chlamydospores can be seen.

Trichosporum ovoides Behrend, 1890

Found by Behrend in the nodosities present on the moustache of a European patient; vegetates parasitically on the surface of the hair under the form of ovoid elements; 3 to 4 μ long and $1\frac{1}{2}$ to $2\frac{1}{2}$ μ wide. Grows easily on culture media; on potatoes the colonies are white, while the medium takes a brownish-black colour.

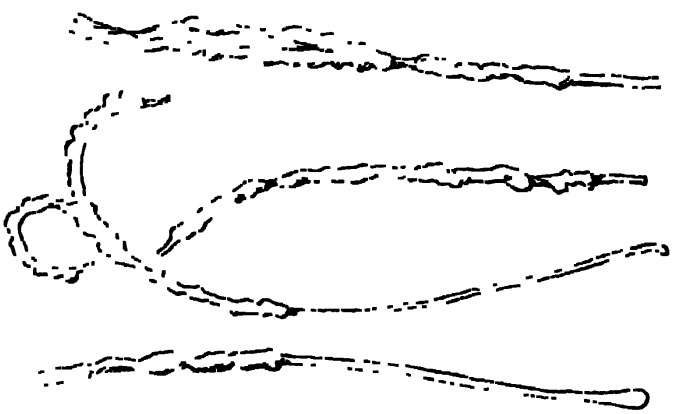


Fig. 585.—Hair affected with Trichosporosis. (After Vuillemin.)

Trichosporum ovale Unna, 1890.

Found by Unna in the nodosities present on the moustache of a European patient. Very similar to *T. ovoides*; in cultures, however, the mycelial threads are often corkscrew-like, and the spores have thick walls.

On potatoes the colonies are white-yellowish, and the substratum takes a brownish-black colour.

Trichosporum glycophile du Bois, 1910.

Found by du Bois in a nodular affection of the pubic hairs in a diabetic patient. In the nodules roundish elements, 3 to 4 μ, were present, together with a coccus. The fungus was easily cultivated in symbiosis with the coccus on sugar media.

Genus Madurella Brumpt, 1905, *emendavit* Pinoy, 1912.

Definition.—Arthrosporineæ with sterile septate hyphæ, reproducing the thallus by fragmentation and secreting a black pigment The spores are produced secondarily by binary division of the articles. Found in black maduromycosis and grow well at 37° C.

Type Species.—*Madurella mycetomi* (Laveran, 1902).

Historical.—In 1901, Brumpt, Bouffard, and Chabaneix wrote an account of a case of black mycetoma which they observed at Djibouti. In the following year the organism found in this case was studied by Laveran, who gave it the name *Streptothrix mycetomi* Laveran, 1902. Brumpt also found the same organism in a maduromycosis in the centre of Somaliland, and also in an amputated foot sent from Madagascar.

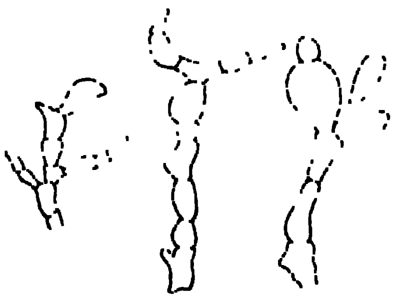


FIG. 586.—*Madurella mycetomi* LAVERAN.

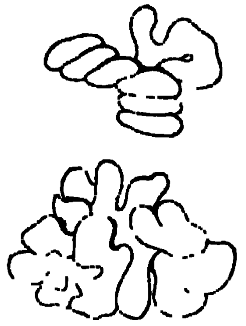


FIG. 587.—GRAINS OF *Indiella reynieri* BRUMPT

(After Brumpt)

Bouffard, in 1905, reported the presence of the same disease in Senegal and in the French Sudan.

In this variety the grains are black or deep brownish red, and always hard and generally small, from 1-2 millimetres in diameter, when single, and not in accumulated masses. The surface is irregular, with projecting points. On clearing with Eau de Javelle, the fungal elements can be clearly seen.

Brumpt (1905) formed a new genus, '*Madurella,*' for this fungus, defining it as follows:—

> 'Mucedine with white thallus, living parasitically in various animal tissues (bone, muscle, connective tissue), possessing during its vegetative life filaments with a diameter greater than 1 micron, and even reaching to 8-10 microns. These filaments are septate and branch from time to time; they secrete a brown substance. When old, these filaments form a sclerote, and their walls sometimes become impregnated with a brown pigment. In this sclerote there are a number of rounded corpuscles, from 8-30 microns in diameter (chlamydospores).'

The type species is the organism called *Streptothrix mycetomi* by Laveran, in 1902, which therefore becomes *Madurella mycetomi* (Laveran, 1902), first cultivated by Brault (1911) in material from Algerian cases.

This form of mycetoma was reported by Balfour (1911) to be present in the Anglo-Egyptian Sudan.

It is generally assumed that this and the Asian, together with the American type, are one and the same disease, but this still requires proof.

In 1908, Nicolle and Pinoy described a maduromycosis which they found in Southern Tunisia, near the Oasis of Tozeur, with hard dark brown grains about the size of a pin's head, in which segmented and ramified hyphæ about 1-4 microns in diameter were seen, as were rounded bodies arranged in chains and resembling the mycelial spores of a trichophyton, the whole being embedded in a brownish cement substance. Cultures were obtained at 35° C., and the growths were identical on maltose agar, glycerine agar, potato, and carrot, and all the media became pigmented black, due to a tyrosinase produced by the fungus, while the colonies which developed in twenty-four hours at 37° C. were white. Microscopically the growths showed the 'favic nails' so commonly met with in cultures of *A. schoenleini*. The authors looked upon the organism as belonging to the genus *Oöspora* Wallroth, 1833, with which Vuillemin considers *Achorion schoenleini* Lebert, 1845, should be classified. Its name, therefore, became *Oöspora tozeuri* (Nicolle and Pinoy, 1908).

Inoculation experiments were unsuccessful in the rabbit, the guinea-pig, and the monkey, but two successful infections were obtained in pigeons.

Brumpt, however, considers the fungus to be a *Madurella*, and therefore its name becomes *Madurella tozeuri* (Nicolle and Pinoy, 1908).

Brault (1911 and 1912) cultivated the fungi *Madurella mycetomi* and *M. tozeuri*.

The former grew at 20° C. and 37° C. on broth, various agars, potato, carrot, and some vegetal liquid media.

In the liquid media the growth appeared as a whitish grey puff-ball, which later became yellowish or brownish, while the medium remained clear and the growth fell to the bottom of the tube.

On solid media it formed a greyish-white, duvet-covered growth, which possessed a central button, surrounded by a radiation, and later, when the culture was drier, the medium became coloured.

Glycerine agar was best, as the growth thereon was luxurious, and when old became yellowish in colour, while the medium showed a caramel tinge in its entirety.

Glucose glycerine agar produced a growth of the colour of touchwood. This culture is thrown into black wrinkles, producing an appearance seen on some seashores.

When the growths of *M. tozeuri* were compared with those of *M. mycetomi* a number of differences were observed.

The cultures of *M. tozeuri* grew more quickly, were more luxuriant, and were white, resembling powdered flour. Those of *M. mycetomi* were more discrete, grey, *duveteuse*, radiated, and sometimes showed concentric circles, and disassociated more easily than the preceding.

Old cultures on glucose agar or on glycerinated glucose agar were quite different in the two species.

On carrot *M. tozeuri* attained a deeper brownish-yellow colour, while in old cultures on this medium it produced spores in a manner resembling an Oöspora.

Pinoy, in his remarks upon the mycology of these two species, says that Brault's *M. mycetomi* very closely resembles that isolated by Nicolle under the name of *Oöspora tozeuri*. Its filaments are 2-8 microns in diameter, and do not possess apparatus for fructification, reproducing by a breaking up of the hyphæ of the thallus into articles 5-10 microns in length, which divide into two spores. These spores are of the same diameter as the hyphæ from which they arise, varying from 2-5 microns, while the membrane becomes yellowish with age. In addition, chlamydospores can be observed forming at the end of the filaments, more or less like favic nails. The spores of *M. tozeuri* are smaller, but are formed in the same manner.

On Sabouraud's gelatine *M. mycetomi* gives rise to black sclerotes in the depth of the medium. These are very numerous, measure ½-1 millimetre in diameter, and are composed of hyphal segments, more or less cylindrical. Sometimes the sphere attains a diameter of 10 microns, and usually contains only one nucleus; but, though studied for a long time, these sclerotes were never observed to have any higher form of fructification. In *M. tozeuri* it is very rare to see the formation of sclerotes, which takes place on the surface of the medium.

On the bases of the researches on *M. mycetomi* and *M. tozeuri*, Pinoy classifies the genus Madurella as follows:—

A. Sclerotes 0·5-1 millimetre in diameter, formed in the depths of medium in cultures—*Mycetomi*.

B. Sclerotes rarely produced, and then on the surface of the medium—*Tozeuri*.

Madurella mycetomi (Laveran, 1902).

Synonym.—*Streptothrix mycetomi* Laveran, 1902.

Mycelium greyish white; when old, yellowish and darkening the media in sugar cultures. Spores varying in dimension from 2-5 microns. Sclerotes black and sterile, with a diameter from 0·5-1 millimetre, formed in the depths of the medium in cultures. Can invade the skin, bone, muscles, and connective tissue of man, giving rise to black grains, which are small, hard, round, and more or less warty, and which morphologically resemble the sclerotes formed in the cultures. Up to the present the inoculation into animals is negative. Very widely spread in Africa. Isolated by Brault from a mycetoma with black grains in Algeria.

Madurella tozeuri (Nicolle and Pinoy, 1908).

Synonym.—*Oöspora tozeuri* Nicolle and Pinoy, 1908.

Mycelium white, becoming yellowish with age and darkening the medium in sugar cultures. Spores generally small, 2 microns or sometimes even 5 microns in diameter. Sclerotes are only rarely produced, and then they appear on the surface of the medium. Occasionally it gives rise to a mycetoma in man, in which it forms black amorphous grains, which are often made up of mycelial rings, enclosing some degenerate cellular elements, which are impregnated with the pigment of the fungus, and also of small diffuse masses, formed solely by the filaments of the fungus, which have a yellow membrane. Inoculation into pigeons positive. Isolated by Nicolle from a mycetoma at Tozeur.

Genus **Indiella** Brumpt, 1906.

Definition.—Arthrosporineæ with septate, ramified hyphæ, without black pigment, and hence sclerotia white or yellowish.

Type Species.—*Indiella mansoni* Brumpt, 1906.

Remarks.—White thallus, living parasitic in various animal tissues—connective tissue, muscles, and bones. Mycelial threads 1-8 or 10 μ, septate, ramified, never secreting—in contrast to the fungi of genus *Madurella*—any black pigment. Masses of mycelial threads form sclerotia-like bodies or grains of various shape containing chlamydospores.

Classification.—The species may be recognized as follows:—

A. Sclerotia hard and bean-shaped —*Mansoni*.
B. Sclerotia soft and in coiled masses—*Reynieri*.

Indiella mansoni Brumpt, 1906.

Mycelial threads are septated, white, thin, 1·5-2 μ when young, larger (3-5 μ) and of irregular shape when old. Numerous spherical chlamydospores, generally terminal, 5-12 μ in diameter. Grains (sclerotia) very small, of $\frac{1}{3}$-$\frac{1}{2}$ millimetre, white, lenticular or reniform, very hard, do not soften by keeping in caustic potash. The fungus has not been grown.

Pathogenicity.—It is the cause of Manson's white mycetoma, of which only one case is known.

Indiella reynieri Brumpt, 1906.

White thallus. Most mycelial filaments are very thin, 1-1½ μ, septated; some—those at the periphery—are of irregular shape, much broader (4-5 μ), moniliform. Nearly every mycelial thread has at the peripheral extremity a terminal chlamydospore, 5-20 μ, often septate in two or three cells. Grains or sclerotia are small, less than 1 millimetre in diameter, coiled up like the excrementa of earth-worms.

Pathogenicity.—This fungus causes a variety of mycetoma with white grains (Reynier's white mycetoma), of which there is only one case on record—a European patient who had never left France. The case was observed and reported on by Reynier.

ORDER III. HEMISPORALES Vuillemin, 1910.

Definition.—Hyphales with the mycelium composed of abundant hyphæ, thin, but more than 1 micron in diameter, septate and branched conidiophores ramified basally, each branch terminating in a protoconidium, preceded by an annular construction produced by a brown, rigid thickening of the wall. The protoconidium is transformed completely or partially into deuteroconidia, but occasionally it elongates, forming a new conidiophore, or puts out branches which are capable of becoming conidiophores.

Classification.—There is only one genus, *Hemispora* Vuillemin, 1906.

Genus Hemispora Vuillemin, 1906.

Definition.—Mycelial filaments, thin, hyaline, septated, ramified. Each conidiophore terminates into an ampulliform structure (protoconidium), which later divides into several spore-like segments (deuteroconidia).

Hemispora stellata Vuillemin, 1906.

Definition.—Hemispora composed of white, sessile discs covered with conidiophores, arranged like brown stars in relief on the surface. Deuteroconidia subspherical, measuring 2·6-3·5 microns, with a dark coloured granular membrane except at the point of attachment, sometimes elongated and barrel-shaped. Habitat, parasitic on man and fungi.

Remarks.—This species was first found in 1904 by Vuillemin, growing on *Aspergillus repens* (De Bary, 1870). In 1909 Gougerot and Caraven first found it parasitic in man, and this has since been confirmed by other cases described by Auvray, De Beurmann, Clair and Gougerot, and by Thiry. So far it has not been found in the tropics.

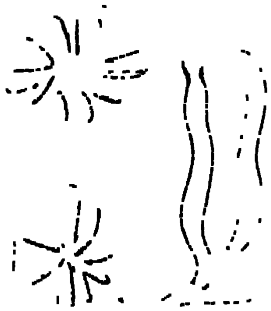


FIG. 588.—*Hemispora stellata* VUILLEMIN. (After Vuillemin.)

Pathogenicity.—It is the cause of hemisporosis, characterized by bony lesions and cold abscesses simulating tertian syphilis, tuberculosis, or sarcomata.

Biology.—It grows well on sugar media at the temperature of the room, and when separated in pure culture can be tested by sero agglutination and complement fixation. Typical colonies asteroid.

Treatment.—Iodide of potassium gives good result.

Hemispora rugosa Castellani, 1910.

Synonym.—*Monilia rugosa* Castellani, 1910.

Definition.—Hemispora growing on all ordinary media, with a crinkled surface without asteroid colonies.

Remarks.—Isolated from cases of bronchitis and a case of tonsillitis by Castellani, and recently from a case of thrush by Pijper.

Name of Fungus.	*Motility*	*Gram.*	*Gelatine.*			*Serum.*			*Litmus Milk.*			*Lactose.*			*Saccharose.*			*Dulcite.*			*Mannite.*			*Glucose.*			*Maltose.*		
Number of Days.			4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12
Hemispora rugosa Cast.	O	+	O	+vs	+	O	O	O	O	O	O	O	O	O	Avs	Avs or O	Avs or O	O	O	O	O	O	O	A	As	As	As	Avs	O or Avs

Name of Fungus.	*Dextrin.*			*Raffinose.*			*Arabinose.*			*Adonite.*			*Inulin.*			*Starch.*			*Salicin.*			*Levulose.*			*Galactose.*			*Glycerine.*		
Number of Days.	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12
Hemispora rugosa Cast.	O	O	O	O	O	O	As	Avs	Avs	O	O	O	O	O	O	O	O	O	O	O	O	O	O or Avs	Avs	O	O	O	O	O	O

Abbreviations used in the Tables.—A = acid; C = clot; G = gas; S = slight; vs = very slight; O = negative result—viz., non-production of acid or gas in sugar media, non-production of indol, non-liquefaction of gelatine or serum, as the case may be; + = positive result.

The growth on glucose agar is abundant, crinkled, or at times somewhat cerebriform; and in colour is amber, yellow, or brownish. Grows well on gelatine, which it liquefies very slowly, so much so that at first it was believed to be a non-liquefier. Gram-positive. Milk is not changed as a rule, but occasionally it undergoes a certain degree of peptonization, with a very small coagulum at the bottom of the tube. For sugar reactions see the table.

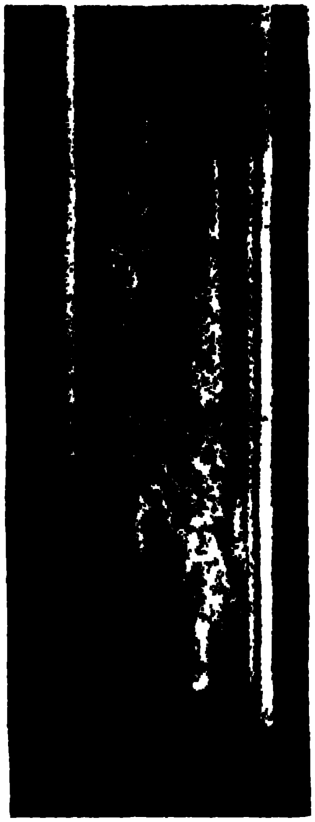


FIG. 589.—*Hemispora rugosa* CASTELLANI, 1910: GLUCOSE AGAR CULTURE.

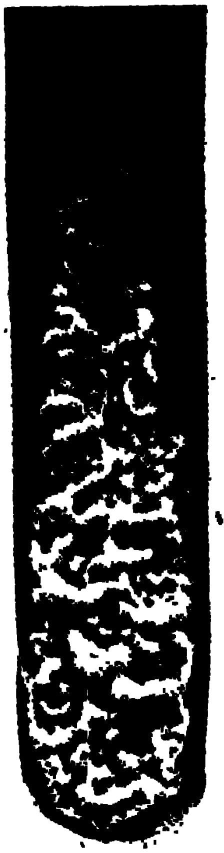


FIG. 590.—*Hemispora rugosa*: GLUCOSE AGAR CULTURE.

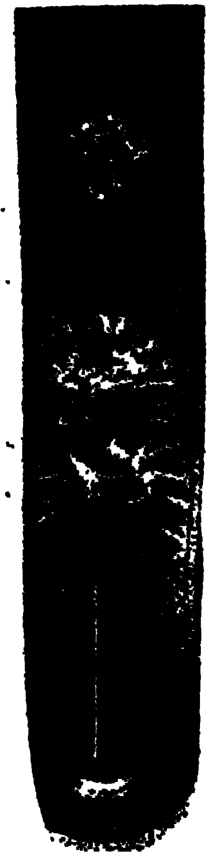


FIG. 591.—*Hemispora rugosa*: GLUCOSE AGAR CULTURE.

ORDER IV. CONIDIOSPORALES Vuillemin, 1910.

Definition.—Hyphales with the mycelium composed of abundant hyphæ, more than 1 micron in diameter, septate and branched, with or without true conidiophores, and with reproduction by means of true conidia.

Remarks.—The reasons for the formation of this order, which contains a large number of families, have already been given, as well as its advantage over the more fully worked out system of Saccardo (p. 1037).

Classification.—The order Conidiosporales is divided into five suborders, which may be recognized as follows:—

A. *Conidium imperfect:* Aleuriospore.
  Suborder 1: *Aleuriosporineæ* Vuillemin, 1911.
B. *Conidium perfect:* Conidium verum.
  I. True Conidiophores absent:—
    Suborder 2: *Sporotrichineæ* Vuillemin, 1910.
  II. True Conidiophores present:—
    (*a*) Conidia borne on sporophores.
    Suborder 3: *Sporophoralineæ* Vuillemin, 1910.
    (*b*) Conidia borne on phialides.
      1. Prophialides absent.
    Suborder 4: *Phialidineæ* Vuillemin, 1910.
      2. Prophialides present.
    Suborder 5: *Prophialidineæ* Vuillemin, 1910.

The fourth suborder, Phialidineæ, contains species of the genera *Aspergillus* Micheli, 1729; *Penicillium* Link, 1809; and *Sterigmatocystis* Cramer, 1859, in which asci are unknown; but though logically correct to include these species in the Fungi Imperfecti, it is more convenient to consider them under the heading Ascomycetes, though the genus Scopulariopsis may be placed here.

The last suborder, Prophialidales, does not contain any genera with species parasitic in man.

SUBORDER 1: ALEURIOSPORINEÆ VUILLEMIN, 1911.

Definition.—Conidiosporales in which reproduction takes place by aleuriospores.

Classification.—The suborder contains two families, which can be distinguished as follows:—

A. Conidiophores absent—*Aleurismaceæ.*
B. Conidiophores present—*Monotosporaceæ.*

FAMILY ALEURISMACEÆ Vuillemin, 1911.

Definition.—*Aleuriosporineæ* without conidiophores.

Classification.—The family is divided into two tribes:—

A. Spores simple or appendiculate—*Aleurismeæ.*
B. Spores bi- or multi-cellular—*Blastotricheæ.*

Only the first tribe is of interest to us.

TRIBE ALEURISMEÆ.

This tribe may be classified as follows:—

A. *Hyphæ pale:*—
  I. Hyphæ very short; sporogenous. Apparatus but little differentiated from the mycelium—*Myceliophthora* Costantin, 1894.
  II. Hyphæ elongate, sporogenous apparatus but little differentiated from the mycelium—*Acladium* Link, 1809.
  III. Hyphæ elongate, sporogenous apparatus well differentiated from the mycelium:—

- (*a*) ***Aleuriospore***, smooth, small, acro-pleurogenous:—
    - 1. Aleuriospores coloured—***Aleurisma*** Link, 1809.
    - 2. Aleuriospores pale—***Corethropsis*** Corda, 1839.
- (*b*) ***Aleuriospore***, large, spiny, acrogenous:—
    - 1. Aleuriospore appendiculate—***Mycogone*** Link, 1809.
    - 2. Aleuriospore non-appendiculate—***Sepedonium*** Link, 1809.

B. *Hyphæ dark*:—

- I. Hyphæ pale and dark. Aleuriospores become dark and acro-pleurogenous on light or dark hyphæ, small, generally 6×4, rarely 11×5 microns—*Glenospora* Berkeley and Curtis, 1876.
- II. Hyphæ very dark. Aleuriospores remain hyaline, situate acrogenously on hyaline hyphæ at the base of sterile dark hyphæ, large 11-14 microns—*Botryotrichum* Saccardo and Marchal, 1885.

Genus Acladium Link, 1809.

Definition.—Aleurismeæ with pale elongate hyphæ and with sporogenous apparatus, but little differentiated from the mycelium. Sporophores unbranched. Conidia pleurogenous.

Type Species.—*Acladium conspersum* Link, 1809.

Remarks.—There is only one species which concerns us—viz., *A. castellanii*.

Acladium castellanii Pinoy, 1916.

Definition.—Acladium with small chains of acrogenously placed chlamydospores. The aleuriospores are acropleurogenous.

Remarks.—The parasite was found by Castellani in cases of ulcerative dermatitis, with gumma-like nodules, in Ceylon, the Federated Malay States, and Macedonia, and fully described by Pinoy.

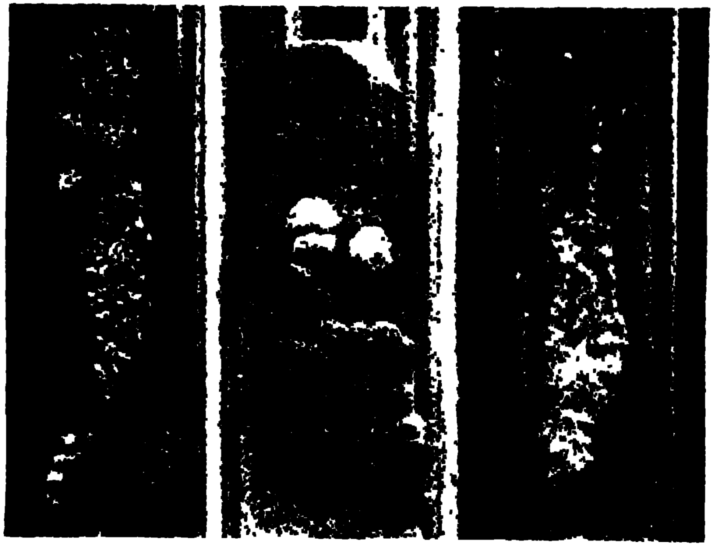


Fig. 592. Fig. 593. Fig. 594.

FIGS 592-594.—*Acladium castellanii* PINOY: CULTURES ON GLUCOSE AGAR POTATO AND CARROT.

The growth on artificial media (such as carrot, potato, glucose agar) consists of many small roundish masses, which later on may coalesce. They are covered by spiculated formations, giving them a prickly appearance, and consisting of erect, straight filaments, parallel to each other, or at times interlacing. These filaments are approximately 2 microns in diameter, and carry laterally pseudoconidia of variable shape, cylindriform, pyriform, or spherical, attenuated in size at their points of insertion. Most of these pseudoconidia are 4 microns in length, with a breadth of 3 microns. This type of fructification recalls the type Acladium decribed by Bodin in certain species of the genus Trichophyton (Malmsten, 1848).

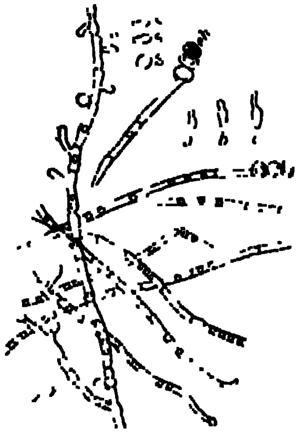


Fig. 595.—Microscopical Appearance of *Acladium castellanii* Pinoy in Hanging-Drop Culture, Five Days Old.

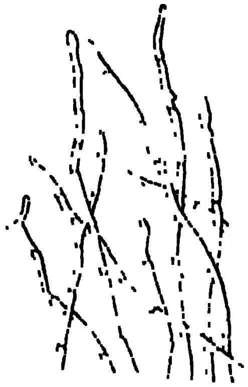


Fig. 596.—Microscopical Appearance of the Fungus in Hanging-Drop Culture, Twenty-Four Hours Old.

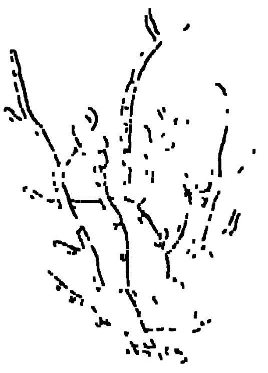


Fig. 597.—Microscopical Appearance of the Fungus in Hanging-Drop Culture, Three Days Old.

S, pseudoconidia; *a*, *b*, *c*, development of mycelial filaments from pseudoconidia; *ch*, chlamydospores.

These pseudoconidia become detached and then develop by sprouting, and mycelial filaments are formed. Certain filaments produce spherical chlamydospores arranged in small strings, as found in certain fungi of the genus Fusarium. These small chains of chlamydospores are very frequently terminal, the dimensions being variable—8 to 10 microns (Figs. 595-597).

In cultures on carrot and potato the colonies are white, on glucose agar often amber colour. Old cultures may show a certain amount of pigmentation, brown or black, especially on potato.

Genus Glenospora Berkeley and Curtis, 1876.

Definition.—Aleurismeæ with pale and dark hyphæ. Aleuriospores become dark, and are situate acropleurogenous on light or dark hyphæ, but are small in size, being generally 6 x 4 microns in diameter and rarely 11 x 5 microns.

Type Species.—*Glenospora curtisii* Berkeley and Desmond.

Classification.—Besides the type, *G. ramorum* (Schweinitz, 1822) and the pathological species are known. The latter are:—

G. graphii (Siebenmann, 1889), found in cases of otomycosis and keratomycosis.

G. sacchari Spegazzini, 1896, in the Argentine.

G. microspora Spegazzini, 1891, in Brazil.

G. khartoumensis Chalmers and Archibald, 1916, found in black maduromycosis.

G. semoni Chalmers and Archibald, 1917.

The various species may be recognized as follows:—

Fig. 598.

Fig. 599.

FIG. 598 AND 599.—*Glenospora khartoumensis* CHALMERS AND ARCHIBALD ALEURIOSPORES.

A. Aleuriospores large, usually measuring 10 or more microns in diameter:—
   Parasitic on plants—(1) *Curtisii*, (2) *Ramorum*.

B. Aleuriospores medium, measuring 6-8-9-11 microns—(3) *Sacchari*.
   Parasitic on plants—(4) *Microspora*.

C. Aleuriospores small, usually measuring 5 or less microns in diameter:—
   - I. Parasitic in man, causing otomycosis and keratomycosis—(5) *Graphii*.
   - II. Parasitic in man, causing black maduromycosis:—
     - (*a*) Growth on clear maltose agar twelve days, uncapped tube at 30° C. Central black rounded mass surrounded by an abundant white fringe—(6) *Semoni* (in India).
     - (*b*) Growth in exactly same conditions as in (*a*). Central series of small elevations from which radiate furrows cutting in black plateau. Fringe very slightly marked—(7) *Khartoumensis* (in Africa).

Glenospora graphii Siebenmann, 1889.

Synonyms.—*Graphium penicillioides* Hallier, 1869; *Stemphylium polymorphum* Hallier, 1869; *Verticillium graphii* Siebenmann, 1889; *Glenospora praphii* Vuillemin, 1912.

Definition.—Glenospora with aleuriospores large, 10 or more microns in diameter.

Mycelium at first white, later dark brownish. The filaments are septated, 2 to 3 μ in breadth, ramified. Fertile hyphæ are erected, often dichotomous or trichotomous, with terminal conidia, which are ovoid with a smooth surface, and of a greyish-brownish colour. It is easily grown on the usual laboratory media; gelatine is not liquefied. This fungus has been found in cases of otomycosis by Hassestein, Bezold, Siebenmann, etc., and in a case of keratomycosis by Morax and Pinoy.

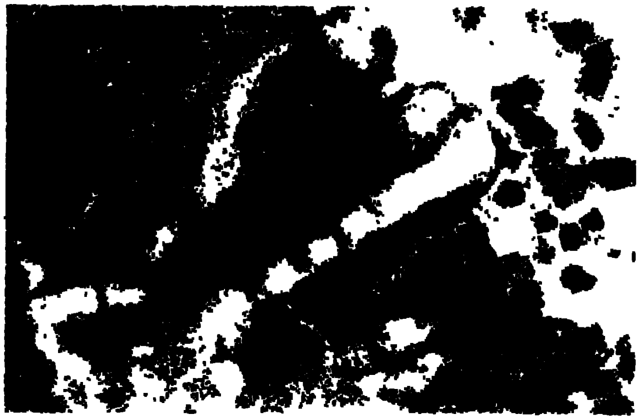
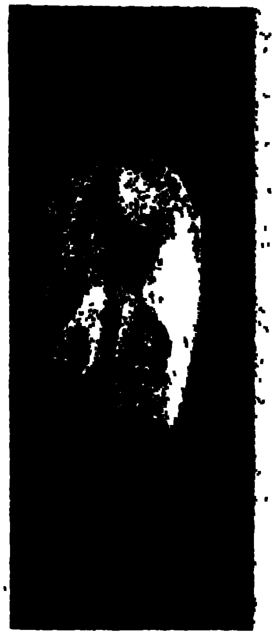


Fig. 600.—*Glenospora khartoumensis* Chalmers and Archibald in Mycetoma Grain.

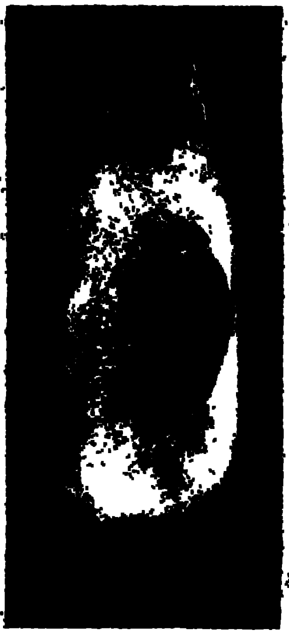


A

Fig. 601.

B

Fig. 602.



A

Fig. 603.

B

Fig. 604.

Fig. 601 and 602.—*Glenospora khartoumensis* Chalmers' and Archibald: Culture on Clear Maltose Agar.

A, Twelve days; B, fourteen days.

Fig. 603 and 604.—*Glenospora semoni* Chalmers and Archibald: Culture on Clear Maltose Agar.

A, Twelve days; B, fourteen days.

Glenospora khartoumensis Chalmers and Archibald, 1916.

Definition.—Glenospora with aleuriospores small, 5 or less microns in diameter; parasitic in man, causing black maduromycosis, and differing from *G. semoni* in cultural characters.

History.—Found by Chalmers and Archibald in a case of black maduromycosis in Khartoum, Anglo-Egyptian Sudan. It occurred in the sole of the foot of a native boy.

Morphology.—All cultures show septate branched hyphæ, varying in diameter from 2·8-1·4 microns, and increasing in very old cultures, when all the hyphæ are dark, to 2·4 microns. At first the hyphæ are pale, but when older they become dark, being of a greenish-black tinge. Thick walled, clear, or dark coloured. Chlamydospores (14 × 11·3 microns) are present, and are especially marked in the black masses on the surface of potato infusions and nutrient gelatine. Aleuriospores are to be found acropleurogenously situated in the surface growth of old potato infusions.

Cultures.—The fungus grows well aerobically in glucose peptone at 30° C., which is the optimum temperature. It also grows well on maltose agar, on glycerine agar, glucose agar, and agar agar. It does not liquefy inspissated blood serum or gelatine. It grows on potato and carrot, but not on cheese or lard. It grew well on litmus milk, but formed neither acid nor clot, though it produced a flaky precipitate. On maltose agar the typical growth was in colour, Ridgway's Standard Colour 'Dusky Drab,' and had a central elevation surrounded by a depression, which separated it from a grooved raised plateau which had a slight fringe.

Habitat.—So far it is only known in man, and all experiments with grains or with cultures failed to infect monkeys, rabbits, or pigeons intraperitoneally, subcutaneously, intramuscularly (with or without a thorn), or into the anterior chamber of the eye. Attempts to find a similar fungus on plants have so far failed.

Pathogenicity.—It causes a variety of *African black maduromycosis.*

Glenospora semoni Chalmers and Archibald, 1917.

Definition.—Glenospora closely resembling *G. khartoumensis*, but differing markedly in cultural characters on maltose agar when grown under exactly similar conditions.

Remarks.—This fungus was isolated by Semon from a case of black maduromycosis occurring in a native Indian soldier serving in France.

It is very like *G. khartoumensis*, but differs markedly in cultural appearances, as may be judged by a comparison of Figs. 601 and 602 with Figs. 603 and 604.

Pathogenicity.—It causes a variety of *Asian black maduromycosis.*

Genus Trichothecium Link, 1824.

Fertile hyphæ are erect, grouped together, each terminating in an oval, pear-shaped, or globular conidium. The only species so far observed in man is *Trichothecium roseum.*

Type.—*Trichothecium roseum* (Persoon, 1801), *emendavit* Link, 1824.

Trichotheclum roseum Persoon, 1801.

Synonyms.—*Trichoderma roseum* Persoon, 1801; *Sporocephalum roseum* Persoon, 1801; *Puccinia rosea* Corda, 1837.

This species vegetates on decaying vegetable matter; the colour is at first white, then pinkish. Each fertile hypha terminates in a pear-shaped conidium, 10 to 20 μ in length and 8 to 12 μ in breadth.

This fungus has been found in cases of otomycosis by Stendener, who did not succeed in cultivating it. Some authorities believe it to be identical to *Glenospora graphii*.

SUBORDER 2 SPOROTRICHINEÆ VUILLEMIN, 1910.

Definition.—Conidiosporales in which reproduction takes place by means of true conidia, but in which true conidiophores are absent.

Type Genus.—*Sporotrichum* Link, 1809, which has a very large number of species scattered over the world, of which 100 are described in Saccardo's 'Sylloge Fungorum,' vol. iv.

Genus Sporotrichum Link, 1809, *emendavit* Saccardo, 1882.

Synonyms.—*Miainomyces* Corda; *Chromelsporium* Corda.

Definition.—Sporotrichales with the characters of the suborder.

Type Species.—Possibly *Sporotrichum obducens* Link, 1809.

Human Species.—There has been considerable discussion as to whether the human species belonged to this or another genus—*e.g.*, Oöspora, Botrytis, Trichosporum, Rhinocladium or Torula—but Smith, de Beurmann, and Gougerot's belief that Sporotrichum is the correct genus has been supported by Matruchot, Vuillemin, and Pinoy, and may be considered as settled as far as our present knowledge goes.

The first species ever associated in any way with man was:—

Sporotrichum inquinatum (Link, 1809), which was found growing on dry human fæces. This was probably a saprophyte. The first ever found in diseased men was *Sporotrichum bronchiale* Montagne, 1844. It was discovered by Gubler in the bronchi of sick persons.

Species Parasitic in Man.—It is customary at the present time to give the following species as parasitic in man, and it may be noted that they do not correspond to any known species living saprophytically or parasitically on plants:—

1. *S. schenki* (Hektoen and Perkins, 1900).
2. *S. beurmanni* (Matruchot and Ramond, 1905).
3. *S. dori* de Beurmann and Gougerot, 1906.
4. *S. indicum* Castellani, 1908.
5. *S. asteroides* Splendore, 1908.
6. *S. gougeroti* Matruchot, 1910.
7. *S. jeanselmi* Brumpt and Langeron, 1910.
8. *S. lesnei* (Vuillemin, 1910).
9. *S. councilmani* Wolbach, Sisson and Meier, 1917.

And one may add:—

10. *S. bronchiale* Montagne, 1844.

There is, however, some difference of opinion with regard to some of these species; thus de Beurmann and Gougerot consider that the fourth and fifth are only varieties of the second.

4. *S. beurmanni* Matruchot and Ramond, 1905, var. *indicum* Castellani, 1908.

5. *S. beurmanni* Matruchot and Ramond, 1905, var. *asteroides* Splendore, 1908.

Considering them all provisionally as separate species, they may be recognized as follows:—

- A. Conidia large (4-11 microns in greatest diameter), with well-developed pedicle and presence of lateral spore clusters:—
  - Mycetomas in Madagascar—*Lesnei*.
  - Conidia large with absence of lateral spore clusters:—
  - Traumatic arthritis in America—*Councilmani*.
- B. Conidia usually small with very short pedicle, which may be absent:—
  - I. With radiating bodies. Conidia very polymorphic, round, oval, or bacilliform, varying from 4-8 microns in greatest diameter—*Asteroides*
  - II. Without radiating bodies:—
    - (*a*) Conidia not numerous. Ferments lactose, not saccharose—*Schenki*.
    - (*b*) Conidia numerous:—
      - 1. Hyphæ 2 or more microns in diameter:—
        - (A) Cultivated:—
          - (i.) Colonies dark from the first—*Gougeroti*.
          - (ii.) Colonies whitish at first:—
            - (1) Colonies finally black. Ferments saccharose, not lactose—*Beurmanni*.
            - (2) Colonies lightish brown—*Dori*.
            - (3) Colonies whitish grey to black. Hyphæ wide, 3 to 4 microns—*Indicum*.
        - (B) Not cultivated. Hyphæ 5 to 7 microns in diameter—*Bronchiale*.
      - 2. Hyphæ less than 2 microns in diameter. Hyphæ 0·5 to 1 micron in diameter—*Jeanselmi*.

Pathogenicity.—They usually give rise to lesions in the skin and deeper tissues, resembling those of tertiary syphilis (gummata, etc.) or tuberculosis, but *S. lesnei* produces a disease like mycetoma.

Treatment.—As a rule the diseases are amenable to iodide of potassium.

Sporotrichum schenki Hektoen and Perkins, 1900.

Synonyms.—*Sporothrix schenki* Hektoen and Perkins, 1900; *Rhinocladium beurmanni* Verdun, 1913.

Discovered by Schenk in a case of gummatous lymphangitis in 1896 in North America. Easily grown on glucose, maltose, and other sugar media. Optimum temperature 30° to 38° C. Growth with an irregular surface, generally of white colour, but old cultures may present some brownish or black pigmentation. Glucose gelatine is slowly liquefied. Mycelial threads as a rule not very straight, rather bent, curved, or undulating; they are about 2 μ in diameter. Conidia present in small numbers, oval, supported by a short sterigmata. Ferments lactose, producing acidity but no gas; has no action on saccharose.

Pathogenicity.—It is the cause of Schenk's sporotrichosis, found in North America. According to de Beurmann, this fungus is very little or non-pathogenic to rats and mice.

Sporotrichum beurmanni Matruchot and Ramond, 1905.

Synonym.—*Rhinocladium beurmanni* Verdun, 1913.

Discovered by de Beurmann in France, and completely investigated by himself and Ramond, Gougerot, Dor, Sicard, Pinoy, etc., in that country; by Adamson in England; by Lutz and Splendore in South America; by Carougeau in Madagascar, etc.

Parasitic Life.—In the tissues oval, yeast-like, or short bacillary forms are seen, 3 to 5 μ in length and 2 to 3 μ in breadth, free or engulfed by phagocytes. Pinoy has described some minute oval forms the shape and size of piroplasmata inside the macrophages. In a case of general infection he has made the important observation that typical fructifications may be seen in the blood capillaries.

Cultures.—The best media are Sabouraud's maltose agar and glucose agar. The growth begins to appear between the fourth and the twelfth day. Optimum temperature 22° C. The growth may be whitish at first, but soon becomes completely black or of a brownish chocolate-like colour. The surface is cerebriform. Glucose gelatine is slowly liquefied. Mycelial threads about 2 μ in diameter, rather straight. Conidia oval, 5 to 6 μ in length and 3 μ in breadth, supported by short sterigmata. In contrast to *Sp. schenki*, the conidia are extremely numerous.

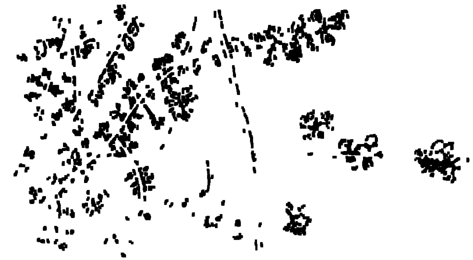


FIG. 605. *Sporotrichum beurmanni* MATRUCHOT AND RAMOND.
(After Gougerot.)

Ferments saccharose, producing acidity, but no gas; has no action on lactose.

Pathogenicity.—Is the cause of by far the greatest number of cases of sporotrichosis in Europe (see p. 2086). Is very pathogenic to rats and mice.

Sporotrichum dori de Beurmann and Gougerot, 1908.

Found by Dor in a case of gummatous sporotrichosis. In contrast to the typical *Sp. beurmanni*, the growth on maltose and glucose agars is slower; the colonies do not coalesce into a large mass, but remain separate and small, not exceeding 1½ millimetres in diameter. The colour is light brownish; never becomes black. Does not grow on gelatine. The mycelial filaments are very thin (0·5 to 1 μ), with short mycelial segments occasionally dichotomous.

The fungus is not pathogenic, or very slightly so, for rats and mice.

Sporotrichum gougeroti Matruchot, 1910.

Synonym.—*Rhinocladium gougeroti* Verdun, 1913.

Differs from the typical *Sp. beurmanni* only in small details, the principal ones of which are the black pigmentation of the colonies from the very beginning, and the extremely abundant sporulation.

Sporotrichum indicum Castellani, 1908.

Found by Castellani in Ceylon. It is doubtful whether it is a separate species, or merely a variety of *Sp. beurmanni*. The mycelial threads are often somewhat larger (2 to 3 μ wide); conidia roundish (3 to 5 μ) or oval (4 to 5 μ long and 3 to 4 μ in breadth). The colonies on maltose and glucose agars may be of various colour —white-greyish, light brownish, dark brownish, black.

Sporotrichum jeanselmei Brumpt and Langeron, 1910.

Was isolated by Jeanselme and P. Chevalier from a case of gummatous sporotrichosis, and was studied botanically by Brumpt and Langeron. It differs from *Sp. beurmanni* by the mycelial filaments being thinner. These are septate, ramified with short lateral branches supporting clusters of spores. The spores are oval or roundish, 2·5 to 3·5 μ.

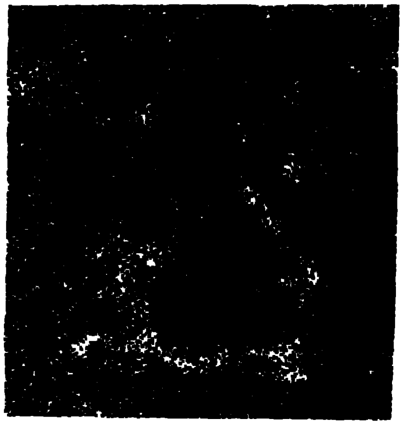


FIG. 606.—*Sporotrichum asteroides* SPLENDORE IN THE TISSUES.
Note radiate body.

FIG. 607.—*Sporotrichum asteroides* SPLENDORE.
Young culture.

(From photographs by Dr. Splendore.)

Sporotrichum asteroides Splendore, 1908.

Synonym.—*Rhinocladium asteroides* Verdun, 1913.

Discovered by Splendore in South America. Is characterized by the presence in the infected tissues of spherical bodies, 4 to 12 μ in diameter, from which some bacillary-like formations radiate. The fungus grows well on maltose and glucose agars, the colonies being first white and later black. Pathogenic to man, rats, and mice.

Sporotrichum lesnei (Vuillemin, 1910).

Synonym.—*Rhinocladium lesnei* Vuillemin, 1910.

Differs from all the other species of *Sporotrichum* by the elongated shape and large dimensions of the conidia, which are 4 to 11 μ in length and 2·5 to 4 μ in breadth. Old cultures are of a dark sooty hue, and black chlamydospores may be present.

Sporotrichum councilmani Wolbach, Sisson and Meier, 1917.

Found by Wolbach, Sisson and Meier in a case of acute arthritis of the knee following injury, in America. This species is characterized by the large size of the spores with absence of lateral spore clusters and by the occurrence in the lesions of septate branching filaments.

SUBORDER 3. SPOROPHORINEÆ VUILLEMIN, 1910.

Definition.—Conidiosporales reproducing by true conidia borne on conidiophores.

Remarks.—A number of families and a large number of genera are included in this suborder, but we are only concerned with four, which may be separated from one another as follows:—

A. Conidiophores unbranched:—
    I. Single hyaline or lightly coloured terminal spore—*Acremonium* Link, 1809.
B. Conidiophores branched:—
    I. Conidiophores erect—*Monosporium* Bonorden, 1851.
    II. Conidiophores decumbent—*Scedosporium* Saccardo, 1911.

Monosporium is only mentioned because *Scedosporium apiospermum* used to be *Monosporium apiospermum*.

Genus Acremonium Link, 1809.

Definition.—Sporophorineæ with creeping sterile hyphæ but little branched, and carrying laterally simple unbranched conidiophores, broad in the middle and gradually reduced towards the distal extremity, terminating in a single hyaline or lightly coloured spore.

Type Species.—*Acremonium alternatum* Link, 1809.

Remarks.—A small number of species are known, which mostly live, saprophytically, on decaying wood, leaves, etc. Two species only are known in man.

Acremonium potroni Vuillemin, 1911.

Found by Potron and Noisette in a case of subcutaneous gummata with fever, somewhat resembling typhoid before the gummata appeared. Easily grown on Sabouraud's agar; colonies white, then pinkish, and, later, orange-yellow. Serum is liquefied. In cultures the mycelial filaments are septated; numerous conidiophores are present of a peculiar elongated type, 15 to 20 µ in length. Conidia ovoid, with a smooth surface, 4 to 5 µ in length and 2 to 2·2 µ in breadth; of *pinkish colour*. This fungus is pathogenic to guinea-pigs.

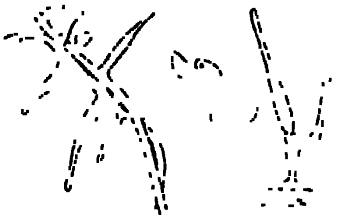


FIG. 608.—*Acremonium potroni* VUILLEMIN.
(After Vuillemin.)

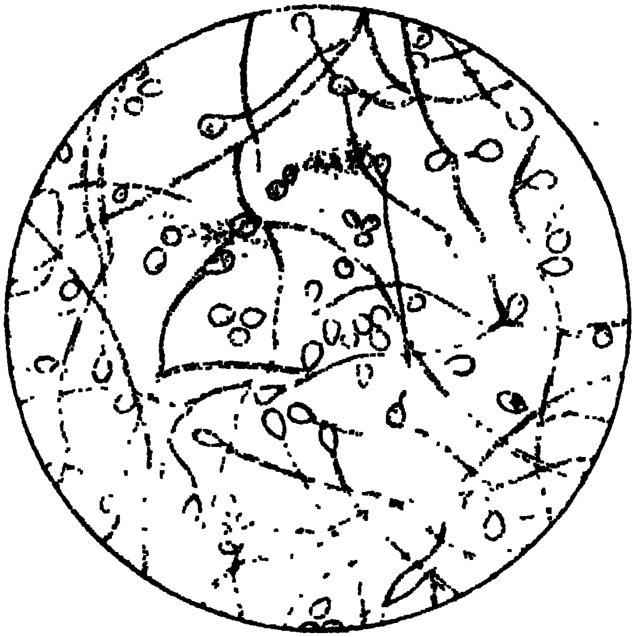


FIG. 609.—*Scedosporium apiospermum* SACCARDO.
(After Radaeli.)

Acremonium niveum Boucher, 1918.

Very similar to *A. potroni*, but colonies are generally white.

Genus Scedosporium Saccardo, 1911.

Definition.—Sporophorineæ with unbranched decumbent conidiophores.

Type Species.—*Scedosporium apiospermum* (Saccardo, 1911).

Remarks.—The other known species are *Scedosporium acremonioides* Harvey, which does not concern us, and *S. sclerotiale*.

Scedosporium apiospermum (Saccardo, 1911).

Definition.—Scedosporium with mycelium at first white and later slightly brown; bundles 3-5 mm. broad in cultures. Mycelial hyphæ creeping, filiform. Conidiophores decumbent, very slightly branched, hyaline, 2·5-3 microns, with one spore oblong, 14 × 5·6-11 × 5·7, rarely subround; at first hyaline, later dilute, dirty rose yellow. Scedosporium, causing white maduromycosis.

Remarks.—Easily grown, the cultures are whitish and covered with duvet; may become brownish when old.

Mycelial tubes septated and of various size; may reach 4 to 5 µ in breadth. Each conidiophore supports a terminal spore, which is either ovoid, 12 to 14 μ in length, and 5 to 6 μ in breadth, or roundish, 6 to 7 μ in diameter. No other kind of fructification is seen.

Pathogenicity.—This fungus has been found in Italy, in cases of mycosis of the foot resembling madura foot, by Tarozzi and Radaeli. Tarozzi considered the fungus to be a *Nocardia*, while Saccardo and Radaeli described it as a new species of the genus *Monosporium*. Saccardo placed it later in the genus Scedosporium. Radaeli made a complete pathological and clinical investigation of the condition.

Scedosporium sclerotiale (Pepere, 1914).

Synonym.—*Monosporium sclerotiale seu nigricans* Pepere, 1914.

Definition.—Scedosporium causing black maduromycosis.

Remarks.—This fungus resembles *S. apiospermum*, with the exception that it produces black pigment. It was ably investigated by Pepere, who grew it on various media, studied it mycologically, studied complement fixation with it, and finally obtained successful inoculations in the anterior chamber of the eye in guinea-pigs.

Pathogenicity.—It was found in a case of black maduromycosis in a peasant, aged thirty-three years, living at Domusnovas, in the province of Cagliari, in Sardinia.

SUBORDER 4. PHIALIDINEÆ VUILLEMIN, 1910.

Definition.—Conidiosporales with conidia borne on phialides.

Remarks.—As already stated, the species of *Aspergillus*, *Sterigmatocystis*, and *Penicillium* in which asci are unknown could be classified, here but we will only consider Scopulariopsis, which is closely related to Penicillium.

Genus Scopulariopsis Bainier, 1907.

Synonym.—*Penicillium pro parte.*

Definition. — Phialidalineæ resembling Penicillium, with unbranched erect conidiophores, bearing phialides, which carry a chain of large ovoid or roundish spores.

Type Species.—*Scopulariopsis brevicaulis* Saccardo, *emendavit* Bainier, 1907.

Remarks.—In addition to those found in man, *S. rubellus* Bainier, 1907, *S. rufulus* Bainier, 1907, *S. repens* Bainier, and *S. communis* Bainier, are known.

Species found in Man.—Two species are found in man, which may be differentiated as follows:—

A. With white creamy formation in old cultures—*Blochi*.

B. Without such formations in old cultures—*Koningii*.

Scopulariopsis blochi Matruchot, 1911.

Synonyms.- *Mastigocladium blochi* Matruchot, 1911; *Scopulariopsis blochi* Vuillemin, 1911.

Found by Bruno Bloch in a case of gummatous lymphangitis, clinically very similar to an ordinary case of sporotrichosis. In cultures the mycelial threads are slender (0·5 to 1·5 μ in breadth), colourless, septated, very little ramified. Conidiophores, 20 to 30 μ in length, are tapering, and from the pointed ends chains of conidia take origin. Conidia elongated, ovoid, 3 to 4 μ in length and 1·5 to 2 μ in breadth. In old cultures white-creamy formations may be seen, which may possibly be undeveloped perithecia.

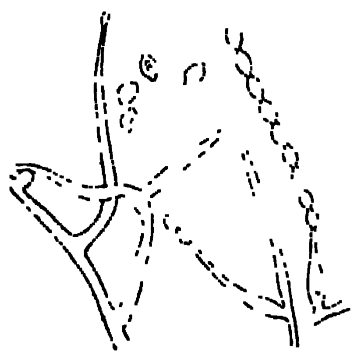


Fig. 610.- *Scopulariopsis blochi* MATRUCHOT. (After Vuillemin.)

Scopulariopsis koningii Oudemans.

Synonyms.—*Monilia koningii* Oudemans; *Scopulariopsis rufulus* Bainier; *S. koningii* Vuillemin, 1912.

A scopulariopsis isolated by Yanin in a case of subcutaneous gummata has been identified by Vuillemin as *S. koningii* Oudemans. The cultural characters are very similar to those of the previous species, but the peculiar white-creamy formations as observed in old cultures of *S. blochi* are not seen. Boucher in cases of gumma-like swellings in Madagascar has isolated a species which he calls *S. ivorensis.*

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PART III

THE DISEASES OF THE TROPICS

SECTION A: FEVERS
SECTION B: GENERAL DISEASES
SECTION C: SYSTEMIC DISEASES

SECTION A

FEVERS

DIVISION I. CAUSATION PROTOZOAL OR PROBABLY PROTOZOAL.

SUBDIVISION A: CARRIED BY MOSQUITOES.

The Malarial Fevers.
The Tropical Hæmoglobinurias.
Yellow Fever.
Dengue and Allied Fevers.

SUBDIVISION B: CARRIED BY SAND FLIES.

Pappataci Fever.

SUBDIVISION C: CARRIED BY TSETSE FLIES, CONE-NOSED BUGS AND UNKNOWN ARTHROPOIDS.

The African Trypanosomiases.
The South American Trypanosomiasis.
The Kala-Azars and Pseudo-Kala-Azars.

SUBDIVISION D: CARRIED BY LICE, TICKS, AND MITES.

The Relapsing Fevers.
Typhus Fever.
The Spotted Fever of the Rocky Mountains.
Tsutsugamushi Fever.

SUBDIVISION E: CARRIED BY MAMMALS.

Rat-Bite and Cat-Bite Fevers.

DIVISION II. CAUSATION BACTERIAL OR PROBABLY BACTERIAL.

The 'Enteroidea' Group of Fevers.
Plague.
Undulant Fever.

DIVISION III. CAUSATION PHYSICAL OR PROBABLY PHYSICAL.

HEAT STROKE AND HEAT SYNCOPE.

DIVISION IV. UNCLASSIFIED, COSMOPOLITAN, AND WAR ZONE FEVERS.

DIVISION V. DIFFERENTIAL DIAGNOSIS.

CHAPTER XL

THE MALARIAL FEVERS

General account—Quartan fevers—Tertian fevers—Subtertian fevers—Pernicious malaria—Chronic malaria—Relapses—Reinfections—Complications—Sequelæ—Diagnosis—Prognosis—Treatment—Prophylaxis—References.

I. GENERAL ACCOUNT.

Definition.—The *malarial fevers* are a group of *specific fevers of protozoal causation*, being due to infections with the parasites *Plasmodium malariæ* (Laveran, 1881), which produces the quartan fevers, *Plasmodium vivax* (Grassi and Feletti, 1890), the agent of the tertian fevers, and *Laverania malariæ* (Laveran, 1890), the exciting cause of the subtertian fevers, which are carried from man to man by the agency of many species of anopheline mosquitoes.

Nomenclature.—The name '*malaria*' is derived from two Italian words, *mal aria*, meaning 'bad air,' and was intended originally to signify that the bad air arising from marshes was the cause of the fevers.

Synonyms.—*English Names:* Ague, paludism, marsh fever, remittent fever, intermittent fever, climatic fever, jungle fever, coast fever.

French Names: Fièvre palustre, paludisme, fièvres paludiennes, fièvres des marais, impaludisme, fièvres malariques, fièvres telluriques.

Italian Names: Paludismo, malaria, febbre intermittente, febbre palustre, febbri malariche, febbri di stagione, febbri d'aria, infezione malarica.

German Names: Wechselfieber, Kaltes Fieber, Intermittens, Sumpffieber, Klimafieber. Marschfieber, Kaltes Fieber.

Local Names.—In all countries local names have been applied to the malarial fevers—for example, Roman fever, Sierra fever, fever of Batavia, Kurunegala fever (Ceylon), Dambul fever (Ceylon), Kamerun fever.

Seasonal Names.—As malarial fevers are more abundant in spring than in winter, and still more so in summer and autumn than in spring, it is natural that seasonal names should be applied to them—*e.g.*, spring fevers, summer to autumn fevers, autumn fevers.

Remarks.—The malarial fevers cover such a wide field of clinical symptoms and pathological phenomena that it is necessary first of all to give a general account, which will comprise such subjects as ætiology, climatology, pathology, chemical pathology, and morbid anatomy, and then to consider the type of fever caused by each of the three parasites mentioned above—viz., the *quartan fevers*, the *tertian fevers*, and the *subtertian fevers*—in their typical and atypical acute phases. Having completed this, we have still to consider the subject of chronic malaria, and we are then in a position to review the complications, sequelæ, diagnosis, and prognosis. Finally, the important matters of treatment and prophylaxis must be discussed.

It may be thought that it would be better to write three separate chapters detailing what is known, considering the three types of fever separately; and though scientifically this would be more accurate, still, clinically it would not benefit, because it is in its atypical forms that malaria is mostly seen by the physician of to-day, and therefore clinically it is better to treat the malarial fevers together and not separately.

It is, however, necessary to preface the account of the disease with a very short note on the history, in order that the reader may understand the salient features of the evolution of knowledge with regard to it.

History.—It is suggested that the references in the 'Charaka-Samhitā' to fevers spread by mosquitoes refer to malaria, and that this fever was recognized at the time of Homer.

In any case, Hippocrates clearly distinguished intermittent from continuous fevers, while among the former he noted the tertian and quartan types, and observed their frequency in summer and autumn and their occurrence near stagnant water and after rains. In 116 B.C. Varro drew attention to the relationship between malaria and marshes, a fact so well realized in the Middle Ages that illustrations are given of mosquito-nets as the only way to live near these collections of water.

We thus see that very early in the history of medicine mosquitoes were associated with fever, which was also associated with stagnant water, and that fevers were divided into the intermittent and the continuous. The introduction of cinchona bark into medicine, as noted in Chapter I., made a distinction as to those fevers which are and those which are not curable by that drug, and this was emphasized by the cure of 'Le Grand Dauphin' in the days of Louis XIV. The medicine used in this celebrated case appears to have been cinchona bark soaked in Rhine wine and presumably strained, and having a small quantity of tincture of opium added thereto.

The pernicious fevers were brought into special prominence by Torti, in 1712, in his celebrated 'Theraputice Specialis Mutinæ.'

As to the actual cause of the disease, it was believed to be minute forms of animal life arising in the exhalations from decaying vegetal matters in marshes. This is the *miasm* theory of malaria, which was fully accepted until modern times, but in 1847 Meckel noticed black pigment (hæmozoin) in the organs of people dying from malaria. There was much discussion as to the origin of this pigment, till, in 1881, Laveran discovered the parasite of malarial fever, and thus laid one of the principal foundations of modern tropical medicine. Golgi in 1886 demonstrated its life-cycle in man, showing the relationship between the attacks of fever and the sporulation of the parasite, as well as the origin of the hæmozoin. Golgi's researches firmly established the parasites of quartan and tertian malaria—*i e.*, *Plasmodium malariæ* and *P. vivax*—while Marchiafava and Bignami in 1891 demonstrated the existence of *Laverania malariæ* and its relationship to subtertian malaria.

During these researches the presence of the peculiar crescent bodies in cases of subtertian infection became known, and caused much speculation; and it was now that King, in 1883, suggested anew that mosquitoes might be the carrier of malaria, a suggestion which we have already noted to be present at the dawn of written medicine. In 1884 Laveran pointed out that Manson's researches on filariasis opened a possibility that malaria might be conveyed in the same way, but these suggestions did not lead to anything, and it was not till Manson, in 1894, emphasized the importance of this possibility that any serious notice was taken of the problem involved. In 1898 Ross, working on Manson's hypothesis, discovered the important fact that the malarial parasite could grow in the stomach of a mosquito, and eventually traced out the whole cycle of the parasite of bird malaria in that insect, and this was subsequently completed as regards the human parasite by Grassi, and confirmed by Marchiafava and Bignami with regard to the infection in man.

Experimental proof of the truth of this carriage was effected by Manson producing typical attacks of malaria, in persons who had never left England, by anopheline mosquitoes infected with the parasites in Italy, and by Low and Sambon living during the malarial season in the Roman Campagna, with no other protection except good anti-mosquito measures, and failing to become infected with the disease.

We therefore have reached this stage of knowing the parasitic cause and its life-cycle in man and the mosquito, but there are some things which we do not know, and these are the reason of the persistence of the infection, in spite of quinine therapy, in some people, while others are without doubt cured, and the reason why the disease appears at times as epidemics. There can be no doubt that the realization of a reservoir for the disease is most important, and there is equally no doubt that this reservoir is man, especially native races, and perhaps more especially the children of native races.

The following additional points appear to us to require further study:—

1. The form in which the malarial parasite lies dormant in the human body (with special reference to the parthenogenesis of the macrogametocyte).

The question of parthenogenesis is still much debated. Neeb has investigated it in *L. malariæ*, and has contrasted it with the schizont stage of the same parasite as follows:—

Character.	*Segmenting Macrogametocyte.*	*Schizont.*
Size	Almost fills the erythrocyte.	Fills about two-thirds of the erythrocyte.
Shape	Oval, not quite centrally situated.	Circular, and centrally situated.
Chromosomes ..	Large, coarse, purplish-brown in red-violet basis, which runs in a band-like curve along periphery.	Small, fine, separate, purple, arranged in a circle around the hæmozoin.
Cytoplasm ..	Resembles that of a typical macrogametocyte.	Resembles that of the trophozoite.
Hæmozoin ..	Coarse yellowish-brown granules excentrically placed.	Fine, dark brown or black granules, usually concentrated into one centrally placed clump.

Thompson believes that Schaudinn probably mistook for parthenogenesis a double infection of a corpuscle with a gametocyte and a schizont.

Ross believes that the ordinary asexual forms persist in the blood in small numbers, and undergoing schizogony, are sufficient to account for the indefinite persistence of the infection. Karrewij has found parthenogenesis to occur in *P. vivax* at the height of the febrile attack.

2. Whether Schaudinn is correct in believing that the eggs of the mosquito can become infected, and, if so, whether that infection is capable of being spread by the next generation of mosquitoes.

With regard to this point the tendency at present is to believe that Schaudinn's observations will not be confirmed.

3. Whether any mosquito other than the Anophelinæ carry the parasites. So far, no evidence in favour of this has been brought forward.

4. Whether there is any animal other than man in which the parasites live in nature.

The investigations of Fermi and Lumbau in 1912 are steps in answering this question negatively, but many more observations in different countries are necessary before a final answer can be given. Mesnil has succeeded in infecting an orang-utan with simple tertian malaria. The attacks of fever in this animal were mild, but for several weeks typical parasites were found.

5. Whether there are any malarial parasites of man which have so far not been recognized.

Thus Stephens has insisted upon *Plasmodium tenue*, which does not appear to us to be specifically distinct, and Oswaldo Cruz has invited attention to a peculiar quartan type of parasite found in the valley of the Amazon and associated with *œdema of the legs* as a pronounced symptom. Laloir's parasite is mentioned in the next chapter, and several other observers have described new varieties of the malarial parasites which require confirmation.

6. Usually it is believed that all fevers regularly recurring every third or fourth day are malarial, but this, while correct as a general rule, is open to doubt in certain instances, and in any case requires careful watch.

Ætiology.—The ætiology may be divided into:—

I. The Exciting Causes.
II. The Predisposing Causes (p. 1142).

I. EXCITING CAUSES.—Malarial fevers are produced by the parasites *Plasmodium malariæ* Laveran, 1881, *P. vivax* Grassi and Feletti, 1890, and *Laverania malariæ* Grassi and Feletti, 1890, because they are always found in the blood or organs of persons suffering from the disease, and can be injected into healthy persons, producing in them typical fevers, the different stages of which correspond to the stages of the life-cycle of the parasite. These parasites can be spread from human being to human being by mosquitoes, in whose bodies they undergo development as already described. Infected mosquitoes can convey the parasites to healthy persons, living in either non-malarial or malarial climates, by their bites, producing attacks of fever typical for the type of parasite with which the mosquito was infected. The classical experiment is the infection of Sir Patrick Manson's son with tertian malaria by means of infected anophelines sent from Rome to London.

There are, therefore, three factors necessary for the production of malarial fever: (1) the blood parasite; (2) the mosquito; (3) man.

1. **The Blood Parasite.**—We have drawn attention to three parasites in connection with malaria, and we believe these to be the only three at present known to cause the fevers, but it is necessary to say that this view is by no means universal. Some authorities believe in a quotidian form of fever due to a species of *Laverania*, or to two separate species of the same genus. These parasites, however, if they exist as distinct species, which we believe to be very doubtful, have not come within our observation, and we therefore agree with those writers who only acknowledge the three types mentioned above.

The descriptions of the structure and life-histories of these parasites have been given in Chapter XXI. (p. 504), and need not be referred to here.

Infection.—The parasites are introduced into the human body as sporozoites, which pass from the salivary glands down the hypopharyngeal canal of the mosquito's proboscis into the blood when a human being is bitten by an infected anopheline.

Incubation.—Once in the blood, three possibilities confront the parasites: they may either be killed and no infection result, or they may remain dormant in some form in the spleen, and not develop until predisposing causes, by lowering the vitality, give them opportunity, or they may at once proceed to develop and give rise to fever.

In this latter event, there is usually an interval between the period of the bite and the attack of fever, for it is evident that in order to influence the metabolism of the body so profoundly as to produce a rise of temperature a certain amount of toxin must be generated. This requires a definite number of parasites, and hence the ***incubation period*** may be short if many parasites are simultaneously inoculated by the mosquitoes, or long if but few. As a rule it may be said that some ***nine to twelve days*** are required for the development of a sufficient number of parasites to produce fever. Acton gives the following table of the length of the incubation period:—

Parasite.	*Maximum in Days.*	*Minimum in Days.*	*Average in Days.*
Quartan	18	11	14
Tertian	21	6	11
Subtertian	14	2	6

During the incubation period, however, there may be slight symptoms of lassitude, or pains in various parts of the body coming on at regular intervals, and often not much regarded, as they may pass off quickly. We are inclined to consider these as being due to parasites as yet not numerous enough to produce fever, and we think these symptoms of importance, as an attack of fever may be prevented by the prompt administration of quinine. This subject will, however, be further discussed under the Pathology of Latent Malaria.

The Fever.—The life-history of the parasite has a definite relationship to the disease, as can be noted by studying the diagrams. The rise of body temperature is always associated with the sporulation of the parasite and the liberation of pyrogenetic toxins, the apyretic interval with the growth and maturation of the parasites in the red corpuscle. This point has been recently carefully studied by Ross and Thomson by their enumerative methods, and they find that there is a distinct correlation between the number of the asexual forms found in the peripheral blood and the fever, and that no fever exists unless these forms exceed some hundreds per cubic centimetre of blood. These forms persist through the apyretic interval before a relapse, but in small numbers, which increase for some days before the relapse takes place. The pigmentation of the cells and organs is due to the hæmozoin liberated by the disruption of the infected red cell. The liberated spores attack new erythrocytes, and so the numbers of the parasites may increase, until in certain pernicious cases it appears as though the majority of the red cells were infected with parasites, and, indeed, two or more may be noted in one cell. Such a condition must, of course, lead to death.

But this does not by any means always happen: for it is well known that a malarial, especially a quartan fever may wear itself out, the attacks becoming less and less severe until they cease.

This would appear to be due to acquired immunity, which no doubt explains the known fact that the European in West Africa on first arrival generally suffers from repeated attacks of fever, but he gradually becomes partially immune, and can then live there, with care, for years. Further, it would certainly explain, in part, the relative immunity of the native races in that region who are infected from earliest childhood, and no doubt this is the true cause of the racial immunity which some allege to exist. It is now known that the merozoites can, although very rarely, penetrate the placenta, and infect the fœtus, giving rise to congenital malaria.

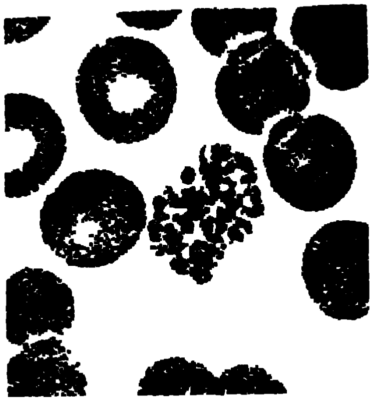

FIG. 611.—*Plasmodium vivax.* (× 1,000 DIAMETERS.)

Schizont or sporulation stage is shown enclosed in a red blood-corpuscle, which will presently rupture and liberate the pyrogenetic toxins, which will cause the fever. At the same time the merozoites and hæmozoin will be liberated.

(From a photomicrograph by Norman.)

The three parasites produce very different results, apparently due to their habitats. Thus *Plasmodium malariæ* and *P. vivax* as a rule live mainly in the circulating blood, in which the former sporulates, while the latter develops in the spleen; their toxins will therefore produce general symptoms. *Laverania malariæ,* on the other hand, seems to affect the red corpuscles so profoundly that they are liable to adhere to the walls of the capillaries of the organs in which the parasite sporulates. Hence this parasite may produce severe local symptoms, due to the mechanical blocking of capillaries or to the more intense local action of the toxin, or to both of these causes, and therefore it is associated with what are called the pernicious fevers—that is to say, the fevers which produce severe effects on one or more organs—*e.g.*, on the brain, causing coma or paralysis; or on the pancreas, causing hæmorrhagic pancreatitis.

At the onset, all three types of fever are apt to be irregular, because the parasites are of different ages, due to the different times of inoculation, but they settle down to a regular type, possibly because the amount of antitoxin generated is able to kill off those parasites which do not conform to the age-period of the majority. Sometimes, however, two distinct broods may exist, producing double fevers, or three distinct broods, causing triple fevers.

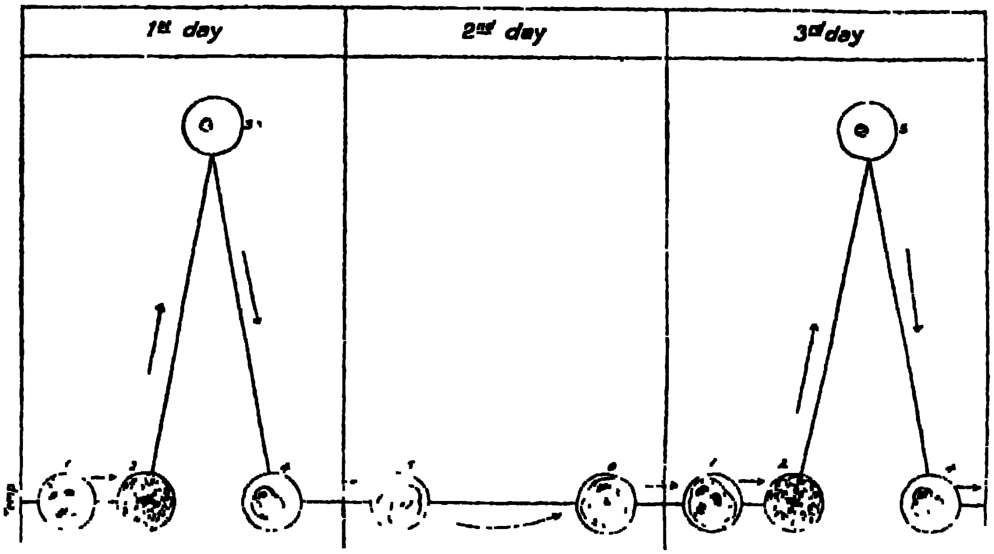

FIG. 612.—DIAGRAM OF A TEMPERATURE CHART IN SIMPLE TERTIAN MALARIAL FEVER.

1, Schizont, with commencing sporulation; 2, sporulating schizont; 3, young trophozoite; 4, 5, trophozoites; 6, schizont.

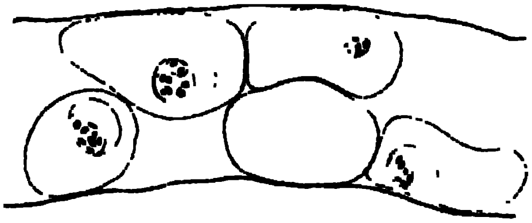

FIG. 613.—*Laverania malariæ.*

Diagram showing parasites in red corpuscles blocking a brain capillary in the cerebral type of pernicious malaria.

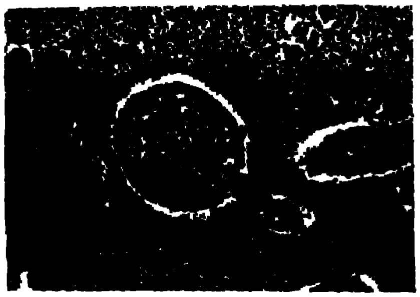

FIG. 614.—*Laverania malariæ.* (× 250 DIAMETERS.)

Photomicrograph showing parasites *in situ* in red blood cells blocking capillaries of the brain.

(After Norman.)

The malarial parasite acts not merely by destroying the corpuscle in which it lives and by altering the metabolism of the body by the pyretic toxin of Rosenau and his collaborators, but it also has a hæmolytic toxin, first described by Casagrandi and De Blasi, which destroys the red corpuscles, thus throwing more work on to the liver and leading to excessive formation of bile, with, as a result, diarrhœa and urobilin in the urine. If the blood-destruction is excessive, the liver is unable to convert the whole of the hæmoglobin liberated into bile, with the result that some may be left unaltered, and may produce hæmoglobinuria.

It appears, however, that an antitoxin is quickly formed, of the nature of an anti-auto-complement, which neutralizes this hæmolysin, and it further appears, from the experiments of Casagrandi on pigeons infected with *Hæmoproteus* (*Halteridium*), that the antitoxin may be a cause of the natural disappearance of the parasites and the cure of the disease. Of course, this antitoxin is produced by the cells of the body, and anything which lessens its formation, such as starvation, gives the parasite a chance to grow and cause disease. Thus Casagrandi found that out of twenty-one birds infected in 1904, ten were still infected in 1905. On semi-starving two of these, he produced relapses, while two others treated with antitoxin obtained from guinea-pigs inoculated with pigeon's blood did not relapse.

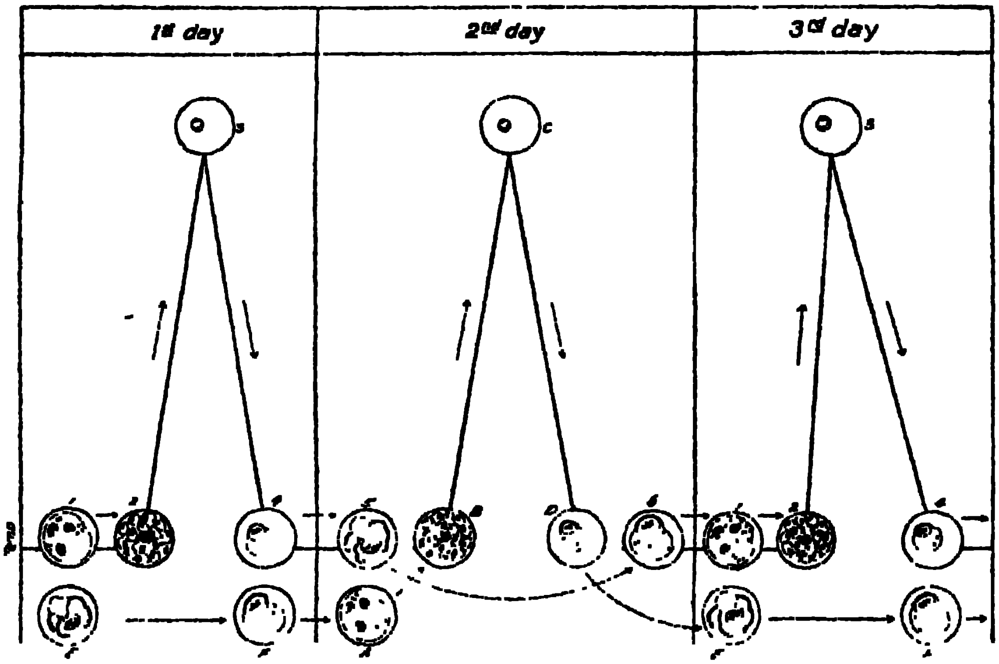

FIG. 615.—DIAGRAM OF A TEMPERATURE CHART IN DOUBLE TERTIAN MALARIAL FEVER.

The fever of the first and third days is due to one brood of parasites, and that of the second day to another brood.

1, Schizont of first brood; 2, sporulating schizont of first brood; 3-5, trophozoites of first brood; 6, schizont of first brood; *A*, schizont of second brood; *B*, sporulating schizont of second brood; *C-E*, trophozoites of second brood; *F*, schizont of second brood.

It will thus be seen that a relapse may be due entirely to predisposing causes which lower the vitality of the body and prevent the production of sufficient quantities of the antitoxin.

Besides the difference pointed out above as to the place of sporulation, there is also a great difference in the time occupied by the cycle of schizogony. *Plasmodium malariæ* requires seventy-two hours to complete its schizogony, or, in other words, it will liberate its toxins and cause an attack of fever in its human victim every seventy-two hours, while in an infection with only one brood of parasites the intervening period will be without fever. This intermission is so marked that it was noted by the ancients, and formed one of their types of intermittent fever, and as the attack of fever occurred on the fourth day, after an interval of seventy-two hours, it was called a 'quartan,' or fourth-day fever, and as such is clearly described by Hippocrates. *Plasmodium vivax* requires forty-eight hours to complete its schizogony, and in single infections produces fever every forty-eight hours—*i.e.*, on the third day—and therefore this type of fever is called 'tertian.'

Laverania malariæ, on the other hand, does not appear to be so regular in the time of its schizogony, and may require from thirty-six to forty-eight hours for the purpose; but though typically producing a tertian fever, the effects due to its sporulation in the organs are much more severe and protracted than those produced by *P. vivax*. Clinically, therefore, there are two types of tertian malarial fever—a benign and a malignant. The former, caused by *P. vivax*, is generally called 'tertian malarial fever,' while the latter, caused by *L. malariæ*, is called 'subtertian malarial fever,' or malignant tertian.

In addition to these clearly defined parasites, others have been described by various authors, and have been named *Hæmamœba præcox* and *H. immaculata* by Grassi and Feletti. The former was said to be pigmented, and the latter to be unpigmented. These parasites require only twenty-four hours for the completion of the cycle of schizogony; consequently they cause fever every twenty-four hours, which is therefore of the nature of a 'quotidian malarial fever.' Many authorities, with whom we agree, consider these parasites to be only stages in the development of *Laverania malariæ*. Quotidian fever can be produced by three broods of *P. malariæ*, or two of *P. vivax* or *L. malariæ*, and does not require a special quotidian parasite. *Plasmodium tenue* Stephens, 1913, appears in part to be related to *P. vivax* and in part to *L. malariæ*, while *P. vivax minutum* of Emin, *P. falciparum quotidianum* of Craig and Oswaldo Cruz's parasite require confirmation.

Therefore, there are only three parasites and three classes of fever to be considered—viz.: (1) *Plasmodium malariæ*, causing quartan malarial fever; (2) *P. vivax*, causing tertian malarial fever; (3) *Laverania malariæ*, causing subtertian malarial fever.

2. **The Mosquito.**—With regard to the Anophelinæ, we know positively that some can carry the germ, while others cannot (see p. 883). Further, it appears quite evident that *Culex* and *Stegomyia* are not carriers of malaria. Daniels, as we have already stated, is inclined to suspect the Ædinæ as being possible disseminators of malaria in jungles, but there is no complete proof of this. Therefore we have at present only the Anophelinæ to consider.

For the various species of the Anophelinæ which are more or less definitely known to carry malaria see Chapter XXXV., p. 883.

The presence of Anophelinæ, however, does not indicate that there must be malaria in the locality, an important point to which Celli was the first to call attention.

England, for example, though it possesses three species of the Anophelinæ—viz., *Anopheles maculipennis* Meigen, 1818; *A. bifurcatus* Linnæus, 1758; and *A. nigripes* St., of which the two former certainly can carry malaria—is practically free from the disease. Nuttall, Cobbett, and Strangeways-Pigg believe that this condition has been arrived at by the reduction of the numbers of the mosquitoes by drainage.

Since the war, however, a certain number of indigenous cases of benign tertian malaria have been reported.

On the other hand, there is no evidence of the existence of malaria without some of the Anophelinæ. On the contrary, there is evidence that where there are no Anophelinæ there is no malaria (Barbados, for example, as first noted by Low). Further, it is highly probable that the endemic malaria of Mauritius and Réunion is due to the introduction of *Pyretophorus costalis* Loew, 1866, as has been pointed out by Ross. There is also the evidence that in places where successful anti-anopheline measures have been carried out, as in Ismailia, malarial fever has ceased to exist.

In order that there may be plenty of these insects, there must be a certain degree of warmth; for as a rule they hibernate in the winter of the temperate zone, coming out in the spring, and increasing in numbers, to reach a maximum in the warm days of autumn. In the tropics, of course, the heat is present all the year round. Heat alone, however, will not suffice for the mosquito, for there must be water for the development of the larvæ and pupæ. Hence, in the dry season in the tropics, there may be few mosquitoes visible, while their numbers will increase remarkably after the rains. In the dry season the mosquitoes and their larvæ æstivate, and wait for more suitable conditions.

There is, however, a third factor to be considered, and that is the effect of the temperature upon the parasite in the mosquito. For ages it has been noted that the fevers due to *P. malariæ* and *P. vivax* occur in the temperate zone in the earlier period of the year—*i.e.*, in the spring—while the worst fevers, due to *L. malariæ*, do not occur until the summer or autumn. This point has been carefully studied by Grassi, Jancsó, Holländer, and others, and the result of their experiments tends to show that temperature has most effect upon the oökinete before it pierces the wall of the stomach of the mosquito and becomes encysted. It would appear that if the temperature is below 15° to 16° C., no further development of the oöcyst will take place in any form of parasite. Further, *P. malariæ* will develop at a lower temperature than the other two, while *P. vivax* will also develop at a low temperature, but *L. malariæ* requires a distinctly higher one.

This may be the reason of the scarcity of *L. malariæ* in the temperate zone, except in the summer and autumn, and its common occurrence in the tropics, and, possibly, this is also the reason of the rarity of *P. malariæ* in the low country of the tropics, while its presence in the hills is common.

Here may also lie the explanation of the universal distribution of *P. vivax* in both the tropics and temperate zone; for Jancsó's researches show that it can develop through a wide range of temperatures.

But these are not the only factors concerning the Anophelinæ and malaria, for Schaudinn showed that the mosquito eggs may possibly be infected by the malarial parasites, and this at once raises the question whether they cannot be carried via eggs, larvæ, and pupæ into a second generation of mosquitoes. If so, this would explain some outbreaks of malaria, but so far Schaudinn's work has not been confirmed.

Another point of importance is the fact that when new lands are opened, it is asserted that people suffer more severely from malaria than can be explained by any theory brought forward at present. For example, it is stated that if a zone of forest on a steep hillside be burnt in the dry season, and then cleared by coolies, who return every night to the quarters where the other estate coolies also sleep, these clearing coolies will suffer severely from malaria, while their fellows working on other portions of the estate will be but little affected. The explanation of this is not that emanations have arisen from the soil and invaded the bodies of the coolies— indeed, after the description of the life-history of the malarial parasite already given, this would be a *reductio ad absurdum*—but merely that the exposure to the sun or the harder work has lowered the vitality of these coolies, and has given the germs already in their system a chance to develop.

It has also long been thought that the mechanical opening of new ground by digging produced the disease, but Ross has pointed out that in Mauritius the digging of earth for years caused no malaria, until some new factor was introduced which occurred in the sixties of last century: this factor we now know to have been the introduction of *Pyretophorus costalis* into the island.

When an attack of malarial fever occurs in a person living in a place where there are no Anophelinæ, it is the result of infection obtained in some other place where these mosquitoes are to be found.

It may safely be concluded that, as far as our present knowledge goes, certain of the Anophelinæ are the only carriers of malaria, and upon this public prophylaxis must be based.

A female mosquito, apparently, can live for at least a month (Ross), if not longer. This does not include such dormant periods of its life as the hibernation in the cold or æstivation in dry seasons, when it may live for a long time in damp places.

The eggs of the Anophelinæ are laid only in natural collections of water supplied with water-plants, such as the back eddies of streams, close under the banks, which are especially good breeding-places. The young imagines, apparently, do not usually travel, but remain near the place where they are developed. Occasionally they can be carried long distances by ships, trains, coaches, carts, etc., but this is the exception, and not the rule. Winds do not appear to carry them far, as they generally take shelter from a high wind. The natural enemies of the Anophelinæ are numerous, including all insectivorous animals, such as bats and birds, together with fish, which eat the larvæ.

The anopheline not merely carries the germ, but because of its length of life, a single individual may be capable of infecting several human beings; for it must be remembered that there is no proof that the mosquito is in any way deleteriously affected by the malarial parasite, and in this way it forms a reservoir of infection.

3. **Man.**—The female anopheline requires blood for the purpose of providing its eggs with sufficient nourishment, and will, therefore, bite any vertebrate it may come across in order to obtain the same.

The malarial parasites have, so far, only been found in man, and hence, until they are found in some other vertebrate, we are not justified in assuming that the anophelines can obtain them from any other source. In the tropics the native population is undoubtedly the great source of the gametocytes by which the infection of the mosquito is brought about, because the majority of them do not protect themselves against mosquito-bites. Of the native population, the children are the greatest source of infection, because, as has already been explained, the adults obtain a partial immunity. But in considering the native as a source of infection, care must be taken not to forget the European, whose blood is sometimes swarming with gametocytes.

Ross has pointed out that, in considering the amount of malaria in a particular locality, imported cases must be distinguished from indigenous cases, and that the latter should be further classified according to the month in which they are infected. He has also attempted, by mathematical formulæ, to investigate the infection-rate of the disease, which method he terms 'pathometry'; but it is very difficult to obtain the necessary data for these calculations. He points out that the number of infections in a given locality during a given period depend upon—

1. The number of persons with gametocytes in the blood.
2. The number of anophelines which have bitten these people and become infected.
3. The number of infected Anophelines which live long enough to transmit the infection—*i.e.*, at least a week.
4. The number of these surviving infected Anophelines which get the chance of biting man again.

It is by no means easy to determine, even approximately, in a district the number of Anophelines capable of carrying malaria; but an attempt might be made to follow Ross, and determine the output from one or two of the more important breeding-places by enclosing a given area with mosquito-netting, and counting daily the numbers of Anophelines which hatch out. A calculation of the areas of the breeding-places, together with the numbers hatching per diem, will give a rough estimate of the increase during that time. Associated with this, a census may be taken of the Anophelines found inside damaged mosquito-curtains very early in the morning. This is a method we have used in Tropical Africa and found of service, for it supplies not merely the number of the Anophelines, but also the percentage which are infected, though of course the error is likely to be considerable. Ross proceeds to show

mathematically that the increase or diminution of the malaria really depends upon the ratio to the population of Anophelines capable of carrying the parasite; and also how an epidemic gradually increases, and how it diminishes when the Anophelines are reduced; and proves that, in order that there may be a reduction of the malaria in man, there need only be a reduction in the numbers, and not an extermination of the Anophelines, which is what would appear to have happened in England, and to be the cause of the disappearance of malaria therein.

Investigation of an Endemic Region.—In investigating malaria in an endemic region, it is necessary to find out—

1. The specific diagnosis of the parasite or parasites causing the malaria.
2. The population of the area.
3. The average number of infected persons.
4. The average number of infected persons carrying the gametocytes in their blood.
5. The species of Anophelinæ in the district, and their breeding-grounds.
6. The species which carry the parasite.
7. The species in which the parasite is found in nature.
8. The number of Anophelines in the affected area.

No remarks need be offered with regard to 1, 2, 4, 5, 6, and 7.

With regard to 8, the method suggested by Ross should be adopted; and as regards 3, the quickest and the best method is to estimate the spleen-rate, but it must be remembered that the spleen is palpable in 1·07 to 2 per cent. of non-malarial children living in London.

Ross suggests that the term 'endemic index,' which was introduced by Stephens and Christophers to denote the percentage of persons carrying parasites in their blood, should be extended to include not merely that factor, but also the proportion of people with spleens enlarged by malaria.

He therefore proposes that the endemic index should be made up of a parasite-rate and a spleen-rate, of which the latter is the more convenient, and if applied to children under fifteen years of age, is useful, provided that kala-azar does not occur in the locality investigated. Children are chosen because the adults have acquired a partial immunity, as already explained.

But the endemic index as defined by Ross is sure to be higher than the mere spleen-rate, and therefore the blood must be examined in the children whose spleens are not enlarged, and the parasite-rate must be added to the spleen-rate to obtain the true endemic index.

In all calculations such as the above the statistical error must be borne in mind, and Poisson's formula, or the modification by Pearson which Ross recommends, must be applied.

Let N=total number of children under fifteen years of age in a locality.
n=number examined for spleen-rate.
x=number with enlarged spleen.
$\frac{x}{n}$ 100=spleen-rate.
e%=percentage of error.

Then by the Poisson-Pearson formula the percentage error will be :—

$$e\% = \frac{200}{n}\sqrt{\frac{2x(n-x)}{n}}\sqrt{1-\frac{n-1}{N-1}}.$$

Latent Malaria.—This term is employed to denote cases in which, without any sign of illness, malarial parasites can be found in the blood in small numbers. These cases form a reservoir of transmission to the anopheline. Craig states that out of 1,267 cases in which malarial parasites were demonstrated in the blood, 21 per cent. were latent, and the majority of these were found to be caused by the subtertian parasite.

Congenital Infection.—The question of congenital malaria has been much debated, but Dumolard and Viallet have recorded a case in which a woman suffering from malaria gave birth to a child, in which blood from the umbilical cord during life and from the heart after death contained malarial parasites identical with those in the maternal blood and placenta. A similar case has been recently reported by Léger.

II. PREDISPOSING CAUSES.—These may be classified into:—

1. Those which promote infection with the parasite.

2. Those which promote the increase of the parasite in man after its inoculation.

1. THOSE WHICH PROMOTE INFECTION WITH THE PARASITE.—The first of these is residence in an area which contains not merely persons with gametocytes in their blood, but also mosquitoes capable of carrying the disease, associated with an atmospheric temperature suitable for the development of the parasite in the mosquito.

The second is any cause which produces large numbers of mosquitoes capable of spreading the disease. This will be not merely a suitable air-temperature, but also moisture. Hence low-lying, marshy places, and the wet season, are important predisposing causes.

The third is occupation, for this may compel people to live in malarial countries, to reside in the low-lying marshy portions of the same, to work in rice fields covered with water, etc. Age is a predisposing factor, as mosquitoes have more opportunity of biting a young child than an adult. Sex has no influence.

2. THOSE WHICH PROMOTE THE INCREASE OF THE PARASITE AFTER ITS INOCULATION.—These predisposing causes are subdivisible into: (*a*) racial; (*b*) personal; (*c*) meteorological.

(*a*) *Racial.*—There is no doubt that the native races suffer less than an immigrant race in a tropical country, where there is always malaria present, and this we believe to be mainly due to the acquired partial immunity of the native races, as already explained.

(*b*) *Personal.*—It will be obvious from the above remarks that the parasite cannot produce the markedly deleterious effects which we term malarial fever, unless there be a sufficiently large number present. Further, there appears to be a tendency on the part of the body to manufacture protective substances, which keep the growth of the parasite in check. Anything, therefore, which interferes with the production of these checking materials will enable the parasite to grow and multiply, and will thus become a predisposing cause of the disease. Such conditions are: (1) chills; (2) starvation or overfeeding; (3) the onset of another acute disease; (4) the presence of some chronic ailment, which may often be but slight.

(c) *Meteorological.*—We have already drawn attention to the relationship between the temperature of the external air and the development of the parasites in the mosquito. It now remains to point out that a similar relationship exists between that condition and the development of the parasite in the human being.

Ross is of the opinion, not merely from observations upon man infected with malaria, but also upon birds infected with *Halteridium*, that high air-temperatures are favourable to the increase of the malarial parasites in man. High air-temperatures are therefore a cause of the relapses met with so frequently in the hot dry season of the tropics.

The reverse is also true; hence the benefit of sanatoria at high altitudes in the tropics, and also of sending a fever-stricken patient to cooler climates, provided the change from the hot to the cold climate be not sudden, but gradual.

Climatology.—The geographical distribution of malaria is determined by a combination of the conditions suitable for the production of large numbers of mosquitoes capable of carrying the germ, and of those suitable for the development of the parasites in the mosquitoes, together with the presence of human beings with numbers of gametocytes in their blood.

The virulence in one region more than in another may depend upon the type of parasite. Thus, *Laverania malariæ*, which is a more virulent parasite than *Plasmodium malariæ* or *P. vivax*, being very common on the West Coast of Africa, renders that area peculiarly dangerous.

Generally speaking, malaria is most prevalent in the region of the Equator, and diminishes gradually north and south till the Arctic and probably Antarctic Circles are reached. The malarial area lies between 63° north latitude (mean summer isotherm of 15° to 16° C.) and 35° south latitude. Its geography may alter considerably in the course of years. Thus regions in England, Holland, France, Germany, and Austria-Hungary are much less malarial than they formerly were. On the other hand, it has been known to affect countries which at one time were immune. Thus Ross says that he believes that Mauritius was infected in the early sixties of last century by the introduction of a mosquito capable of spreading the disease, and hence the epidemic which occurred in that island. Réunion is another example. Barbados is said to have no malaria and no anophelines. Therefore the geography to be described is that known to exist at present.

AFRICA.—The worst malarial region in the world is probably the West Coast of Africa, from Senegal to the Congo, but the whole of Africa, except portions of Cape Colony, is malarial.

ASIA.—Malaria is widespread throughout Asia, being very marked in certain districts of India, especially the swampy land at the foot of the Himalayas, in Ceylon, and Borneo; while Arabia, Syria, the Straits, Siam, and China are also malarial. Little is known about Siberia.

AUSTRALASIA AND POLYNESIA.—Malaria occurs in the north of Western Australia, the Northern Territory, North Queensland, Torres Straits Islands, New Guinea, Finschafen, the Solomon Islands, and the Bismarck Archipelago.

AMERICA.—Malaria exists in Central America, the West Indies, with the exception of Barbados, the coast of the Mexican Gulf, the north of South America, including British Guiana, and the north of Brazil as far as Rio de Janeiro. Paraguay and Bolivia are infected, as are Peru and Chili, but the south part of South America is less infected. Many places in the United States are malarial, but Canada is not markedly infected, except about the northern shore of Lake Ontario, while Greenland is supposed to be free.

EUROPE.—Great Britain and Norway are practically free, but most of the other countries have endemic foci, particularly Russia, Italy, Serbia, Greece, Turkey, and Austria-Hungary.

In France malaria exists in the south and west; in Switzerland in the canton of Tessin; in Germany along the course of the Rhine, and in the lowlands watered by the tributaries of the Danube. Sweden has also some endemic spots.

Apart, however, from mere geographical distribution, it will be obvious that the necessary conditions for malarial propagation are best supplied in the tropics, especially near the Equator, where there is generally a considerable amount of atmospheric moisture and rain as well as heat.

The wet season has also a great influence, supplying the necessary moisture which at other times may be lacking. The effect of altitude has already been mentioned.

Pathology.—In malaria the body is invaded by protozoal parasites, which grow and increase at the expense of the red cells of the blood, and in doing so manufacture toxins, of which we know two—viz., a pyrogenetic toxin and a hæmolysin.

Red blood cells are found in the whole of the circulatory organs, but are generally contained in arteries, veins, and capillaries. In two places, however—viz., the spleen and bone-marrow—they come intimately into relationship with the parenchyma cells. Whatever function the spleen may in future be found to possess as regards the malarial parasites, it probably acts as a purifier to the blood which passes through it. Perhaps the bone-marrow assists in such a function.

Parasites contained in red cells should, therefore, be able to pass all over the body, and should be found equally distributed, no matter what organ is examined. This would be so if the parasite did not seriously damage the red cell, and, by its toxins, the endothelium of the vessels, especially that of the capillaries, in which the blood-flow is slowest. It would appear as though the damage done to the red cell by the quartan parasites is not severe enough to cause them to be caught in the capillaries. Therefore the whole life-history of the quartan is spent in the circulation, and sporulating forms can be readily seen in finger-blood.

Tertian parasites, on the other hand, seriously affect the red cells, causing swelling, degeneration, and decolorization. The trophozoite and schizont stages are easily seen in the peripheral circulation. Still, the sporulating forms are more common in the spleen, which may be looked upon as having filtered them off from the blood which passes through it.

The subtertian parasites act deleteriously on the corpuscles, making them smaller and darker. They rarely appear in the peripheral circulation in the sporulating condition, while they abound in the spleen and internal organs. On examining the organs post mortem, it will be found that the schizont and sporulating forms are found in the capillaries, while the trophozoites are found attached to the walls of the arterioles and venules.

The sporulating parasites give rise to hæmozoin, which escapes from the corpuscle along with the merozoites, and will therefore be most commonly found in those tissues and organs in which sporulation takes place—*e.g.*, spleen, liver, and bone-marrow—and will give them a definite coloration, varying from a reddish-brown to a black, according to the quantity present.

This pigment will, of course, be also met with in the peripheral blood, both free and inside mononuclear leucocytes, for, on escaping from the parasite, the hæmozoin is seized by the mononuclear leucocytes, macrophages, and the endothelial cells of capillaries; therefore, in acute malaria, it will be distributed evenly through the organ affected. The pigment is later conveyed from the blood-vessels into the tissues by the phagocytes, and is found in the connective tissue of the organ close to the bloodvessels. Eventually it disappears, being partially digested by the phagocytes and tissue cells and partially removed by the lymph. This process, however, cannot continue without causing irritation of the connective tissue.

Not merely does pigment escape from the sporulating parasite, but also hæmolysin, which damages the red cells, and causes the appearance of another pigment, yellowish in colour, called 'hæmosiderin.' This is deposited in the parenchyma cells of the organs—*e.g.*, the liver—and may perhaps damage them. The presence of this hæmolysin has been confirmed by the researches of Simpson.

Another toxin—this time pyrogenous—also escapes from the sporulating parasite, and may be the cause of the hyperæmia found in the internal organs—*e.g.*, the spleen and the liver in acute malaria—and may also cause the destruction of the parenchyma cells of those organs. After a series of attacks the blood capillaries and lymph spaces in the liver and spleen remain permanently dilated, and separated by only a slight amount of damaged parenchyma tissue. Later, regeneration of the parenchyma takes place, but the organ will remain permanently altered, even though all pigmentation may have disappeared.

In the case of the subtertian parasite, serious local damage may be caused to the brain, the intestine, the pancreas, or other organs, by the parasites massing in the capillaries and forming, with free pigment and swollen endothelial cells laden with pigment and parasites, regular thrombi, sufficient to impede the circulation, and thus to still further damage the toxin-poisoned organ. Finally, the toxins are excreted by the skin and by the kidney, and in doing so may damage the latter organ.

There are two main conditions, the pathology of which must be explained—viz., acute and chronic malaria. In acute malaria there are the effects produced by each of the three parasites, of which the subtertian is liable to seriously damage important organs.

Chronic malaria should also be described according to the three types, but there is at present lack of material to evolve such a description. Chronic malaria may, however, pass to an advanced condition called 'malarial cachexia,' which shows itself in three ways—as (1) a rare acute cachexia; (2) a more common chronic cachexia; (3) cachexia with amyloidosis.

In addition, there are the pathological features of latent malaria and the relapses.

Before, however, proceeding to describe the actual morbid anatomy of these conditions, a few words must be said upon what we know of the chemical pathology of the disease and on the blood changes which take place.

Chemical Pathology.—The pyretogenous toxin has already been mentioned among the poisons of animal origin, and, though long suspected of being present, its actual occurrence was first proved by Rosenau and his collaborators. Probably it is the poison which acts deleteriously upon the tissues of the organs and causes metabolic changes, but this is only a matter of conjecture.

We know that the heat output in the cold stage of the attack is markedly diminished—a condition met with in many fevers—but the chemistry of the metabolic changes is but little known. During the attack the urine is at first increased in quantity, which is thought to be due to the rise of blood-pressure internally, owing to the contraction of the cutaneous vessels during the cold stage. Notwithstanding this increase in quantity, the specific gravity is raised, because of the increased metabolism caused by the toxins, as is shown by the large increase in solids. The colour is dark, and the acidity of the urine is increased, as in most fevers. Nitrogen is excreted in excess, which is largely due to the increase of urea. Chlorides, sulphates, and bases, especially potassium, are all increased in quantity. Phosphates, however, are diminished during the actual attack, but increased as it is passing off, and are considerably increased in the intermission. Phosphoric acid is therefore retained in the body during the attack.

As would be expected, iron is excreted in increased quantity, probably due to hæmozoin and hæmosiderin, but this increase does not really appear until after the actual attack is over, and then continues for some days.

As before remarked, the urine may contain a considerable quantity of urobilin, and the indigo-blue may be also increased.

Schlesinger's test for urobilin in the urine is performed by adding to the unfiltered urine an equal quantity of a solution of 10 parts of zinc acetate in absolute alcohol, shaking the mixture, and adding a few drops of a solution of lugol, stirring and filtering, when a fluorescence will appear, varying in intensity according to the quantity of urobilin present.

The diazo-reaction is said to be obtainable in about 5·5 per cent. of cases. Serum-albumen may be present after severe attacks, and protcose has been reported, as well as nucleo-proteid.

When the intermission comes, the urine diminishes in quantity, but nitrogen is still excreted at a higher rate than it should be, though less than during the attack.

Chlorides are diminished, phosphates increased; sulphates, though still higher than normal, are less than during the attack, while the excretion of the bases is diminished. The excretion of iron is marked, and the toxicity of the urine is said to be considerable.

During convalescence the most marked features are the polyuria, with low specific gravity, which in subtertian fevers may be so marked as to alarm the patient, while in quartan and tertian it may be so slight as to escape attention. There is also increase of chlorides and potassium salts excreted.

Urriola states that if the urine in malarial ca[illegible] is centrifuged, four types o pigment granules may be found: (1) very fin[illegible]ranules; (2) larger granules in groups; (3) large masses; (4) granules in [illegible]cocytes and hyaline casts It is, however, difficult to exclude extraneous matters.

As regards the fæces, the most noticeable feature is the increase in the excretion of bile and iron, both of which are related to the blood-destruction. Ross and Thomson have shown that the quantity of fæcal urobilin (stercobilin) shows a marked correlationship with the occurrence of the fever, being increased during the attack.

The sweat of a malarial patient is well known to have a peculiar odour, and contains substances very toxic to rabbits.

The above chemical features point to the fact that the toxins of malaria are excreted from the body by the sweat and the urine, and that during the fever there is very active nitrogenous, potassic, chloride, and sulphate metabolism.

That there may be other toxins as yet unknown is obvious from the fact that the *Plasmodia* cause marked shivering and a sensation of coldness, even though the actual blood temperature is rising. It would appear as though this is due to the constriction of the cutaneous vessels by some poison which acts on non-striped muscle, for the arrectores pilorum are also affected, producing goose-skin. *Laverania malariæ*, however, because it sporulates internally, and not in the peripheral blood, causes chills more rarely than the other two.

De Blasi has shown that an antihæmolysin is formed in the human body, and Casagrandi, as already mentioned, has performed experiments on *Halteridium* in birds, tending to show that this substance has a restraining power against increase of the parasites.

The only other remarks we can offer on the chemical pathology are limited to the nature of the pigments, hæmozoin and hæmosiderin.

HÆMOZOIN.—Hæmozoin is the black pigment formed from hæmoglobin by the malarial parasites while living in the erythrocytes, and is afterwards distributed over the body on the disruption of the red cells. It is taken up by phagocytes, as already described, and removed from the bloodvessels to the connective tissue, in which it can be seen in the liver and spleen. It is soluble in alkalis, but not in water, alcohol, chloroform, ether, or acids. It contains iron, but in the form of an organic compound, which will not give the Berlin-blue reaction. Eventually it disappears from the connective-tissue cells, but whether it is eliminated from the body or used in some altered form we do not know. As it is formed by malarial parasites, it is peculiar to the diseases caused by them. Brown considers that it is formed by the action of a proteolytic enzyme from the parasite acting upon the hæmoglobin of the erythrocyte, and that therefore it is formed from hæmatin, a conclusion also arrived at by Carbone and V. Ascoli.

HÆMOSIDERIN.—This is the yellow pigment found in the form of yellow granules in the parenchyma cells of the liver, spleen, kidney, bone-marrow, endothelium of capillaries, and occasionally in leucocytes, after any great destruction of blood cells. In malaria it is undoubtedly due to the action of hæmolysins destroying the red cells. It contains iron in the form of an inorganic compound, and gives the usual Berlin-blue reaction. It is insoluble in alkalis and acids, but is soluble in alcohol.

The Blood.—The parasites live in the blood, in which they produce changes by their own action and by that of their toxins.

The malarial parasites, being true blood parasites and living in the red cells, form the most important feature of the pathology of the blood, but their structure and life-history having already been described in Chapter XVII., it only remains to estimate their numbers.

Ross estimates that a medium-sized person of 68 kilogrammes (150 pounds) body weight possesses 25,000,000,000,000 erythrocytes. In a severe infection he estimated the parasites as numbering 12 per cent. of the corpuscles—*i.e.*, 3,000,000,000,000—and, further, he considers that if they fall below 1 to 100,000 corpuscles—*i.e.*, 250,000,000—they will cause but little disease. Certainly, large numbers of parasites can exist in the body and go through their life-cycle in the spleen without causing symptoms. This condition is called 'latent malaria,' and can be easily converted into active malaria by any cause which depresses the vitality of the body.

ERYTHROCYTES.—In quartan malaria the corpuscle containing the parasite is a little smaller than a normal corpuscle, and, if anything, more darkly coloured. In tertian malaria it is swollen and more lightly coloured, and on treatment with Leishman's stain exhibits fine red granules (Schüffner's dots), which are to be looked upon as a sign of degeneration of the corpuscle. In subtertian malaria the corpuscles when stained in the same way may exhibit Maurer's dots or clefts, which appear as large, irregular red formations, and also Marshall-Plehn's bluish dots, the significance of which is uncertain. The red cells may become transformed into brassy bodies, which are shrunken red corpuscles which have taken on the colour of brass. These are corpuscles which have undergone some form of necrosis, probably due to the hæmolysin, though it has been thought that they were infected corpuscles in which the parasite had died as a result of the necrosis.

FIG. 616.—BLOOD FILM SHOWING SCHIZONT OF *Plasmodium vivax*.

(From a microphotograph by J. J. Bell.)

FIG. 617.—BLOOD FILM SHOWING HEAVY INFECTION WITH *Laverania malariæ*.

(From a microphotograph by J. J. Bell.)

Partial decolorization of the erythrocytes has been recorded in subtertian infections, and is especially well marked in those containing crescent bodies. Bignami thinks that in the subtertian fever the red corpuscles, which are infected with the parasite, have a diminished elasticity, and therefore are not so capable of circulating, and cling to the walls of small capillaries.

As every sporulation causes the destruction of red cells, anæmia is one of the marked features of malaria. This destruction takes place at each paroxysm, and though in quartan and tertian fever it may be slight, in subtertian fever it is apt to be considerable.

After a certain number of attacks of fever the loss becomes much less than in the earlier seizures.

When the fever is intermittent, regeneration takes place quickly, so that before the next paroxysm the normal number of erythrocytes may be nearly reached; but even in quartan and tertian fevers, if long-continued, anæmia will result.

The histological changes in the unaffected corpuscles are pallor and poikilocytosis, with demi-lune and crescentic forms, and in severe cases megaloblasts, with polychromatophilia and basic granular degeneration, together with normoblasts, may be noted. The tonicity of the corpuscles is increased after a number of attacks, according to Viola. In the blood of malarial cachectics the brothers Sergent have described basophile formations having the shape of a figure 8, with a double contour, and Brumpt and others have described basophile rings with a single contour. Laveran considers these appearances to be due to artefacts.

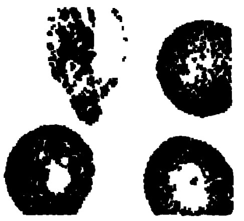

FIG. 618. — BLOOD FILM SHOWING PARTIAL DECOLORIZATION OF AN ERYTHROCYTE BY A CRESCENT BODY OF *Laverania malariæ*. (X 1,000.) (After Norman.)

LEUCOCYTES.—The leucocytes are at first increased during the paroxysm, and then markedly diminished, so that a leucopenia is the characteristic of the simple malarial fevers. The normal ratio of white to red corpuscles is 1 to 500 or 600. From observations of Stephens and Christophers this may be 1 to 90, 1 to 200, 1 to 290, or 1 to 300 during the rigor (*i.e.*, leucocytosis), becoming 1 to 764 (*i.e.*, leucopenia) when the rigor is completed, and when the temperature falls altering to 1 to 968. Billet has shown that if curves are made of the leucocytic count and the temperature in simple tertian and quartan fevers, the two curves follow one another in their rises and falls. In pernicious malaria there may be leucocytosis.

Another important matter is the relative increase of the large mononuclear leucocytes, and this is better marked during the leucopenia of apyrexia than during the leucocytosis of the attack, for Thompson finds that it is usually low during the rigor and the febrile stage, but with the decrease of the fever it may become as high as 90 per cent. of the total leucocytes. This mononucleosis is observed for a long time after an attack of fever, even when quinine therapy is persisted in continuously.

The following are some examples of the differential count according to various observers:—

Kind of Corpuscles.	*Da Costa.*	*Billings.*	*Christophers and Stephens.*	*Bastianelli.*
Polymorphonuclears	67·00	65·04	50·2	39·0
Large mononuclear and transitional	15·94	16·90	31·4	41·9
Lymphocytes	15·33	16·90	18·1	19·1
Eosinophiles	0·83	0·96	0·4	0·0

It must be remembered that this relative increase in the mononuclears has been noted in other protozoan infections.

Phagocytosis is particularly seen in the large mononuclear and transitional leucocytes, and to a less degree in the polymorphonuclear leucocytes and very rarely in the eosinophiles. In these cells clumps of pigment and the residue left after segmentation of a schizont are not uncommonly seen. If, however, something abnormal takes place in the red corpuscle, a phagocyte may engulf it and its parasite, or only the parasites if they have escaped from the red cell, or only the débris of the red cell.

Vacuolization and diminution of the staining power of leucocytes are to be seen. Myelocytes are said by Da Costa to be found in subtertian infection up to 0·51 per cent. Eosinophiles diminish during the paroxysm, and increase during the apyrexia.

HÆMOGLOBIN.—This is, of course, reduced, but the colour index may vary sometimes, being less than normal. Ross and Thomson find that it falls markedly with an attack of fever, but rises rapidly during convalescence.

THE SPECIFIC GRAVITY OF THE BLOOD.—Diminution of the density of the blood begins at the onset of the attack, and becomes more marked as it proceeds, and may amount to a diminution of 6·2 degrees. This fall is probably due to destruction of red cells and the breaking up of large parasites, which more than balances any loss of liquid by vomiting, diarrhœa, sweating, and polyuria.

The diminution is most marked in full-blooded persons, in primary affections, and first attacks, less in later attacks, and least in chronic malaria. The density recovers after treatment by quinine.

CHRONIC MALARIA.—In chronic malaria there is a leucopenia and a marked decrease in the numbers of the red cells, which is but little affected by febrile attacks.

POST-MALARIAL ANÆMIA.—Bignami points out that there are cases in which, in spite of the cessation of the malarial fever, the anæmia tends to progress, and these he calls post-malarial anæmias. They are generally induced by age, malnutrition, overwork, pregnancy, nursing, etc., and are not due merely to the malarial infection. Bignami divides these into four types, according to the characters of the blood.

First Type.—This form of anæmia comes on after attacks of ordinary acute malaria, and is characterized by well-marked diminution in the erythrocytes, the presence of normoblasts, diminution of the colour-index, and leucopenia associated with relative mononuclear increase. In this type the prognosis is good.

Second Type.—The second type is severe, and the prognosis is exceedingly bad. It is characterized by great diminution in the red cells, presence of poikilocytes, megalocytes, normoblasts, and megaloblasts, with leucopenia and relative mononuclear increase.

Third Type.—This is rapidly fatal, and has similar characters to the second type, but is without normoblasts.

Fourth Type.—This type is really grave chronic anæmia, resembling the first type, but being specially characterized by the paucity of the normoblasts and the marked leucopenia.

Wassermann reaction is in our experience generally negative.

Morbid Anatomy.—The morbid anatomy of malaria has been most carefully studied in recent years by Bignami in Italy and Ewing in America. It may be considered under the following headings:—

A. ACUTE MALARIA.

1. Lesions caused by *Plasmodium malariæ.*
2. Lesions caused by *Plasmodium vivax.*
3. Lesions caused by *Laverania malariæ.*

B. CHRONIC MALARIA.

1. Lesions caused by *Plasmodium vivax.*
2. Lesions caused by *Laverania malariæ.*
3. Malarial cachexia.
4. Latent malaria.

A. MORBID ANATOMY OF ACUTE MALARIA—1. LESIONS PRODUCED BY *Plasmodium malariæ.*—*Plasmodium malariæ* goes through the entire process of schizogony in the circulating blood, and hence is evenly distributed all over the body, and therefore does not especially accumulate in any one organ. Marchiafava and Bignami mention that they have made two autopsies, one on a case of acute quartan malaria, in which the patient died of nephritis, and the other in a case of the same fever, in which the patient died of spinal disease.

The visceral lesions are: *Spleen* enlarged, not softened nor very melanotic; *liver* and *bone-marrow* not markedly melanotic; *parasites* in the spleen and in the blood, but not in the brain.

Leishman has mentioned that he has received films from the peripheral blood and spleen of a fatal case, in both of which the parasites were very numerous, but he was not in a position to state whether the patient died of malaria or not. If *P. malariæ* is to produce severe symptoms, it would appear necessary for it to exist in very large numbers.

2. **LESIONS PRODUCED BY *Plasmodium vivax*.**—It is rare for death to ensue as the result of an infection with *P. vivax*. Still, this does occur at times when there is a heavy infection. Ewing has described a case of tertian infection causing coma, hæmoglobinuria, and either causing or associated with catarrhal colitis.

The principal features are the pigmentation of the bone-marrow, liver, and spleen, which last is also enlarged. The blood and spleen show large numbers of *P. vivax*. The kidneys and colon are inflamed, and the endothelial cells of the brain are swollen and contain pigment.

3. LESIONS PRODUCED BY *Laverania malariæ*.—We have already insisted several times upon the fact that *L. malariæ* differs from the other malarial parasites in sporulating in the organs, generally in the spleen, but at times choosing one organ and at other times another. The organ in which it sporulates in large numbers suffers most, and produces symptoms which give the characters of that particular type of malarial fever.

Thus the parasite may attack principally the brain, the intestine, the heart, or the pancreas, producing marked signs of disease therein. Therefore the conditions of the organs vary with the localization of the parasite.

Macroscopical Examination.—In general the body is pale, with a yellowish tinge, which may be noted superficially in white races, but which may only be observed in the subcutaneous tissues in native races. The heart may be small or dilated, the muscle flabby and pale or brownish, and ecchymoses may be present in both the epicardium and endocardium. The lungs may be normal, anæmic, or hyperæmic and congested. Hæmozoin is not easily detected in the lungs, because of the usual pigmentation. As first described by Laveran, a sclerosis of the lungs is not infrequently met with.

The liver is generally enlarged, and varies from a dark brown to a slate colour. It is soft and congested, and the outlines of the lobules are usually indistinct. The gall-bladder is full of dark-coloured bile.

The spleen is enlarged, with a tense capsule, but its consistency is usually much less than normal, and at times it may be almost diffluent in very acute cases. We have, however, seen it quite firm in a recent infection. Its colour varies from a deep brown to black

The stomach and intestines may show but little change, except in the choleraic forms, in which their mucosa may be intensely congested and dark red in colour, except where the Peyer's patches and the solitary glands stand out clearly. The intestine is darker red in certain places, giving it a mottled appearance, and the contents may be blood-stained fluid with flakes of mucus. In fact, the appearance post mortem and the history, if death takes place rapidly, so much resemble those of cholera that in regions where that disease is prevalent mistakes may arise, though, indeed, the dark pigmentation should enable errors to be avoided. We have not infrequently met with dark pigmentation of the small and large bowels in cases of pernicious cerebral malaria, and in general infection without cerebral symptoms. This pigmentation is due to hæmozoin, as can be easily proved by microscopical examination.

The lymphatic glands may be swollen, while the pancreas is usually normal, but it may be very rarely swollen and hæmorrhagic—*i.e.*, in a condition of hæmorrhagic pancreatitis. We have seen it quite brown, and pigmented with capillaries choked with infected corpuscle débris, pigment, etc.

The suprarenal capsules may be congested. The kidneys are more or less normal, but sometimes they are congested, with punctiform hæmorrhages in the pelvis and cloudy swelling in the parenchyma, or brownish. The serous membranes, pleura, and peritoneum, show as a rule nothing remarkable, except, perhaps, a little pigmentation. The bone-marrow is generally hyperæmic and chocolate-brown in colour. The brain may appear normal, but in the cerebral type of pernicious malarial fevers there will be marked changes. In slight cases there may be only œdema without pigmentation or petechiæ. Sometimes there is brownish pigmentation without petechiæ, and with or without œdema. Typically, however, there are:—(1) Hyperæmia of the leptomeninges, which may be œdematous and thickened; (2) brownish, or even blackish, pigmentation of the cortex; and (3) punctiform hæmorrhages in the white matter under the cortex or elsewhere. The spinal cord exhibits changes similar to those in the brain, while the retina shows numerous hæmorrhages.

Microscopical Examination.—After death, parasites may be found in the blood of the heart, spleen, bone-marrow, and at times in the capillaries of the brain, intestines, pancreas, etc.

The parasite, however, is much shrunken, and the typical forms seen during life are not distinct after death. Thus the ring form shrinks and becomes a rounded disc, with the chromatin particle situated at the periphery. The fully developed schizont is more typical, the merozoites being arranged in a ring around the central pigment block. If the post-mortem is made quickly this shrinking is not noted. The mononuclear leucocytes will be noted to have pigment granules, while the polymorphonuclears may show phagocytosis. In films from the internal organs macrophages with parasites and red cells may be seen.

In the heart there may be a few parasites, but very rarely the capillaries will be found filled with red cells containing numerous parasites, and the heart muscle laden with hæmosiderin as has been described in a pernicious cardiac form of malaria, but may also be seen in cases of general infection.

The lungs may contain parasites in all stages of their existence, as well as pigmented macrophages and leucocytes. It is, perhaps doubtful whether there is a true form of malarial pneumonia. Bignami has stated that the pneumococcus is always present, and that a pneumonia in a malarial patient is a double infection.

The capillaries of the liver are much enlarged, with swollen endothelial cells often laden with pigment. These capillaries are filled with blood cells containing parasites and leucocytes with pigment. The perivascular lymph-spaces are swollen, and Kupfer's cells contain pigment. The liver cells are compressed between the dilated capillaries, and contain hæmosiderin and bile-pigment, and, in addition, isolated cells or groups of cells may be necrosed, but this is rarely extensive. The portal canals are infiltrated with red cells containing parasites in all stages of development.

In the spleen the red cells of the pulp are seen to be filled with schizonts and crescents, while pigment is present in leucocytes and macrophages. The kidneys show pigmentation in the walls of the capillaries of the glomeruli, as well as those lying between the tubules; but parasites are rare in the former, though common in the latter situation. Phagocytes are not uncommon, containing pigment, red cells, and parasites. The cells of the glomeruli degenerate, and are thrown off into the capsule along with exudation, and the epithelial cells of the convoluted tubules degenerate, and are cast off into the lumen.

The suprarenal capsule shows irregular areas of vascular dilatation full of erythrocytes, many of which contain parasites, while macrophages may also be present.

The capillaries of the abdominal fat are often full of red cells containing parasites. The bone-marrow is chocolate-coloured in the small bones, and brownish-red in the long bones. Often it is soft and diffluent, and contains sporulating parasites and, in particular, crescents (gametocytes), which are thought to start their life here.

When the intestine shows the choleraic appearances described above, the capillaries of the mucosa and villi are filled with parasites in all stages of schizogony, and leucocytes with pigment masses. The epithelial cells are necrotic, but the submucosa and deeper layers escape injury, and their blood-vessels contain nearly normal cells.

The brain in pernicious cerebral fevers has its capillaries filled with sporulating parasites and mononuclear macrophages containing degenerated parasites, while the arterioles and venules are freer, and only contain young forms. Sometimes no parasites are to be seen, and only pigment in the endothelial cells, which may be swollen and fatty, or may be found free in the vessel, and may have parasitic inclusions. The nerve cells may be affected, showing damage to or disappearance of Nissl's bodies, and at times degeneration of their nuclei, the whole cell being sometimes filled with small granules. There may be fibrolysis—*i.e.*, degeneration of the neurofibrils—only small argentophile granules remaining. Rod-like cells attached to the processes of the ganglion cells may be seen. The punctiform hæmorrhages are due to the diapedesis of apparently normal red cells. Occasionally the cerebro-spinal fluid is increased, and there may be a slight lymphocytosis.

B. Morbid Anatomy of Chronic Malaria.—The lesions of chronic malaria fall principally upon the spleen, the liver, and the bone-marrow. There are no records of post-mortems on persons suffering from chronic malaria due to *Plasmodium malariæ*.

1. Lesions due to *Plasmodium vivax*.—The best recorded case of this infection is that given by Ewing of a man who suffered from the disease for about a year, and died from endocarditis about three months after the last attack.

The spleen was enlarged, firm, and dark, and contained parasites and pigment in endothelial cells about the Malpighian bodies. Some hæmosiderin could also be seen. The liver showed no gross signs indicating malaria, but microscopically, pigment was collected in large intracellular masses in the portal canals and slightly in a few endothelial cells throughout the lobule. Macrophages also contained pigment. The marrow was but slightly pigmented, showing a few endothelial cells with black pigment.

2. Chronic Malaria without Definition of the Parasite.—These lesions are generally due to *Laverania malariæ*, and, as stated above, affect the spleen, liver, and bone-marrow.

The spleen is always enlarged, often considerably, and is firm in consistence, but its colour varies from a slate to a dark red, which depends upon the amount of pigment deposited therein. Usually there are some adhesions, indicating old perisplenitis. On section it generally appears quite black, but this depends upon the amount of pigment; the capsule is thickened; the Malpighian follicles stand out clearly, as they are enlarged and non-pigmented. Microscopically the capillary vessels are seen dilated and separated by splenic pulp, or by connective tissue containing giant cells. The pigment may be diffused through the organ, but is generally either collected around the follicles or extracellular, and contained in the lymphatics of the arterioles or septa, both of which are thickened.

The liver is larger and harder than usual. If pigment is present, it will usually be gathered around the periphery of the lobules, which will, therefore, stand out clearly. Later the pigment becomes perivascular, and finally disappears. The capillaries or lymph-spaces may be considerably dilated, and the liver cells atrophied by pressure. On the other hand, proliferation of the hepatic cells and repair of the damage may be seen taking place. Atrophy of the liver is not usual, but may occur in old people from thrombosis of the portal vein, and is then associated with necrosis.

The bone-marrow is usually pigmented, and of a chocolate hue in the small bones, while in the long bones it may be reddish, except, perhaps, in the very centre. This colour is due to the replacement of the fat by vascular tissue.

3. Malarial Cachexia.—This may be acute when it develops after a few attacks of fever, but more commonly it comes on as a sequela to chronic malaria.

The anæmia is marked, and there is fluid about the ankles and in the abdominal cavity. The spleen is enormously enlarged, as is also the liver, while the bone-marrow is yellow, sclerotic, or gelatinous Parasites may be found or they may be absent.

A special form of cachexia is that in which amyloid changes are found in the kidney along with parenchymatous nephritis, associated more rarely with amyloid changes in the intestine, spleen, and liver, with sometimes simple ulceration of the intestine.

4. Latent Malaria.—*Plasmodium vivax* and *Laverania malariæ* can exist in the spleen of persons who show no sign of fever or malarial cachexia. These parasites can go through their life-cycle in that organ, and in the case of *L. malariæ* in the liver also, but it would appear that they are restrained from invading the circulation by the action of some antitoxin, and therefore do not increase to such numbers as to cause toxic symptoms.

It is obvious from the above that, if the restraining influences which conduce to the condition of latent malaria are removed, an attack of malaria will follow, or if there has been a previous attack, a relapse will take place.

Observers have always had a difficulty in admitting that the ordinary form of the parasite could be latent and cause a relapse, though there appears no doubt that this can take place. Schaudinn, as has already been mentioned, considers that the macrogametocyte is capable of undergoing parthenogenesis and forming merozoites, thus starting a cycle of schizogony anew and causing fever. Craig and other observers insist upon conjugation, causing a rejuvenescence of the parasite and a relapse of the fever.

Classification.—As there are three parasites—*Plasmodium malariæ*, *P. vivax*, and *Laverania malariæ*—there are therefore three clinical entities—quartan malarial fever, tertian malarial fever, and subtertian malarial fever—due to these parasites.

Quartan and tertian parasites go through their whole life-history in the circulating blood, and though the tertian sporulating forms are found in internal organs, such as the spleen, yet they do not tend to accumulate in those organs or to produce special effects. On the other hand, the subtertian parasite sporulates entirely, or almost entirely, in the internal organs; and if one particular organ is especially attacked by the parasites, there will be special clinical features to that phase of the disease. This is the cause of the ***atypical subtertian fevers***, and is also the basis of those serious symptoms which have for many years been alluded to as the perniciousness of this type of fever. The nature of these pernicious symptoms will depend upon whether the parasite is principally localized in—(1) the cerebro-spinal nervous system; (2) the gastro-intestinal mucosa; (3) the pancreas; (4) the heart; (5) the lungs; (6) the liver, etc.

We will give clinical descriptions of the different quartan, tertian, and subtertian fevers.

II. THE QUARTAN FEVERS.

Quartan malarial fever depends for its symptoms and course upon the life-history of *Plasmodium malariæ*, introduced into the blood of man by an anopheline mosquito. Its clinical course will depend entirely upon whether the parasites are of approximately the same age, or whether they have been introduced into the body on different days.

If only parasites of approximately one age exist in the blood, a typical quartan malarial fever ensues, with an interval of seventy-two hours (the length of time which a merozoite takes to become the fully developed schizont). Such a fever is called '*quartana simplex*,' or simple quartan fever.

If the parasites have been introduced on two different days, and are therefore of different ages, the patient will develop fever on two successive days, and be free from it on the third day; such a fever would be called '*quartana duplex*,' or double quartan fever.

If, however, the parasites were introduced on three successive days, the fever may be daily—that is to say, may be a quotidian fever—and this could only be recognized as belonging to the quartan fevers by its parasite being discovered microscopically; such a fever would be called a '*quartana triplex*,' or triple quartan fever.

If the parasites exist in greater numbers and groups than usual, the fever may be irregular and subcontinuous.

There are, therefore, several types of quartan fevers—viz.:—

A. *Acute quartan malaria* :—
   1. Simple quartan fever.
   2. Double quartan fever.
   3. Triple or quotidian quartan fever.
   4. Irregular subcontinuous quartan fevers.
   5. Mixed infections.

B. *Chronic quartan malaria.*

Simple Quartan Fever.

Definition.—*Simple quartan malaria* is characterized by attacks of fever recurring every seventy-two hours and separated by apyrexial intervals which occupy the time required by *Plasmodium malariæ* to pass from the merozoite to the fully developed schizont.

Incubation.—This has not been determined with any degree of certainty. It is without doubt longer than either tertian or subtertian. Celli, by experiment, came to the conclusion that it might be very long—two months or more.

By the experimental inoculation of blood, Marchiafava and Bignami calculated the maximum incubation at 18 days, the minimum at 11 days, and the mean at 14·3 days. We are not aware of any accurate experiment to determine the incubation period after the bite of infected mosquitoes. The only observation which we know is the very doubtful one recorded by Buchanan in 1901, when anopheline mosquitoes of undetermined species were allowed to bite men in India from the 9th to the 21st of January, with the result that one developed a temperature of 38·9° C. on the 5th of February, but parasites were not found, and the other cases were negative.

Remarks.—The clinical description may be divided into the febrile attack and the apyrexial interval.

THE FEBRILE ATTACK.—Generally there are prodromata before an attack of quartan fever. Some few hours previously the patient may complain of giddiness, weakness, malaise, headache, or even nausea and vomiting. If the blood is examined during the occurrence of these symptoms, the parasites will be seen to be schizonts, and the commencing formation of merozoites may also be noted.

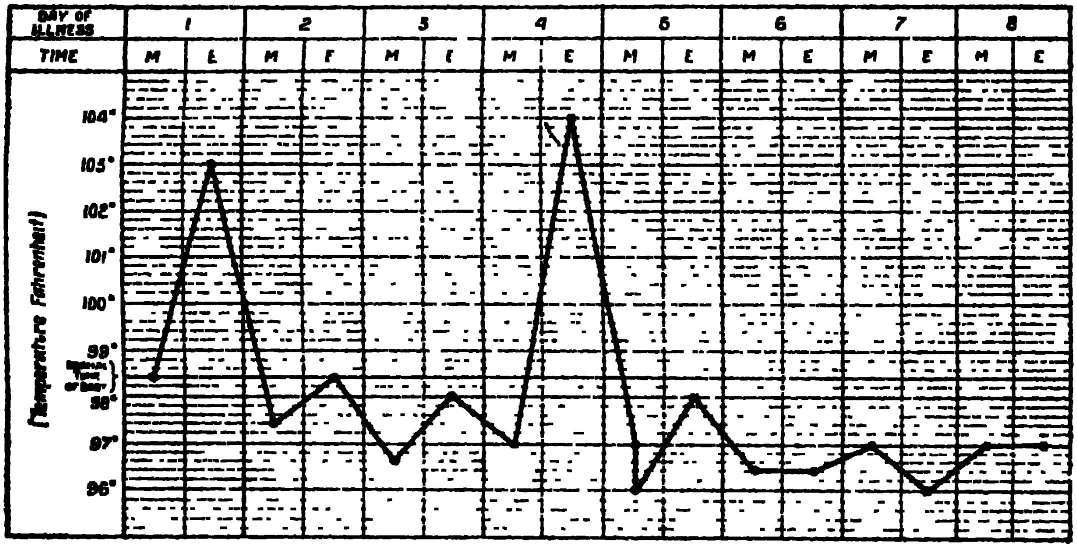

FIG. 619.—TEMPERATURE CHART OF A CASE OF SIMPLE QUARTAN MALARIAL FEVER IN THE GENERAL HOSPITAL, COLOMBO.

In a short time the definite attack begins. It may roughly be divided into three stages: (1) The cold stage; (2) the hot stage; (3) the sweating stage.

1. *The Cold Stage.*—The patient begins to feel cold, either in the legs, arms, or back. This sensation increases until actual shivering sets in. In quartan fever the rigors are well marked and characteristic, and the patient may shiver until he shakes the bed; the teeth may chatter, the lips become blue, the arms and legs cold, and goose-skin may be present. If the blood is examined in this stage, some of the parasites may be seen fully sporulated, or only young parasites may be found.

During this cold stage, which is the most uncomfortable of the three stages, the internal temperature is rising rapidly, and the internal organs must be somewhat congested during the chill; for there are symptoms of intense headache, visual disturbance, vomiting, and at times diarrhœa. The temperature, which rises before the chill begins, varies at first from 100·4° to 102·2° F., but generally rises rapidly to its maximum—about 104° or 105° F.

The cold stage does not last long, fifteen to thirty minutes being the average time, but it may be longer or shorter, and may be irregular, being preceded by a transient sensation of heat.

2. *The Hot Stage.*—Gradually the shivering ceases, and the patient begins to feel warmer and more comfortable, though sensations of cold and heat may succeed one another. By degrees the sensation of heat increases, until the patient becomes burning hot, and as in the cold stage he desired to wrap himself up with coverings, now he desires to throw these off. The skin feels hot and dry, the pulse and respirations increase, the conjunctivæ become injected. Vomiting and diarrhœa may take place, and an erythematous rash sometimes appears. The temperature reaches its maximum, and soon declines.

This stage may last about three to four or more hours.

3. *The Sweating Stage.*—Towards the end of the hot stage the forehead is noticed to be damp, and presently the sweat begins to appear profusely, and great relief is felt by the patient. As the sweating increases, the temperature falls rapidly and the pulse-rate declines. As the temperature approaches normal the patient may fall into a sleep, from which he will wake feeling much better, and with a normal or subnormal temperature. The total duration of the attack may be about eight to ten hours.

THE INTERVAL.—After awaking from his sleep the patient feels quite well, though weak, and generally goes about his ordinary work during the two days of this interval. But signs are not wanting that everything is not well; for the temperature is often subnormal and the pulse slow, while in the blood the developing parasites may be traced, and leucopenia with relative mononuclear increase noted. At the end of seventy-two hours the apyrexial interval will end in an attack of fever, as described above.

The Course of the Fever.—Quartan, rightly or wrongly, is believed to have a great tendency to relapse, to go on for months, and even, it is said, for years, if not treated. The parasites rarely appear to multiply to any great extent in the blood, and hence pernicious symptoms are usually absent. If left to itself, the fever is supposed to gradually die out, but to recur at times. Spontaneous cure is, however, rare.

Irregularities.—Prolongation of the attack has been noticed. Marchiafava and Bignami state that it may very exceptionally last for more than twenty-four hours, in which case the temperature shows two chief undulations—one near the beginning and the other near the end of the attack—separated by a marked remission.

Children.—Children may show neither cold nor sweating stages. Very often convulsions take the place of the cold stage, but these may be so slight as not to be noticed. On the other hand, they may be very severe.

Double Quartan Fever.

In this form there is an attack of fever on two successive days, and an apyrexial interval of twenty-four hours.

Typically the two attacks should be equal in severity, but often that is not so, for one attack is less severe than the other. As already stated, this may be due to two groups of parasites, inoculated on separate days. But sometimes quartana simplex may become quartana duplex, and this is explained by the fact that there may be a double infection, but that while there are many of one brood of parasites, and hence fever, the other brood may be so few at first that they require time to develop to such numbers as are necessary for the production of fever. Consequently quartana duplex may at first show itself by a very slight rise in the temperature on the second day, which increases gradually till equal to that produced by the stronger infection.

Triple Quartan Fever.

This is a quotidian or daily fever produced by three broods of quartan parasites coming to maturity on three successive days, and can only be diagnosed by an examination of the blood. The three attacks may be similar, and may begin at the same hour, or they may vary in severity and begin at different times. In quartana triplex sometimes an attack may be 'subintrant'—that is to say, the cold stage of one attack may begin before the sweating stage of the other attack is finished; but this is not common, and usually there is a distinct interval of normal or subnormal temperature.

A simple or a double quartan may become a triple quartan in the manner described above for the origin of a double from a simple fever. On the other hand, it may start as quartana triplex, and become a duplex, and finally a simplex. This may be due to the weakening of certain groups of parasites. Sometimes a triplex may directly become a simplex from the linking together of two other groups of parasites at the same time.

Irregular Subcontinuous Quartan Fevers.

Quartan parasites are believed not to cause continuous fever, but very rarely they may cause subcontinuous or remittent fever. Such a condition is due to the presence in the blood of parasites of all ages, which, therefore, are continually sporulating and disturbing the metabolism, thereby producing the remittent type of fever.

Mixed Infections.

Mixed infections may occur with either of the other two parasites —viz., *P. vivax* or *L. malariæ*—and an intermittent irregular fever be produced, only to be diagnosed by the microscope.

Chronic Quartan Malaria.

See Chronic Malaria, p. 1182.

III. THE TERTIAN FEVERS.

Tertian malarial fever depends for its symptoms and course upon the life-history of *Plasmodium vivax*, introduced into the blood of man by an anopheline mosquito. Its clinical course will depend entirely upon whether the parasites are of approximately the same age or whether they have been introduced into the body on different days.

If only parasites of approximately one age exist in the blood, a typical simple tertian malarial fever ensues, with an interval of forty-eight hours (the length of time which a merozoite takes to become a fully developed schizont). Such a fever is called 'tertiana simplex,' or simple tertian fever.

If the parasites belong to two distinct broods, or have been introduced on two different days, and are therefore of different ages, the patient will develop fever every day. Such a fever would be quotidian in type, and would be called 'tertiana duplex,' or double tertian fever.

If many broods of parasites are present, the fever becomes subcontinuous and irregular.

There are, therefore, several types of tertian fevers—viz.:—

A. *Acute tertian malaria :—*
   1. Simple tertian fever.
   2. Double or quotidian tertian fever.
   3. Irregular subcontinuous tertian fevers.
   4. Mixed infections.

B. *Chronic tertian malaria.*

Simple Tertian Fever.

Definition.—*Simple tertian malaria* is characterized by attacks of fever recurring every forty-eight hours, and separated by apyrexial intervals which occupy the time required by *Plasmodium vivax* to pass from the merozoite to the fully developed schizont.

Incubation.—The natural incubation period is believed to be from eight days upwards. The period of incubation in experimental cases in which quantities of infected blood were inoculated varied from four to twenty-two days. The period of incubation after the experimental bites of infected anophelines varies from seven to twenty-five days.

Remarks.—The clinical description may be divided into—(1) the attack of fever; (2) the apyrexial interval.

The Attack of Fever.—There may be no prodromata, or, on the other hand, these may be most characteristic. When present, they take the form of pain in the head and the back, and especially in the bones of the limbs—more particularly the joints—which lead to their being considered to be rheumatic, together with a feeling of lassitude and illness. On the day succeeding these sensations the patient may feel quite well, but on the next day they may recur.

If treated in this stage, the fever may never develop, but if neglected, it will appear in the course of a few days.

After a feeling of illness, giddiness, nausea, or vomiting, with perhaps a slight rise of temperature, the patient suddenly becomes very cold and shivers, and his symptoms resemble in detail those already described for quartan malarial fever, except that they may not be so severe. In about ten to thirty minutes the warm stage begins.

As the chills diminish, sensations of warmth appear; at first pleasurable, they soon become intense, and the patient feels burning hot. The skin is hot, flushed, and dry: the conjunctivæ injected; the pulse full, quick, and often dicrotic, and the pains in the head, back, and limbs increase. A slight cough may be noted; vomiting is common, and sometimes diarrhœa occurs. Very often the white skin shows a sallow or slightly yellowish tinge, which is also present in native races, but can only be seen in the conjunctivæ. The heart-sounds are usually normal, but sometimes a soft systolic murmur can be heard. In the lungs, at times, sonorous and sibilant râles occur. The spleen is enlarged and tender, which is characteristic, and a soft murmur over the splenic area, like a uterine souffle, is said to be sometimes heard. Skin eruptions have been described; the commonest in our experience is erythematous or urticarial. Herpes may occur on the lips.

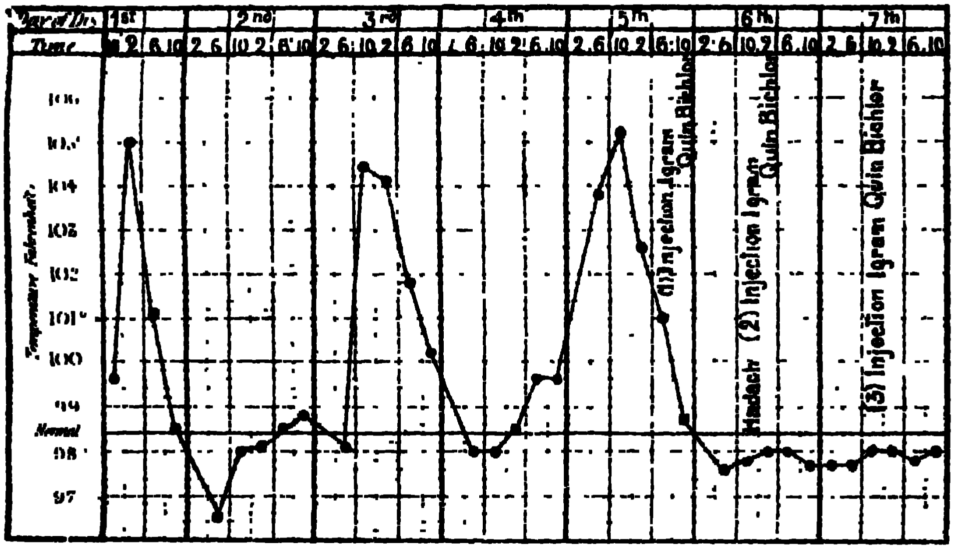

FIG. 620.—TEMPERATURE CHART OF A CASE OF SIMPLE TERTIAN MALARIAL FEVER, SHOWING THE EFFECT OF INTRAMUSCULAR INJECTIONS OF 1 GRAMME OF QUININE BIHYDROCHLORIDE.

The temperature begins to rise before the chill, and continues to ascend during the cold stage, reaching a maximum in the hot stage, which may be anything from 102° to 108° F., but is generally about 104° or 105° F. The warm stage may last four or five hours, when it passes into the sweating stage.

The mouth becomes moist, and sweat gradually comes out all over the body, and soon a most profuse perspiration may take place, and the pulse, respirations, and temperature may fall to normal in about four hours, when the patient, as in quartan fever, goes off into a sleep. The attack lasts about ten to twelve hours, and generally begins in the morning, but may take place at any time of the day.

Apyrexial Interval.—This lasts about thirty-six hours, during which the temperature is often subnormal. In the interval the patient may feel well, but his blood will show developing parasites, reduced erythrocytes, and a leucopenia with a mononuclear increase.

Peculiarities.—As in quartan, so in tertian fever, children may have neither chill nor sweating stage, but may, on the other hand, show convulsions.

Double Tertian Fever.

When parasites mature on two separate days, fever is produced every day, which is therefore quotidian in type, and is called a double tertian (tertiana duplex). The attacks are similar to those described above, but usually are shorter, and, of course, the apyrexial interval is shorter. As a rule, the attacks begin at the same hour each day, but sometimes one attack is later than the other. Very often one attack is not so severe as the other, but if left to itself without treatment, it may become similar to the more severe attack.

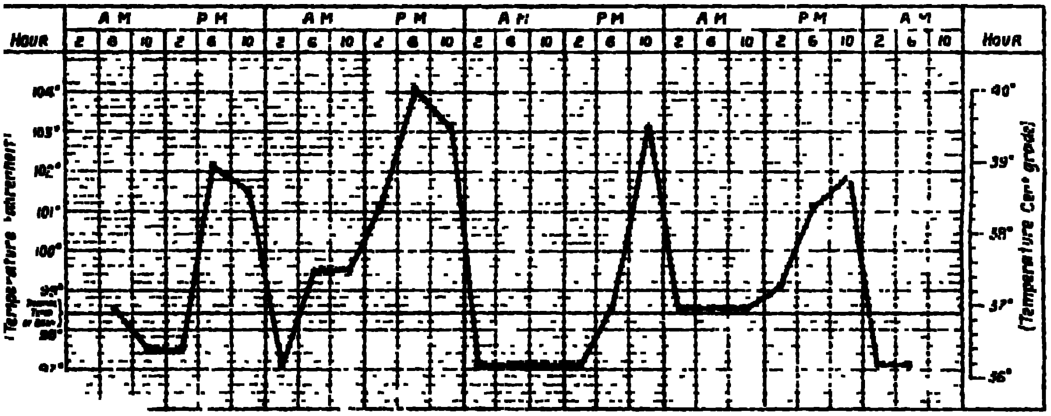

FIG. 621.—CHART OF A CASE OF DOUBLE TERTIAN MALARIAL FEVER IN THE GENERAL HOSPITAL, COLOMBO.

(Note postponement of attack in third and fourth days.)

Double tertians may arise by a simple tertian anticipating. If this is continued after the double tertian is developed, or if one of the attacks of a double tertian anticipates, in course of time it will join in with the originally previous attack, so that a person who is in the sweating stage of one attack may suddenly start the cold stage of the other.

Clinical Course.—Left to itself, tertian malaria tends to a spontaneous cure after a series of attacks, but relapses may occur. Groups of more severe attacks alternate irregularly with groups of milder attacks. Usually, recurring attacks take place about the same time on the succeeding days.

The anæmia of tertian fevers is more easily overcome than that of quartan, and great exhaustion is only seen in old debilitated subjects.

Two interesting points may be noticed—(1) anticipation of the attacks; (2) retardation of the attacks. Anticipation of the attacks means shortening of the apyrexial interval, so that they begin at short intervals. Retardation means prolongation of the apyrexial interval, and is generally due to the action of quinine, but may be due to spontaneous weakening of the parasite.

Irregular Subcontinuous Tertian Fevers.

Irregularity may be brought about by parasites maturing at different times on the same day, and thus producing an almost continuous fever with exacerbations and remissions; but tertian fever is rarely duplicated—that is to say, it rarely shows two distinct attacks in one day. Prolongation of the attack produces a fever resembling the subtertian, while in very chronic tertians just the reverse may take place—viz., prolongation of the apyretic intervals—so that fever appears at the end of seven, eight, fourteen, or sixteen days.

Mixed Infections.

Irregularity may also be produced by mixed infections of *Plasmodium vivax* with *Plasmodium malariæ*, or with *Laverania malariæ*. These mixed infections can only be recognized by the microscopical examination of the blood.

Chronic Tertian Malaria.

See Chronic Malaria, p. 1182.

IV. THE SUBTERTIAN FEVERS.

Synonyms. –*Tropical malaria, Summer-autumnal fever, Malignant tertian.*

Definition.– *Subtertian malarial fevers* depend for their symptoms and course upon the life-history of *Laverania malariæ*, introduced into the blood of man by an anopheline mosquito.

Remarks.–Their clinical symptoms may approximate to the type described for the other two malarial fevers when *Laverania malariæ* lives mainly in the spleen and in the peripheral blood, but more generally the symptoms of these fevers are very different from those produced by the tertian parasites. The essential difference is that *Laverania malariæ* can, and does, live largely in the internal organs, and may even concentrate its forces upon one organ. As clinical symptoms are produced by the derangement of the functions of the organs and systems of the body, so the symptoms of these types of subtertian fever may point to a given organ or to a given system of the body. It is in this way that the subtertian fevers can produce signs and symptoms which medical practitioners are more accustomed to associate with some other disease, and this explains the curious phenomenon of *malarial mimicry*. As the parasite *Laverania malariæ* can live in any organ, it can therefore produce the signs and symptoms of any disease, and we know practically of *no clinical picture* which it is *impossible* for this parasite *to reproduce*, be it an acute illness or a chronic ailment, be it associated with febrile symptoms or free from fever. Hence the great necessity for the practitioner to be careful as to the diagnosis of malaria, and to remember that in atypical cases which are of frequent occurrence it is most difficult, and that the microscope is not infallible in its aid, as *negative microscopical findings do not exclude a diagnosis of malaria*, as will be emphasized in the section on diagnosis.

The subtertian fevers are therefore capable of division from a practical point of view into two great groups:—

A. Typical Subtertian Fevers.
B. Atypical Subtertian Fevers.

In the first group comes *simple subtertian fever*, which shows an intermittency of the symptoms, which is due to the fact that the time required by a merozoite of *Laverania malariæ* to attain to the stage of a schizont is thirty-six to forty-eight hours, while a *double infection* produces a quotidian fever, and *more severe* infections, irregular, remittent, and bilious types of fever. Mixed and chronic infections may also ensue as in the other types.

The fevers of the second group may be subdivided according to the syndrome which is produced, and which depends upon the organ or system of the body which is attacked.

We will now consider these various clinical conditions.

A. TYPICAL SUBTERTIAN FEVERS.

The typical subtertian fevers may be divided into:—

1. Simple subtertian fever.
2. Double subtertian fever.
3. Irregular subtertian fever.
4. Remittent subtertian fever.
5. Bilious subtertian fever.
6. Mixed infections.

1. Simple Subtertian Fever.

Definition.—This form of subtertian fever usually shows intermissions based upon a tertian type.

Incubation.—The incubation period has been studied by Marchiafava and Bignami, who considered it to be of nine to ten days' duration when acquired by natural mosquito infection, and to vary from nine to nineteen days when acquired by experimental mosquito infection. Prodromal symptoms resembling those of tertian fevers may exist before an attack.

Febrile Attack.—The cold stage may be entirely absent, but it often occurs, and is sometimes severe. Sometimes the attack begins with the warm stage, in which the symptoms are very severe pains in the limbs, back, and head, with gastro-intestinal disturbance in the form of vomiting, diarrhœa, and coated tongue. The skin is often flushed and dry and sometimes icteric, while the eyes are injected. The sweating stage is never absent, and may be marked. The spleen is usually tender, as well as the liver. The four-hourly temperature chart is most characteristic, for the invasion takes place with a rapid rise to 104° F. to 105° F., after which the temperature remains high, oscillating about 1° F. The oscillation which immediately precedes the crisis is larger than the others, and is called the pseudo-crisis. After this the temperature rises to its highest point (precritical elevation), and then suddenly falls (crisis) below normal, where it remains, as a rule, until the next attack. It may, however, rise from subnormal to normal, and just prior to the next attack show a distinct depression. This typical temperature may, however, be greatly masked by an absence of the sudden rise at the invasion, or of the precritical elevation, or by an exaggeration of the pseudo-crisis, making the single attack appear double.

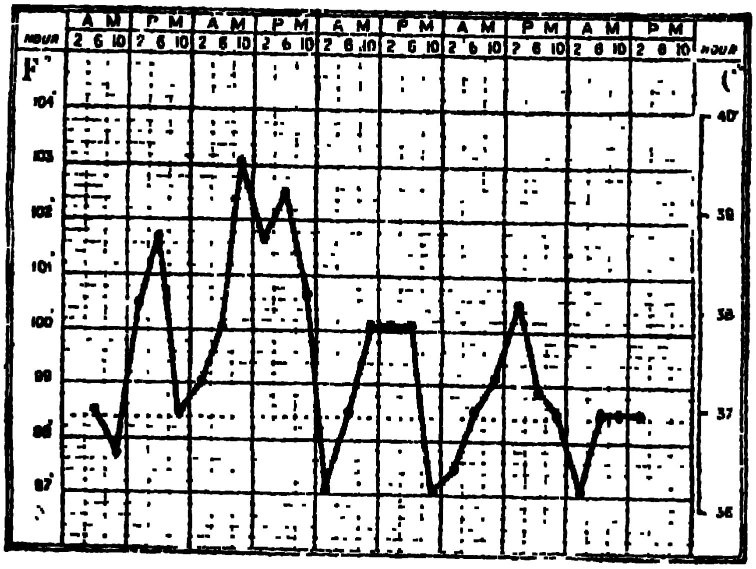

FIG. 622.—CHART OF A CASE OF SUBTERTIAN MALARIAL FEVER.
The curve is most typical on the second day, before quinine was administered.

Lastly, the whole attack may be shorter than usual, and resemble, as regards the temperature, a simple tertian fever.

The duration of the attack in subtertian fever is about twenty-four hours or more.

The Interval.—The interval will be twenty-four, ten, or even eight hours in duration, varying, of course, with the length of the attack.

2. **Double Subtertian Fever.**

This is a quotidian fever, caused by two broods of *Laverania malariæ*. The cold stage is less marked than in a quotidian fever, due to quartan or tertian parasites. The temperature rises rapidly, the fastigium is very short, and the fall is to below normal. There is nothing particular to remark about the warm or sweating stages, which resemble those of the simple subtertian fever. The whole attack only lasts six, eight, or twelve hours.

3. **Irregular Subtertian Fevers.**

When several broods of *Laverania malariæ* exist together in the blood, it is obvious that, instead of sporulation taking place regularly every day or every other day, it will be irregular, and hence the attacks will run into one another and produce an irregular type of fever, which is commonly met with on the West Coast of Africa.

4. **Remittent Subtertian Fevers.**

Remittent fevers arise by prolongation of ordinary attacks, or by anticipation or subintrance, so that two attacks become continuous, the onset of the second attack beginning before the first one is concluded. Duplication may also lead to a remittent fever.

Febrile Attack.—These fevers may be mild or grave, and may become pernicious. The symptomatology is briefly as follows: After one or two days of prodromal lassitude, pains, and sensations of chilliness, etc., fever comes on without any cold stage. The skin becomes hot and dry, and often turns yellowish, and headache, with pains in the different parts of the body, is a source of trouble to the patient.

The tongue is coated; thirst is sometimes intense, and may be associated with vomiting and purging, together with pains in the region of the liver, spleen, and stomach. The toxins affect the brain, causing sleeplessness, restlessness, and delirium. The liver and spleen are both enlarged and tender, and at times there is slight cardiac dilatation on the right side. The temperature is characterized by high fever with remissions.

Interval.—The time of the remission is by no means certain. It may take place in the morning and the rise in the evening. Under treatment the parasites rapidly disappear from the peripheral circulation, but last longer in the viscera, so keeping up the fever.

Course.—Mild attacks get well under the week, but without treatment they would soon become the more serious or grave type of fever, which is part of the atypical group of subtertian fevers which are dealt with in the next section. Three variations may be mentioned here. The first resembles typhoid in its clinical features; the second is distinguished by the bilious vomiting and diarrhœa, with marked enlargement of the liver and jaundice, which is often called bilious remittent fever; and the third shows a tendency to hæmorrhages, local gangrene, hæmoglobinuria, and great weakness, sometimes called 'adynamic remittent fever.'

Remarks.—Only the bilious remittent will be considered here, as *malarial hæmoglobinuria* will be treated in the next chapter on Tropical Hæmoglobinurias, and the atypical subtertian fevers will be described directly after bilious remittent fever.

5. Bilious Remittent Fever.

This is a type of subtertian remittent fever in which there is great blood-destruction, and consequently much bile-production. We have seen it repeatedly in Africa, and more recently in the Balcanic Zone, and it is said to occur in all highly malarious districts.

The attack begins as an ordinary remittent fever, but is associated with jaundice, bilious vomiting, and usually bilious diarrhœa, though in its place there may be constipation. The patient also complains of pain and tenderness in the stomach and liver. After a few days' illness the symptoms may gradually subside, or, with or without hiccough, epistaxis, or hæmatemesis, the temperature may rise considerably, and the patient, becoming comatose, dies.

We have noted at times a curious intermission in the symptoms, of short duration, after which high fever ensues, quickly followed by coma and death (*vide* Yellow Fever-like Type, p. 1172).

6. Mixed Infections.

Mixed infections of *L. malariæ* with the other malarial parasites are not uncommon, and lead to a type of quotidian fever which can only be diagnosed accurately by an examination of the blood and a differentiation of the parasites concerned.

The blood may show only forms belonging to *P. vivax* at times, and only forms belonging to *L. malariæ* at other times.

B. ATYPICAL SUBTERTIAN FEVERS.

The causation of this group of subtertian infections is due to the fact that *Laverania malariæ* undergoes schizogony in the internal organs, and is apt, at times, to specialize upon one particular organ, which becomes seriously affected, not merely because it has to bear the full brunt of the liberated toxins, but also because it suffers from malnutrition, because its capillaries become blocked by swollen endothelial cells belonging to their walls and by red blood-corpuscles filled with malarial parasites, as well as by leucocytes laden with pigment, and by the pigment and merozoites set free during schizogony.

This explains not merely the special character of the symptoms exhibited in any case, but also the multiplicity of clinical types caused by this parasite, and the peculiar conditions called *masked malaria* or *malarial mimicry*.

These various syndromes may for purposes of description be arranged as follows:—

I. Subtertian syndromes without localization.
II. Subtertian syndromes with localization.

I. SUBTERTIAN SYNDROMES WITHOUT LOCALIZATION.

Though it is true that one and the same case may show fever on one day and not on another, still, for practical purposes, it is convenient to subdivide these subtertian syndromes into two groups, according as to whether fever at the time of first examination is or is not a marked feature.

A. NON-LOCALIZED SUBTERTIAN SYNDROMES WITHOUT MARKED FEVER ON FIRST EXAMINATION.

1. Hæmorrhagic non-febrile type.
2. Anæmic type.
3. Mental types.
4. Algide type.
5. Pseudo-alcoholic type.

Hæmorrhagic Non-Febrile Type.—The patients are pale, very weak, and languid, and complain of pains in the loins and limbs. In most cases the whole body is covered with petechiæ, and tense indurated swellings, due to large extravasations of blood, may be present. The gums are often swollen, spongy, and hæmorrhagic. Epistaxis, hæmatemesis, and passage of blood *per rectum* may take place, as well as hæmoptysis and hæmaturia from kidney or bladder. Some patients have large indurated spleens, but febrile symptoms are almost constantly absent. Malarial parasites can be found in the peripheral blood in some cases. Quinine is the infallible remedy.

Anæmic Type.—The patient shows no sign of typical malaria; on the contrary, he is pallid, and possesses the lemon-yellow tinge of *pernicious anæmia.* The liver, and more rarely the spleen, is enlarged. Usually there is no fever, but in some cases the temperature may rise to 99° or 100° F., which is common in *pernicious anæmia.* Malarial parasites may not be found in the blood, even after repeated examinations, while the usual signs of *pernicious anæmia—e.g.*, poikilocytosis, nucleated red blood-corpuscles, high colour index, relative *increase of small mononucleurs* in place of the increase of the large mononuclears which one expects to see in malaria, may be present.

This type of anæmia may lead the physician to suspect *malignant growth* in elderly patients, especially if there is vomiting and pain after taking food.

Quinine acts as the diagnostic and therapeutic agent.

Leukæmia.—Certain authors believe that malaria can cause leukæmia, but this appears to us to be more of the nature of a complication.

Mental Types.—The patient is melancholic or apparently demented, or more rarely acutely maniacal and violent, with usually a normal, subnormal, or but slightly raised temperature. The spleen may or may not be enlarged, but a careful examination of the blood generally reveals a mononucleosis or at times a very few malarial parasites, while quinine therapy effects a disappearance of the symptoms.

The violent cases may be of interest from a medico-legal point of view, because the patient never has the slightest recollection of his acts, and cannot be held responsible for them.

Algide Type.—The patient is, as a rule, first seen in a condition of such extreme collapse as to make the practitioner suspicious of cholera. The nose is sharp, the cheeks sunken, the lips and extremities cyanotic, the nails livid, the pulse small, soft, and frequent, becoming thready and imperceptible, the skin cold and clammy, and the respiration laboured. The patient may, however, be conscious, and be able to answer questions and to complain in a weak voice of severe thirst. This is a very serious and fatal form of pernicious malaria, and generally kills the victim in a few hours.

Pseudo-Alcoholic Type.—The patient may not have been very well for a few days, being capable of doing his work, but irritable and complaining of not feeling fit. In order to carry on his duties he may or may not take a certain amount of alcohol. Suddenly, during or after a dinner or at a public performance, he tumbles off his chair, and the impression at first is that he has taken too much alcohol, and this may be considered to be confirmed by the odour of his breath. It will, however, soon be evident that the patient is seriously ill, and the diagnosis will be revised and apoplexy probably instituted. Finally a blood examination will generally reveal a number, and sometimes a large number, of malarial parasites of the subtertian type. At a post-mortem these parasites will be seen to be blocking the capillaries of the cerebral cortex.

The poorer type of native patient will be taken as a 'drunk' to the local lock-up, and in the morning the so-called drunken man will be found to be seriously ill and may even be dying. Blood examination generally, but not always, reveals malarial parasites. Generally these are serious infections, and the prognosis is grave.

B. Non-Localized Subtertian Syndromes with Marked Fever on First Examination.

The non-localized subtertian syndromes with marked fever on first examination may be divided into—

✓ 1. Subtertian hyperpyrexial fever.
2. Subtertian syndromes resembling a specific fever.
3. Subtertian syndromes not resembling a specific fever.

Subtertian Hyperpyrexial Fever.

This type of fever is characterized by very high temperatures, often commencing at the onset of the illness. It may be continuous or intermittent, and often attains temperatures exceeding 105° F. Sometimes the temperature may reach heights which can hardly be believed—*e.g.*, in two of our cases the temperature exceeded 108° F. These cases have a very serious prognosis, but recoveries are not unknown.

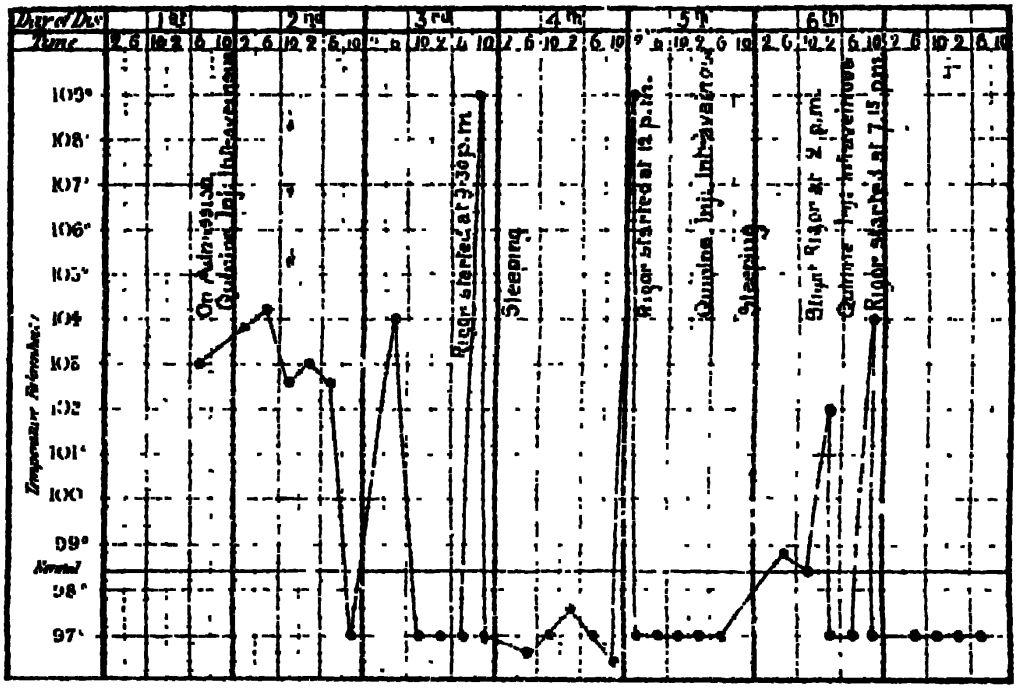

FIG. 62:—TEMPERATURE CHART OF A CASE OF HYPERPYREXIAL SUBTERTIAN MALARIA.

Syndromes resembling a Specific Fever.

The syndromes resembling a specific fever may be divided into types as follows:-

1. Typhoid-like type.
2. Malta-fever-like type.
3. Typhus-like type.
4. Cerebro spinal like type.
5. Yellow-fever-like type.
6. Weil's-disease-like type.
7. Scarlet-fever-like type.

Typhoid-like Type.—This fever resembles enteric fever, as may be judged by the temperature chart (Fig. 624). The onset is slow, the patient apathetic, the tongue coated, and headache present, while the temperature is continuous or subcontinuous. The abdomen is slightly tumid, the spleen usually palpable, but not large or hard. The blood usually shows subtertian parasites, and the bacteriological examination for 'enterica' is negative, but quinine here has but slight action on the course of the fever for some time. The complication of typhoid infections in the course of malaria is mentioned on p. 1184.

Malta-Fever-like Type.—This is very rare, and resembles Malta fever, but malarial parasites can be easily found in the blood; while bacteriological tests for *Micrococcus melitensis* and its allies are absent. Finally quinine effects a cure.

Typhus-like Type.—The cases exactly resemble typhus fever, but malarial parasites are often present in the blood, and the disease yields to quinine therapy.

Cerebro-Spinal-like Type.—The symptoms are those of epidemic cerebro-spinal meningitis, but the cerebro-spinal fluid is clear, though its pressure may be increased; its cellular contents are normal in number and character, while meningococci are absent and the blood shows malarial parasites. The spleen may or may not be enlarged.

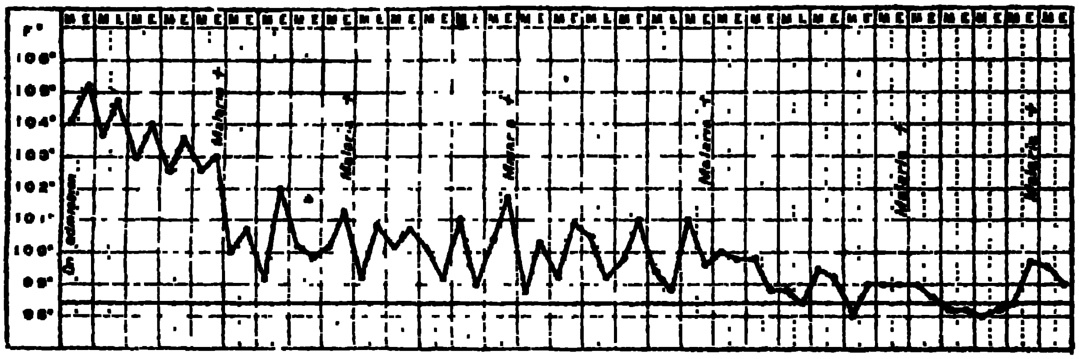

FIG. 624.—ATYPICAL SUBTERTIAN MALARIA SIMULATING TYPHOID FEVER. Hæmocultures and serological reactions for germs of the Enteroidea group of fevers were negative.

Sleeping-Sickness-like Type.—This, which is rare, is characterized by low fever, slight trembling of the hands and tongue, and progressive general weakness, drowsiness, and occasional convulsions. The lymph glands in the neck are not enlarged, and the cases may occur in regions where sleeping sickness is unknown. Malarial parasites may be hard to find, but quinine in large doses cures the affection.

Yellow-Fever-like Type.—This is characterized by fever, without rigors, severe headache, flushed face, pains in the body, pulse quick, full, and bounding at first, severe vomiting, tenderness in the epigastric region, and slight albuminuria. On the third day the temperature falls from 103° to 100° F., and the symptoms abate, while the patient feels better; but the temperature rises again, jaundice appears, the pulse slows to about 60-70 per minute, dark brown vomit appears containing red blood-corpuscles. The symptoms may get worse, the jaundice may deepen, and death ensue. Subtertian parasites may be present in abundance in the blood, and quinine may be ineffective unless given in massive doses.

Weil's-Disease-like Type.—Cases like Weil's disease, with cutaneous hæmorrhages, are occasionally malarial, and may end fatally. The mild type of camp jaundice may also be simulated by malaria, but this is rare.

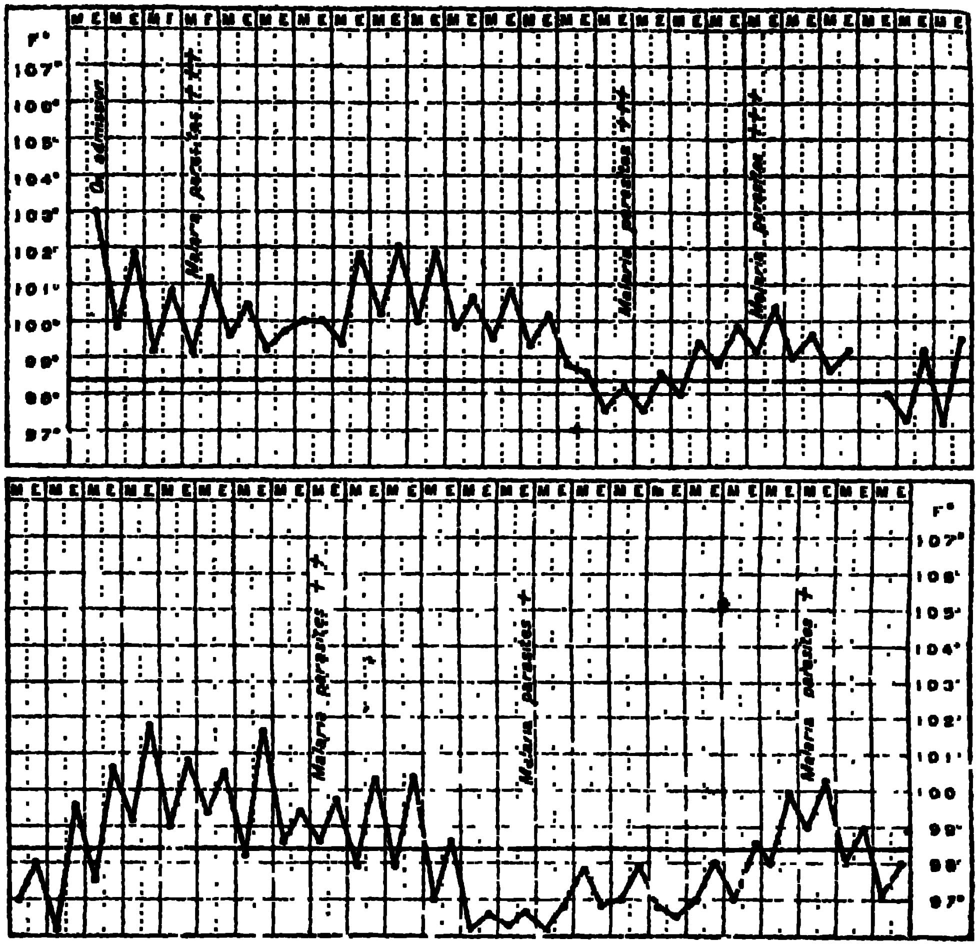

FIG. 625.—ATYPICAL MALARIA SIMULATING MALTA FEVER.
Hæmocultures and serological reactions for *Micrococcus melitensis* and *M. paramelitensis* were negative.

Scarlet-Fever-like Type.—Scarlatiniform pernicious fever is characterized by a diffuse scarlatiniform rash all over the body, with desquamation of the horny layer and erythema of the fauces, and may lead to a typhoidal state in which the patient dies.

Syndromes not resembling Specific Fevers.

The subtertian syndromes not resembling specific fevers are:—

1. Hæmorrhagic febrile type. √
2. Hydrophobia-like type.
3. Kussmaul coma-like type.
4. Diaphoretic-like type.
5. Comatose type.
6. Delirious type.
7. Tetanus-like type.
8. Convulsive type.

Hæmorrhagic Febrile Type.—This form of pernicious fever is apparently rare. It is characterized by hæmorrhages from the skin and mucosæ of the nose, bronchi, intestines, stomach, and generative organs, during the attack, but not during the intermission.

This condition rapidly produces acute grave anæmia, with thready pulse, coma, delirium, convulsions, and death, or may become the milder type, in which fever is not a marked symptom (*vide* p. 1169).

Hydrophobia-like Type.—Signs of hydrophobia associated with fever, a large spleen, and malarial parasites in the blood, call for energetic quinine treatment, when the symptoms disappear, unless it is true hydrophobia in a malarial patient.

Kussmaul Coma-like Type.—Signs of Kussmaul's coma coming and going every alternate day and associated with fever in a diabetic patient call for quinine therapy, even if the spleen is not enlarged, the blood free from malarial parasites and mononucleosis. Occasionally after the exhibition of a small dose of quinine, parasites may be found in the blood.

Diaphoretic Type.—In this type the sweating of the third stage of an attack is so exceedingly copious that not merely is the bed saturated, but a pool may even form on the floor. Such excessive excretion of sweat is dangerous, as the patient becomes more and more exhausted as it goes on, and a most dangerous collapse may ensue.

Comatose Type.—This may begin suddenly or slowly. If the latter, there may be weakness, sleepiness, headache, disturbance of vision, stupor, or delirium, which ends in coma. But more often the patient is brought to the hospital quite comatose. He lies flat upon his back, with usually no paralysis and no alteration in the reflexes. The pupils may be contracted and give the idea of opium-poisoning, while the patient cannot be roused to answer questions, but will only frown or groan.

Hæmorrhages may be found on the skin and in the retina. The urine, which may have casts and a little albumen, is usually passed involuntarily, as are the motions. The heart is dilated, and the pulse, at first slow, soon becomes quick, and towards the fatal termination very quick and thready. Respiration may be quiet or noisy. If death is to take place, the patient becomes colder and colder, the tongue dry and thick, and respiration ceases.

If he is about to recover, the coma will gradually pass away; he will be able to answer questions when roused, and after a time gradually recovers consciousness. The speech is at times most peculiar, being scanning in character.

The coma may be present one day, but the next day the patient may be slightly better, with a subnormal temperature and a slower, fuller pulse; towards evening, however, the temperature rises, and the coma returns. This second attack is, as a rule, fatal. The fever may be remittent or intermittent. In the latter case it returns before death. Quinine treatment by injection and otherwise appears to be of no avail at times, and after two or three days of coma, even when the parasites have disappeared from the peripheral blood, the person may die.

Delirious Type.—In this form delirium is the most marked feature, and in a short time is followed by exhaustion, coma, and death. Such cases are apt to come on suddenly, and to be mistaken for drunkenness, sunstroke, or mania. The fever is usually very high. Recovery is supposed to occur, but we have never seen these cases end otherwise than fatally.

Tetanic Type.—Patients delirious from malaria may show trismus, contraction of the limbs, opisthotonos, retraction of the abdomen, and conjugate deviation of the eyes. The contractions of the muscles may relax and increase as in tetanus, and there may be priapism. The attack may resolve, or end in death with high temperature.

Convulsive Type.—Children during an attack of fever may develop convulsions, followed by stupor, or even coma and death.

II. SUBTERTIAN SYNDROMES WITH LOCALIZATION

The subtertian syndromes with localization may be classified into:—

I. Syndromes with 'nervous system' localization.
II. Syndromes with 'digestive system' localization.
III. Syndromes with 'respiratory system' localization.
IV. Syndromes with 'circulatory system' localization.
V. Syndromes with 'ductless glands' localization.
VI. Syndromes with 'urogenital' localization.
VII. Syndromes with 'cutaneous' localization.
VIII. Syndromes with 'special sense' localization.

1. With 'Nervous System' Localization.

The atypical subtertian malarias with nervous system symptoms may be classified as follows:—

1. Meningitic type.
2. Hemiplegic type.
3. Monoplegic type.
4. Myelitic type.
5. Ataxic type.
6. Disseminated sclerotic type.
7. Bulbar type.
8. Cerebellar type.
9. Cerebral type.
10. Polyneuritic type.
11. Korsakoff type.
12. Aphasic type.

Meningitic Type.—Fever with signs of meningitis may be found in young persons and children. The symptoms are vomiting, headache, retraction of the head, and rigidity of the neck, convulsions, hyperæsthesia, going on to coma and death. There may be hypertension and slight lymphocytosis of the cerebro-spinal fluid.

Hemiplegic Type.—The patient may be suddenly taken ill with fever, and develop a typical hemiplegic attack.

Monoplegic Type.—This simulates a cerebral hæmorrhage, but is associated with high fever, and in both it and the two preceding subtertian parasites can be found in the blood.

Myelitic Type.—This simulates a transverse myelitis.

Ataxic Type.—The symptoms are slow and scanning speech, great muscular weakness, exaggeration of tendon reflexes, ataxia, together with vomiting. Subtertian parasites are found in the blood. At first there is no fever, but this may develop later. Such patients generally recover on quinine treatment, or, indeed, they do so spontaneously.

Disseminated Sclerotic Type.—There is scanning speech, intentional tremor, nystagmus, spastic gait, and increased reflexes, all of which yield to quinine therapy.

Bulbar Type.—A fever with bulbar symptoms—that is to say, difficulty of speech and deglutition, with facial paralysis, or with a weakening of the muscles of the face and also frequently of the legs. This appears to be by no means rare, and yields to quinine therapy if taken in time. Malarial parasites are often absent from the blood, and the spleen need not be enlarged.

Cerebellar Type.—The symptoms of this type are ataxia, the patient walking like a drunken man and complaining of severe headache and almost complete loss of vision. Vomiting is frequent: often there is no fever, and the spleen and liver are not enlarged. The blood may show parasites, and quinine therapy cures the condition, which may be suspected to be cerebellar tumour or abscess, according to the absence or presence of fever.

Cerebral Type.—This type resembles a cerebral abscess to such a marked degree that an operation may be considered to be necessary, when a blood examination reveals the subtertian parasites and quinine cures the condition.

If there is no fever cerebral tumour may be suspected, but the blood examination reveals the true condition.

Polyneuritic Type.—This type closely simulates 'wet beri-beri,' because the patient is œdematous, with the characteristic gait and loss of knee-jerks. There is neither fever nor enlargement of the liver or spleen, but the blood contains subtertian parasites, and the condition is cured by quinine therapy.

Polyneuritis without œdema is also known.

Korsakoff-like Type.—This resembles the preceding in that the patient shows polyneuritis, but in addition he suffers from mental symptoms, among which the most important is the loss of memory for recent events, all of which disappear under the influence of treatment by quinine. Subtertian parasites may or may not be present in the blood, and the liver and spleen may not be enlarged.

Aphasic Type.—In this type motor aphasia develops with or without other paralyses.

II. WITH 'DIGESTIVE SYSTEM' LOCALIZATION.

The subtertian malarias with digestive system symptoms may be classified as follows:—

1. Pseudo-cholera type.
2. Pseudo-dysentery type.
3. Pseudo-appendicitis type.
4. Pseudo-peritonitic type.
5. Pseudo-liver abscess type.
6. Pseudo-cholecystitis type.
7. Pseudo-cirrhosis type.
8. Hæmorrhagic pancreatitis type.
9. Gastritis type.

Pseudo-Cholera Type.—This is merely a great exacerbation of the ordinary gastro-intestinal symptoms often met with in malarial fever. There is vomiting, abdominal pain, and severe diarrhœa, with motions typical of cholera—*i.e.*, rice-water motions. A microscopical examination of the dejecta may show a few leucocytes in stages of degeneration. The spleen may be palpable, and an examination of the blood will show subtertian parasites, while a bacteriological examination shows absence of cholera and of paracholera vibros.

During the attack the patient is pale or cyanotic, the eyes sunken, the skin cold and clammy, but the temperature may be raised, and hiccough, severe thirst, and painful cramps in the lower limbs, may also be present. The urine is scanty or suppressed. Collapse, delirium, or coma, may precede death, or the patient may be sensible to the end. If the patient is to recover, the algidity diminishes, the diarrhœa ceases, and after a long sleep he awakens refreshed and convalescence sets in.

Pseudo-Dysentery Type.—In this type there are two forms—viz., those with typical dysenteric motions containing blood and mucopus, and the other with hæmorrhagic motions without pus and with little or no mucus. Fever may be high, with great distress and prostration and a small rapid pulse, but at times the temperature may be nearly normal. The spleen may be slightly enlarged, there may be history of previous malaria, and there may or may not be malarial parasites in the blood.

Pseudo-Appendicitis Type.—The attack is sudden, with marked pain in the appendicular region, sometimes vomiting, and usually fever, but no rigors. The spleen and liver may not be enlarged, and there may be tenderness and rigidity in the appendicular region. There may or may not be subtertian parasites in the blood, but the condition is cured by large doses of quinine.

Pseudo-Liver Abscess Type.—This type is associated with fever, often of an intermittent character, profuse sweating, loss of flesh, spleen often not palpable, liver enlarged, with pain on pressure all over the hepatic area. Malarial parasites are usually present in the blood, and the condition yields to quinine therapy by proper means. The condition is rare, and must not be mistaken for true liver abscess, which is not uncommon, and the error of making the diagnosis of malaria in abscess of the liver is more common than *vice versa.*

Pseudo-Cholecystitis Type.—There is severe pain, shooting up to the right shoulder, tenderness in the region of the gall-bladder, severe vomiting, and occasionally slight jaundice. The spleen may or may not be enlarged, and the same is true for the liver. The blood usually shows subtertian parasites, and the condition, which resembles an attack of cholecystitis due to gall-stones, is cured by quinine.

Pseudo-Cirrhosis Type.—This is rare, and is characterized by the hepatic facies and ascites. After tapping, the liver and spleen may be felt to be enlarged and hard. On repeated examination subtertian parasites may be found in the blood. Quinine very slowly cures the condition.

Hæmorrhagic Pancreatitis Type.—The attack is sudden, with violent pain in the epigastrium, followed by vomiting and collapse. Tenderness and tympanites may be present in the epigastrium. Blood examination reveals subtertian parasites, and quinine effects a cure.

Pseudo-Peritonitic Type.—This is characterized by fever, pinched face, vomiting, pain and tenderness all over the abdomen. Malarial parasites are found in the blood, and quinine cures the condition.

Gastritis Type.—This is characterized by acute or by chronic indigestion, yielding to quinine treatment. In old people, especially when anæmia is present, cancer may be suspected.

III. With ‘Respiratory System’ Localization.

It will be remembered that during the ordinary attack of any malarial fever there are a few dry, rather coarse, râles to be heard when the temperature begins to fall, and earlier, at the beginning of the attack, there are often—as first noted by Castellani—very minute crepitations at the base, probably of pleural origin, which generally disappear when the temperature has reached its highest point. They both speedily disappear, but every now and then, even in ordinary attacks, they are more pronounced, and the patient suffers from cough or pain on taking a deep breath.

Slight as these usually are, they nevertheless are the basis of the respiratory system types of pernicious malaria, which may be classified as follows:—

1. Pseudo-bronchitic type.
2. Pseudo-pneumonic type.
3. Pseudo-pleuritic type.

Pseudo-Bronchitic Type.—This subacute or chronic dry bronchitis, with little or no fever, is cured by a few doses of quinine.

Pseudo-Pneumonic Type.—This is often of the nature of a broncho-pneumonia, and is accompanied with blood expectoration, in the red corpuscles of which parasites may be seen, dyspnœa, and cough. The symptoms are better in the remission of the fever, and worse during the attack. The blood is full of parasites. In many cases broncho-pneumonia in malarial patients is not due directly to the malarial parasites, but is a complication due to the pneumococcus.

Pseudo-Pleuritic Type.—Intermittent pleuritic pernicious fever has been described, with sharp pricking pain, dry cough, and friction sounds, which improve in the remission, and become worse again in the attack.

Pleurisy of malarial origin is without effusion.

IV. WITH 'CIRCULATORY SYSTEM' LOCALIZATION.

Atypical subtertian malaria with circulatory system symptoms may be classified into:—

1. Pseudo-anginal type.
2. Endarteritis type.
3. Intermittent claudication type.
4. Erythromelalgia type.

Pseudo-Anginal Type.—The right heart has been noticed to be enlarged in attacks of malarial fever, and sometimes these symptoms become marked, with severe pain in the cardiac region of an *anginal nature*, sometimes accompanied by vomiting of blood, a development of the algide condition mentioned above, and death.

Sometimes the anginal syndrome is very marked, but the condition is amenable to treatment by quinine.

Pseudo-Endarteritis Type.—A superficial artery may swell, become hard and knotty to the touch, and extremely painful. There is no fever, and the blood examination may be negative, but the condition yields to quinine.

At other times dry gangrene may be the only sign of an endarteritis of a deeper and more important vessel. Search should be made for malarial parasites, and if there is any reason to suspect malaria as a possibility, quinine should be administered.

Intermittent Claudication Type.—From time to time the patient is unable to put his foot to the ground, because he feels pain in the calf of the leg and there may be an absence of pulse in the dorsalis pedis artery or in the posterior tibial. Quinine cures the condition.

Erythromelalgia Type.—The hands, and at times the feet as well, become flushed, and the patient complains of pain and tingling in the fingers and at times the toes also. Quinine is the correct treatment.

Heart Block.—This may be due to malarial parasites.

***Rarer Forms.*—Certain authors admit endocarditis as being of malarial origin.**

V. WITH 'DUCTLESS GLANDS' LOCALIZATION.

The types with which we are acquainted are those concerning the *suprarenal capsules*—viz., suprarenal hæmorrhage and the pseudo-Addison type, and those affecting the *thyroid gland*.

Suprarenal Hæmorrhage Type.—The sign and symptoms are those of acute peritonitis, but though the blood shows no malaria parasites, it equally shows no signs of polymorphonuclear leucocytosis. There is no enlargement of the spleen. Quinine should be administered, and the blood again and again examined for parasites. So far the cases have ended fatally as far as we know.

Pseudo-Addison Type.—There is a pigmentation of the skin associated with great loss of flesh and severe asthenia, with or without splenic enlargement, with or without fever, with or without parasites in the blood, but benefited by quinine.

Thyroid Type.—Intermittent and slight swelling of the thyroid gland has been observed in cases of malaria.

VI. WITH 'UROGENITAL' LOCALIZATION.

Subtertian malaria with genito-urinary symptoms may classified into:-

1. Orchitic type.
2. Ovaritis type.
3. Priapism type.
4. Functional generative changes.
5. Nephritic type.
6. Polyuric type.
7. Malarial hæmoglobinuria.

Orchitic Type.- Sudden severe pain in the testicles in a person who may never previously have suffered from typical malarial fever. The testicles become slightly swollen and very tender. There is no effusion. The temperature rises and the patient feels very ill, but the symptoms may be intermittent. A blood examination reveals malarial parasites, and quinine cures the condition.

Ovaritis Type.—Neuralgia of the ovaries is met with at times as a malarial symptom.

Priapism Type.—This is rare and is not influenced by the ordinary drugs, but is cured by large doses of quinine.

Functional Generative Changes.—Impotence, amenorrhœa, and metrorrhagia have been assigned to malaria.

Nephritic Type.—A type of malarial nephritis has been described.

Polyuric Type.--After one or two days of malarial fever, due to the subtertian parasites, a patient may begin and continue to pass enormous quantities of urine, which may cause considerable alarm. Energetic quinine therapy will stop this excessive flow.

Malarial Hæmoglobinuria.—This will be considered in Chapter XLI., p. 1213.

Malarial mastitis has been recorded. Quarelli has described a case of malarial chyluria.

VII. WITH 'CUTANEOUS' LOCALIZATION.

Pseudo-Smallpox Type.—This is characterized by high fever, severe pains in the back, associated with the papular eruption which appears on the second or third day, and consists of small shotty papules which never become vesicles or pustules, which are especially abundant on the face. It may require repeated blood examinations to find the parasites, and the spleen may not be enlarged, but quinine quickly cures the condition.

Herpes.—Herpes is not rare in attacks of malarial fever. It recurs with each attack, and usually at exactly the same spot on which it was situate during a previous attack—*e.g.*, on the lips, the tongue, the face, and the genital organs, etc.

It may occur without febrile symptoms, at a time when an attack of fever is due. Herpes zoster is very rarely seen.

Rarer Eruptions.—Malarial erythemata, malarial urticaria, malarial purpura, and malarial patchy œdema, resembling Malabar swellings or Quincke's œdema, may be mentioned. Ulcerative and gangrenous conditions have been recorded.

Pigmentation.—The black hyperpigmentation of malaria is quite common, and may be present in patches, *chloasma malaricum*, or it may be diffused, and in the latter case may be associated with the syndrome of Addison's disease (see p. 1180). In chronic cases the skin takes on a peculiar pale yellow or ashy grey tinge.

VIII. WITH 'SPECIAL SENSE' LOCALIZATION.

Subtertian malaria may concentrate its attacks upon the eye or the ear (see also p. 2004).

Amaurotic Type.—During an attack of pernicious fever a patient may complain that he is unable to see. When treated with quinine, as a rule sight soon returns, but more rarely blindness may result, due to thrombosis of the retinal vessels, and consequently retinal hæmorrhages and optic neuritis. One eye only may be attacked. This condition must be differentiated from quinine amaurosis. In malarial amaurosis the pupils react to light, and vision is, as a rule, not completely lost. In quinine amaurosis the pupils are widely dilated, do not react to light and other symptoms of cinchonism, such as deafness, severe tinnitus aurium, etc., will be present.

Aural Type.—In this there is a deafness which is not due to quinine, but to the lack thereof permitting the subtertian parasites to damage the organ of hearing. It is rare and chronic. Richardson records cases simulating mastoid disease.

Menière's Type.—Buzzing of the ears with giddiness, and at times the patient falls down. These attacks, which are very severe, are of malarial origin, but rare. The practitioner must differentiate this disease from aural symptoms due to quinine, which may induce buzzing, but seldom severe giddiness. Moreover, symptoms due to quinine improve or disappear on the drug being discontinued.

Loss of taste and anosmia may be noted. Symptoms simulating a frontal sinus affection may occur.

PERNICIOUS MALARIA.

When any of the above-mentioned syndromes caused by the *subtertian parasite* become serious, and threaten to endanger the life of the patient, they are called 'pernicious malaria,' which is therefore commonly caused by *Laverania malariæ*.

More rarely pernicious malaria may be due to the quartan or tertian parasites being present in enormous numbers in the blood, when the syndrome usually produced is *without localization* and most frequently of the *comatose type*.

CHRONIC MALARIA.

Chronic malaria may result from infection by any of the three malarial parasites, but is usually caused by *Laverania malariæ*, the subtertian parasite.

The symptoms of chronic malaria are repeated attacks of slight fever, which may pass unnoticed; enlargement of spleen and liver; and pigmentation of the skin and mucosæ. This pigmentation is particularly to be noted in the tongue in dark races, while in white races Gerhardt's urobilin icterus may be seen in the skin. Other symptoms are œdema about the feet, associated with anæmia, which may be marked; the presence of malarial parasites in the peripheral blood during an attack of fever; and often palpitation and dizziness, bronchitis and digestive troubles, and a general disinclination for exertion and work. The urine shows an increase of urea and urobilin. If this state of affairs is allowed to continue, it may pass into malarial cachexia with enormous enlargement of the spleen, which is firm to the touch and not tender or painful, associated with a profound secondary anæmia, and great reduction of red cells and hæmoglobin, with increase of mononuclear leucocytes. In boys and girls the onset of puberty may be arrested (malarial infantilism).

In malarial cachexia the apyrexial intervals are long, during which search may in vain be made for the parasite in the peripheral blood, but it is usually found during the febrile attacks, which may be quite mild. This is a condition, however, in which blood examination does not help the diagnosis as it does in other forms of malaria, and the clinical symptoms require to be studied, for the disease resembles kala-azar, while it may also be mistaken for ankylostomiasis.

Chronic malaria, of course, is due to insufficient treatment of the acute disease by quinine.

MALARIAL RELAPSES.

The cure of an attack of malaria, unfortunately, does not end the disease, for relapses are the rule and not the exception; in fact, using an expression of Mannaberg's, 'Malaria is one of those infectious diseases in which a relapse may be considered as an essential feature.' The reason is that the parasites are not all killed off by the quinine. There are two different types of relapses: the first, after a short interval, may be called the true relapse; the second, after a longer interval, may be called the recurrence. Relapses and recurrences are probably caused by parasites belonging to the cycle of schizogony, and by the parthenogenesis of the macrogametocyte, which belongs to the cycle of sporogony.

Relapses of quartan fevers take place at irregular intervals, and the suggestion that they are most usual at about the twentieth day is not correct. Tertian fevers relapse most commonly from the fifth to the eighteenth day, and subtertian about the end of a week after the original attack, but these times are extremely variable. These relapses are historically interesting, as they probably represent the quintans, sextans, septans, octans, nonans, etc., of ancient authors.

Recurrences take place after long intervals without fever and without reinfection. Exactly how long the parasites can lie dormant in the human body and then wake to activity and cause fever is not known. Intervals of two and three years are readily credited nowadays, but it is in our experience certain that the length of time may be much longer.

Parasites can certainly be found in the blood of persons long after they have left the tropics: thus, Ross mentions that they were found in a case in Liverpool four years after absence from any malarious locality, and also states that his own father suffered from attacks once or twice a year, even after nine years' residence in England.

It is probable, then, that the old idea that the malarial parasite can exist or lie dormant for years in the system, and awake to renewed activity when given a suitable opportunity, is true. During the apyrexial intervals it must, of course, be going through a cycle of schizogony, but not in sufficient numbers to cause disease. These parasites will increase rapidly, and cause fever when the general vitality of the body is lowered by any of the predisposing causes already mentioned, but especially by a chill, coming into action.

MALARIAL REINFECTIONS.

In tropical countries where there are plenty of anophelines and many inhabitants, European and native, adults and children, with numerous gametocytes in their blood, reinfections are found to be common. Many cases of apparent recurrence in these countries must be reinfections, which, of course, may be with the same or a different species of parasite from that causing the first fever. Repeated infections are the great cause of the quotidian and irregular fevers of the tropics.

COMPLICATIONS.

Many other diseases may occur in the human body at the same time as an attack of malaria; but of all, the most important are typhoid, dysentery, pneumonia, and nephritis.

Typhoid as a complication is, of course, due to the *Bacillus typhosus* occurring in a person who is also infected by malarial parasites, and in that sense, therefore, the old term ' typho-malaria ' is correct.

Dysentery may be a complication due to the *Loeschia histolytica* or to the dysenteric bacilli, but it may also be directly caused by the malarial parasite alone (p. 1177).

As to whether there is or is not a malarial pneumonia is a vexed question; personally, we are of the opinion that a severe subtertian fever may produce symptoms resembling a pneumonia, but that true lobar pneumonia, when present in a malarial subject, is due to the pneumococcus, and is therefore a complication.

Nephritis may be found in tertian and subtertian fevers, being directly due to the irritation of the kidney by the malarial toxins.

SEQUELÆ.

Many so-called sequelæ have already been described under Atypical Subtertian Fevers (see p. 1168). The possible sequelæ of malaria are very numerous, and may be classified into those belonging to the nervous system and sense organs, the blood, the liver, and the spleen.

The subtertian parasite may leave severe traces of its action upon the brain after pernicious attacks, and, indeed, the mind may never regain its old condition. Apart from the milder alterations of disposition and character, actual *insanity* in the form of mania or melancholia may result.

Neuritis in some form is sometimes of malarial origin, but it is quite possible that alcoholic and arsenical poisoning, and, indeed, beri-beri, may have been confused with it. We have seen cases of polyneuritis of malarial origin, but the condition is rare. *Neuralgias* have already been mentioned, and are probably in some cases due to the direct influence of the malarial toxins. *Tinnitus aurium, vertigo, deafness, anosmia,* and *loss of taste,* are said in some cases to be malarial in origin.

Severe and long-continued *anæmia* may result as a consequence of malaria caused by the subtertian, and much more rarely by the other parasites. The classification and characters of these anæmias have already been given in the section on Pathology, to which reference should be made (pp. 1144 and 1151).

Cirrhosis of the liver of malarial origin is, in our experience, much less frequent than admitted by many writers. Cirrhosis of the liver is common in the tropics, and in certain cases is due to alcohol; but one of the writers has pointed out that, at all events in Ceylon, a polyfibrosis of liver, pancreas, and kidney can be met with which has no malarial origin.

The *enlargement of the spleen* has already been described, and rupture as the result of blows or injuries is by no means unknown, though not common, and requires prompt surgical attention. We have only come across one case in our experience.

Tremors are not infrequently seen in chronic malaria, though more rare in acute malaria. *Fine tremors*, consisting of bilateral fine oscillations of small amplitude, caused by the alternate action of antagonistic muscles, may occur in the limbs and more rarely in the head. They are most common in the upper limbs, and especially in the hands. In the head there may be nystagmus or the tongue may be implicated. These tremors are increased by effort, fatigue, or emotion. *Coarse tremors* are usually exaggerations of fine tremors, and are often due to emotion, such as examination by the physician. *Intentional tremors* are produced in the hands, and sometimes in the head and neck, and are due to voluntary movement. They are not very uncommon in malarial infections.

The fine tremors must be distinguished from the fine tremors due to quinine, which are not very rare when the drug has been given for long periods. These tremors disappear in days, weeks, or months after the drug has been discontinued.

In malarial patients coming from war zones tremors and ataxic movements are not rarely seen, but these tremors are neither due to malaria nor to quinine, being of hysterical origin (*sensu lato*), and disappear often after treatment by suggestion.

DIAGNOSIS.

The diagnosis of malaria may be simplicity itself, or, on the other hand, it may be most difficult, as there is practically *no sign or symptom of disease of the human body which it cannot mimic.* We venture to impress upon the reader the vital necessity of making a thorough and *careful clinical examination*, as in many cases this alone may be the key to a correct diagnosis.

The positive signs of malarial infections are:—

1. *Tertian or quartan periodicity*, no matter what the symptoms may be.
2. *Tertian, quartan, or subtertian parasites* present in the peripheral blood.
3. *Pigment in the leucocytes.*
4. *Quinine*, properly administered, producing beneficial effect upon the symptoms.

The complementary signs suggesting malarial infections are:—

1. *Spleen enlarged and hard*, no matter what the symptoms may be.
2. *Slightly enlarged and tender spleen* in cases exhibiting syndromes usually significant of another disease, if the usual tests for the causal agent of the other disease are negative.

3. *Presence of mononucleosis* in association with other features of malaria.

4. *Pigmentation of the skin.*

5. *History of old malarial infections.*

Malaria should not be excluded by:-

1. *Absence of malarial parasites from the blood*, even after repeated examinations, especially in people who have taken quinine, and unless the examinations have been repeated many times and at varying intervals.

2. *Absence of mononucleosis.*

3. *Absence of enlargement of the spleen.*

4. *Absence of 'prompt reaction' to quinine.*

The question of driving the malarial parasite from a hiding-place in some organ into the peripheral blood by giving a small 'provocative dose' of quinine, injections of vaccines, of sterile milk, of strychnin, of adrenalin, by spleen douches, violent exercise, by ultraviolet light, etc., has been attempted, but reliance cannot be placed upon these methods as a practical aid to diagnosis.

Splenic puncture, and the subsequent examination of the blood obtained in this way, would help diagnosis considerably, but is not devoid of risk.

It is generally stated that a fever which within four days is not influenced by quinine in full doses is not malaria. This is correct as regards malarial fevers due to tertian and quartan parasites, but not always as regards those caused by the subtertian parasite. We have met with cases in which the fever has remained unaffected, while the parasite can be found in the peripheral blood, notwithstanding several weeks' quinine therapy by various methods.

In malarial cachexia James has pointed out that the microscopical is inferior to the clinical examination, drawing attention to the fact that a four-hourly temperature chart carefully kept during one of the febrile attacks will often show the typical curve of subtertian fever. In such difficult cases the clinical signs, together with the reaction of the disease to quinine, must be utilized.

In latent malaria the frequent increase of the urobilin in the urine may be of some slight help in the diagnosis, as pointed out by Plehn, together with indefinite periodical rheumatoid pains. Thomson has devised a diagnostic method based on complement deviation, using as antigen a culture of malaria parasites from a heavily infected case. The reaction, however, seems to be positive also in cases of syphilis. Details may be found in Thomson's paper, *British Medical Journal*, December 7, 1918.

The *differential diagnosis* of the various forms of malarial fever should be confirmed, no matter how evident the clinical symptoms may be, by microscopical examination.

The most important diseases to differentiate from malaria are typhoid, insolation, liver abscess, kala-azar, Malta fever, influenza, yellow fever, dengue, and seven-days' fever. For the differential diagnosis see Chapter LX. (p. 1511), which deals with the diagnosis of a tropical fever.

The pernicious forms of malaria, in whatever way they attack the patient, will in most cases be readily diagnosed by blood examination, as will also the masked form of the disease.

Fevers due to septicæmia caused by a streptococcus, the pneumococcus, and the gonococcus, may resemble malaria, but can be excluded by bacteriological examination, as can influenza when it gives rise to an intermittent type of fever.

PROGNOSIS.

Quoad vitam the prognosis is usually good if an appropriate quinine therapy is carried out, but it must be remembered that pernicious cases tend to a high mortality, notwithstanding all treatment, and even in the usual benign cases the cure is very often merely clinical and not complete, as is also seen in other protozoal diseases such as syphilis, yaws, and amœbiasis.

There are two further points to be considered under this heading, and they are:—

1. The probability of recovery.
2. The probability of a cure.

1. **Probability of Recovery.**—This depends upon:—

(*a*) The type of fever.

(*b*) The condition of the patient with regard to race, age, sex, physical fitness, the presence or absence of other diseases, idiosyncrasy to quinine, and the duration of the symptoms.

(*c*) The nature of the country in which the patient is living.

THE TYPE OF FEVER.—Quartan and tertian infections, especially in the simple type, give the best prognosis, but quotidian infections and fevers due to the subtertian parasite should be viewed as more dangerous, while pernicious malaria must be regarded as extremely dangerous.

RACE.—The mortality among natives of bad malarial regions is usually low, while that among Europeans is high. The death-rate in a native race which has comparatively recently been subjected to increased danger of malarial infections is sometimes truly appalling.

SEX.—There is a better prognosis for males than for females, and there is a distinctly worse prognosis for an attack taking place during pregnancy.

AGE.—Children often have more severe attacks than adults, but can usually stand quinine well, which rather balances this disadvantage.

PHYSICAL FITNESS.—Persons debilitated by long residence in tropical countries or from existence upon poor food are not in a condition to resist severe malarial infections, and therefore the prognosis is rendered more serious.

COMPLICATIONS.—The presence of complications in any form—*e.g.*, typhoid fever, etc.—naturally makes the outlook more serious.

QUININE.—Idiosyncrasy to quinine of an anaphylactic nature is most serious, but can be combated by commencing with very small doses, and slowly and steadily working upwards.

DURATION OF THE SYMPTOMS.—If the symptoms persist in the face of quinine therapy the prognosis is serious.

2. **Probability of a Cure.**—The probability of a cure—that is to say, of a so-called bacteriological sterilization of a patient with regard to the malarial parasites—is a very doubtful matter, as the

affection is able to lie dormant for months and years, even after the tropics and any source of infection have been parted with entirely. At times one may be lucky enough to catch all the parasites sporulating, and to kill them with one large and properly applied dose of quinine. This has certainly happened to us with regard to the subtertian parasite in certain cases, but it may have been accidental. The infection may remain dormant for years, and be reawakened by any cause lowering the resisting powers of the individual, such as a chill, a traumatism, or an operation. In temperate climates there is often a seasonal dormancy in winter.

TREATMENT.

Essential Treatment.—There is one specific remedy for malaria, and this is *Quinine*, which should be given *immediately* upon the diagnosis of malaria being made, and may be administered as follows:—

A. WHEN THE PATIENT IS FIRST SEEN IN AN ACUTE ATTACK.

I. *In Benign Intermittent Fevers* (Quartan and Simple Tertian) give *quinine in solution* by the mouth, if the patient is not sick, in 10 grain doses three times a day, or in doses of 15 grains in the morning and 15 grains in the evening.

In a certain number of cases it is advisable to give with each dose of quinine 5 grains of *sodium bromide* in solution, in order to combat any nerve effects of the drug. The bowels should be freely opened with calomel, followed by salines.

If the heart is not working properly, *caffeine citrate* in 1 to 3 grain doses may also be administered, either by the mouth or hypodermically.

If this dosage of quinine is found to be insufficient, as judged by the persistence of the symptoms, *increase* it to 10 grains every four hours instead of three times a day.

II. *In Severe Intermittent, Remittent, and All Subtertian Fevers* give *quinine* by intramuscular injection in a dose of 15 grains *as soon as the diagnosis is made*. Repeat the injection daily, and in addition administer the drug by the mouth in 10 grain doses three times a day.

In these fevers as much as 45-60 grains of quinine may be required in twenty-four hours to combat the symptoms, and should be given by a combination of intramuscular injections with oral administration.

Sodium bromide, the purgative and cardiac drugs mentioned in the preceding section, may also be given.

The injection is to be made in a thoroughly antiseptic manner. Use a vial, containing 15 grains of quinine bihydrochloride in 1 cubic centimetre of fluid, manufactured by some reputable firm. The injection may be made *deep* into the muscles of the gluteal region, care being taken to avoid the line of the sciatic nerve, or *deep* into the loose tissue, extending from the lower angle of the scapula to the crest of the ilium. The vials made by different firms vary

very much in the degree of pain or discomfort which they produce, but some (in pre-war preparations) caused very little pain if given, as should always be done, with the strictest antiseptic precautions. For fuller instructions see Method of Administration, p. 1193.

Do not hesitate to give *intramuscular injections of quinine.* They *have saved many lives*, but the strictest antiseptic methods must be used.

III. *In Pernicious Malaria.*—In pernicious fevers give *quinine at once by intravenous injection.*

The quinine injection should be made into the median basilic or median cephalic veins, and not less than 1 gramme (15 grains), dissolved in sterile 5 c.c. of physiological salt solution, should be injected at a time. The skin over the selected vein should be rendered thoroughly aseptic by soap and water and carbolic lotion, or by painting with tincture of iodine, and then a bandage tied round the arm, so as to retard the flow of venous blood and make the selected vein stand out. Then the needle should be inserted into the vein (care being taken that there is no air in needle or syringe) in a sloping direction, with the point towards the heart, so that the injection can flow with the circulation. The point of the needle should be felt to be loose (*i.e.*, in the vein). The bandage must now be loosened and the injection made *slowly*, the effect on the pulse being noted. The needle is now withdrawn, and an aseptic pad fixed in position by a bandage.

The effect of quinine on the circulation must be remembered, and if the pulse is bad, it is advisable to give an injection of ether as a preliminary.

If the serious symptoms persist the intravenous injection may be repeated in four hours, and further medication may then be carried on by intramuscular injections. Not more than two intravenous and two intramuscular should be given, under any circumstances, in twenty-four hours.

When the serious symptoms abate the intramuscular injections alone should be used, and should be given once or twice a day, and supplemented by oral administration, as indicated above.

B. DURING THE COURSE OF THE FEVER.

I. *If the symptoms are abating* the dosage of quinine may be reduced slowly to about 30 grains per diem, but this must not be done too quickly, and care must be taken to increase this dosage at once if there are any signs of a return of the symptoms.

During the course of the fever the bowels must be kept regularly open, the urine must be carefully watched as to quantity and colour, and tested chemically from time to time, while blood examinations should also be made at times and the pulse carefully noted.

II. *If the symptoms are not abating* the probability is that insufficient quinine is being administered, and in such cases the drug should be carefully increased.

If only oral administration has been used it should be at once supplemented by intramuscular injections.

Care should also be taken that the bowels are kept well opened, that a sufficiency of fluid is drunk to provide a good flow of urine, and that the heart's action is well supported by stimulants and by drugs if necessary.

In order to combat severe symptoms, it may be necessary to give 45-60 grains of quinine, or even more, per diem, but this must be done carefully, and the dosage must at once be reduced when improvement appears. As a rule, not less than 30 grains in the twenty-four hours should be given.

Quinine often takes effect before the expiration of four days of thorough treatment, but it may be necessary to continue the administration of large daily doses longer than this period. If quinine appears to be ineffectual in checking the symptoms, care must be taken to exclude any other possible cause for the symptoms.

C. When the Acute Attack has Subsided.

Continue to administer quinine orally for at least *three months*.

During the first month give it in 10 grain doses twice or thrice daily. During the second month 5 grain doses thrice daily. During the third month 5 grain doses twice daily.

The quinine may be administered, as the *bihydrochloride*, in crushed tabloids, but if it is desired to use the more insoluble salts (see the paragraphs on the theoretical considerations lower down in this chapter) a mixture such as the following may be given:--

Quinine sulphate	10 grains.
Dilute sulphuric acid	10 minims.
Syrup of orange	1 drachm.
Distilled water	1 ounce.

Euquinine may be substituted for quinine for the purposes described in this paragraph, but must be given in slightly larger doses.

With the commencement of convalescence it is useful to give some tonic mixture such as:

Iron and quinine citrate	10 grains.
Liquor strychninæ hydrochloratis	3-5 minims.
Syrup of orange	1 drachm.
Distilled water	1 ounce.

This should be taken three times a day half an hour after meals.

See that the patient's bowels are kept regularly open every day.

Notwithstanding all care and energetic quinine treatment, relapses are prone to occur some variable time after medication has ceased.

D. Relapses.

When relapses occur after thorough quinine treatment it is advisable to combine with this drug arsenic and at times tartar emetic and phosphorus.

The following mixture introduced by Castellani indicates the line of medication suggested:—Quinine sulphate, 10 grains; dilute sulphuric acid, 10 minims; tartar emetic, ⅛-¼ grain; codein, ⅛-¼ grain; syrup, 1 drachm; chloroform water, to 1 ounce.

Another formula used by Castellani is: Quin. hydr., gr. x.; tartar emetic, gr. ⅛; liq. Fowleri, ♏i.; syr., ʒii.; aq. chlorof. ad ℥i.

Two tablespoonfuls of this mixture may be taken, well diluted with water, every four hours.

In addition it may be necessary to resort to intramuscular injections of 15 grains of quinine daily, and it is sometimes advisable to alternate this, every other day, by a subcutaneous injection of the *phosphorated oil* of the British Pharmacopœia in doses of from 1 to 4 minims.

The above forms the quinine-phosphorus-tartar-emetic treatment for malarial relapses devised by Castellani, and found useful by Quarelli and others.

Baccelli's mixture, slightly modified, has the following formula: Quin. bisulph., gr. 8; ferri perchlor. (Ital. Pharm.), gr. 3; liq. Fowleri, ♏.½; aq. to ℥i. It is very bitter.

E. CHRONIC MALARIA.

Chronic malaria should be treated by the methods given just above for relapses. Intramuscular injections of quinine are specially useful in this condition, and should be given in courses of fifteen daily injections. The courses should be repeated two or three times after varying intervals.

F. MALARIA IN PREGNANCY.

Give the usual twenty-four hourly dosage of quinine, but divide it up into small individual doses of 2 to 5 grains.

G. MALARIA IN CHILDREN.

The dosage of quinine for children is as follows:—

Age of Child.	*Dose of Quinine.*	*Number of Doses in Twenty-four Hours.*
Under twelve months ..	½ to 1½ grains.	Six.
1 to 3 years	1 to 2 grains.	Six.
3 to 10 years	2 to 3 grains.	Six.
10 to 16 years	3 to 5 grains.	Six.

H. REMARKS.

It may be thought that in the above we have been too dogmatic, but our excuse is that we desire to lay before the practitioner our experience of many years of tropical practice.

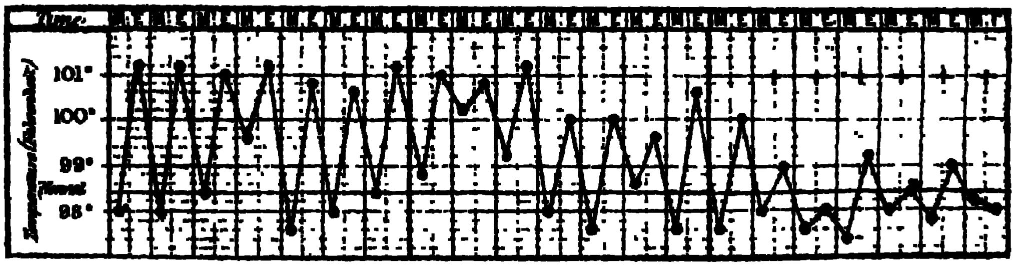

FIG. 626.—TEMPERATURE CHART TO ILLUSTRATE THE BENEFIT OF INTRAMUSCULAR INJECTIONS GIVEN AT + + + + + +, AS COMPARED WITH THE PROLONGED ORAL THERAPY OF DAYS PREVIOUSLY.

The dosage of quinine in use in England and non-malarial countries is perfectly useless in highly malarial tropical districts.

An attempt is made in the above system of treatment to prevent relapses and recurrences as far as is possible.

DETAILS OF TREATMENT.—The various other points connected with treatment may be considered as follows:—

A. Quinine therapy.
B. Symptomatic treatment.

Quinine Therapy.—There are a number of details which require elaboration with regard to quinine therapy, and these are:- (1) The dose; (2) the time of administration; (3) the method of administration; (4) the duration of treatment.

THE DOSE.—To adults we generally give three times a day by the mouth 5 to 10 grains of the ordinary preparations (sulphate, hydrochloride, etc.). The routine mixture is composed of quinine sulphate, 5 to 10 grains; dilute sulphuric acid, 5 to 10 minims; syrup of orange, 1 drachm; distilled water, 1 ounce. We give euquinine in slightly larger doses.

By intramuscular or intravenous injections we give 15 grains, by the rectum 30 grains; but when given by the last method, some tincture of opium should be added, to prevent irritation, which otherwise is liable to occur. Five or ten grains of potassium bromide added to each dose of quinine will, to a certain extent, prevent tinnitus aurium. In cases in which the heart is weak a few minims of tincture of digitalis should be prescribed.

Children suffering from malaria stand quinine well, and the minute doses advised in so many treatises on the diseases of children are, in our experience, utterly inadequate in the tropics. Infants under one year of age may receive from ½ grain to 1½ grains six times a day; children between one and three years of age from 1 grain to 2 grains six times a day, and those between three and ten years 2 to 3 grains six times a day.

Nocht has advised the administration in adults of quinine in small repeated doses of 2½ grains five times a day. This method is useful when there is a tendency to hæmoglobinuria and in pregnant women in whom the administration of full doses may induce abortion; but this action has been greatly exaggerated, many cases ascribed to quinine being due to some other cause. We have often given 15 grains of quinine daily to pregnant women, but divided into small doses of 2 to 3 grains, and in severe cases have pushed the drug without bad effects. The addition of a little opium may prevent bad effects.

In patients showing anaphylactic symptoms such as dyspnœa dysphagia urticaria, etc., Héran and Saint-Girons give quinine as follows: the first day a 'defensive dose' of gr. ½ quinine sulphate mixed with gr. 8 sodium bicarbonate is given, and two hours later, gr. 1½. The second day, two hours after the 'defensive dose,' gr. 3 is administered. The third day, two hours after the defensive dose, gr 6 is given, and so on, gradually increasing the amount of quinine.

TIME OF ADMINISTRATION.—The best time to give quinine to a *healthy person* for purposes of prophylaxis, or to a convalescent for purposes of effecting a cure, will be at meal-times, and preferably directly at the end of the meal, so that it can enter the blood with the products of digestion, and so obtain its fullest action. It has been our rule in most cases to advise that it should be taken directly after the early morning meal.

The hæmolytic action of quinine must be remembered, and the fact that it may by this action give the liver more work by extra bile production. Consequently, it is most necessary to remind the above class of patients to take care that the bowels are open regularly, and to correct by suitable aperients any irregularity that may exist.

With regard to *mild quartan and tertian fevers*, there is not the slightest doubt that excellent effects are obtained by giving the drug four hours before the attack—*i.e.*, before the sporulation of the parasite is due. In this way the merozoites are most likely to be killed. This may be modified by giving the drug twice daily, one dose of 10 grains by the mouth in the morning, and the other dose of 10 grains at the above-stated time. This method we have found most useful, as it allows for irregularity in sporulation.

In many cases, however, we give the drug three times a day, without regard to the conditions of parasitic life, and this method is apparently not less successful.

In more *severe forms of quartan and tertian*, and in cases of *subtertian fever* in which the patient is seen for the first time during the attack, the drug should be given intramuscularly or by the mouth, when it may be administered on the fall of the temperature, when the gastric irritation is lessening, and then continued by one of the above methods.

In cases of *serious and of pernicious attacks*, time must not be wasted in waiting for temperatures to fall or for symptoms to improve, otherwise the patient will die, and there must be no hesitation in giving either an intramuscular or an intravenous injection, according to the severity of the symptoms.

Method of Administration.—For practical purposes there are only four methods of administration:—

1. By the mouth.
2. By the rectum.
3. By intramuscular injections.
4. By intravenous injections.

By the Mouth.—If expense is no object, take the most soluble drug that can be got, and use either the bihydrochloride or the bisulphate; otherwise the sulphate must be used. In cases of women and children, euquinine may be used with advantage, but it should be remembered that it is very insoluble and expensive.

The forms in which the chosen drug may be administered are:—

1. Powder.
2. Solution.
3. Tabloid, tablet, or pill.
4. Cachet or capsule.

It is presumed that no doctor would allow his patient to take quinine in a cigarette-paper, though non-medical people are found who have got into the habit of using this method.

As regards the powder, it is an efficient method of administering the drug to the healthy, if given directly after a meal, but the taste is most unpleasant. It is certainly the cheapest method.

The acid preparations—for example, the bihydrochloride and bisulphate—may be dissolved in water, but should have some flavouring added to disguise the taste, while the sulphate requires an acid, which may be provided by suspending some of the powder in natural limejuice; but in order to dissolve the sulphate properly a mineral acid should be used, in the strength of 1 minim to each grain, but more than this will be required if the unpleasant after-taste is to be avoided.

In hospitals the sulphate must be used, as it is cheap and effective, but it is as well to have it periodically reported upon by an analyst, in order to see what is really being given to the patients. For hospital use it may be dissolved in dilute sulphuric acid, and have some cheap form of flavouring added.

We have used Warburg's tincture on the West Coast of Africa with apparent success in cases of chronic subtertian infection, which resist the ordinary methods of administering quinine, but care is required, as it may have a depressing effect upon the heart.

Tabloids, tablets, and pills are pleasant methods of taking quinine for prophylaxis, convalescence, and mild attacks. Moreover, they are extremely useful for journeys, being readily carried, but in order to be successful they must not be old and hard. The hydrochloride or bisulphate should be used and the solubility tested from time to time in water, otherwise the tabloid must be reduced to powder and taken as indicated above.

Pills and capsules are quite good when fresh, but they are apt to get hard when old, and are then useless, and must be opened and the powder used, if they form the only supply available.

The quinine tannate chocolates are, of course, only used for prophylaxis in children.

By the Rectum.—This method may be useful in gastric disturbance, but is not to be compared with the intramuscular. Twenty grains of the bihydrochloride are made into a solution in water, and then mixed with an ounce of mucilage of starch solution, and used as an injection. It is advisable to add a few drops of tincture of opium.

Quinoform suppositories (gr. iii.) have been used in children by Pedro and others.

Intramuscular Injections.—We are not in favour of hypodermic injections of quinine—*i.e.*, of injections simply under the skin—but strongly recommend intramuscular injections in all cases of malarial fever in which there is gastric disturbance, where, for any reason, the quinine is apparently failing to act, when the disease is becoming chronic, or in serious subtertian infections. For this purpose the bihydrochloride should be dissolved in normal (0·75 per cent.) saline solution, and carefully sterilized. Baccelli's formula is 10 grammes of quinine and 0·075 gramme ($1\frac{1}{6}$ grain) of salt dissolved in 10 grammes ($2\frac{1}{2}$ drachms) of water, one-tenth of which is used for an injection; but the greatest care must be taken that this solution is properly sterile. A good formula for a solution which does not cause pain is Gaglio's or Giemsa's: Quinine hydrochloride, 10 grammes; aquæ destillatæ, 18 grammes; ethylurethane, 5 grammes, of which one-twenty-fifth portion is used for an injection (1·5 c.c. of the solution contains 0·5 gramme of quinine).

If, however, the solution is to be prepared and sterilized while the patient is waiting for treatment, much time is lost. We therefore recommend the tropical practitioner to purchase and keep by him the sterilettes, which are little hermetically sealed vials containing a gramme (15 grains) of quinine in solution. These sterilettes may be purchased from Squire and Sons, or Martindale, of London; Burroughs Wellcome and Co.; or Molteni, of Florence. Giemsa's solution may be obtained in similar sterile vials.

The technique is simple: First cleanse the skin of the patient carefully with 1 in 40 carbolic lotion; then break off the glass seal of the vial at the nick in the neck, and pass the open mouth of the vial through a flame; then draw up the contained fluid into a sterilized all-glass syringe provided with a platinum iridium needle. Plunge the hypodermic needle deeply into the deltoid or gluteus maximus, and make the injection. Withdraw the needle, and place a little pad of wool, wrung out in 1 in 40 carbolic lotion, on the site of the injection. Performed carefully in the above manner, there need be no fear of tetanus or abscess formation, and the injection can be repeated at will. If necessary, a stimulant or an injection of ether may be given in the old and feeble before this intramuscular injection. After repeated injections of quinine, even if administered antiseptically, hard swellings may appear at the seat of the injections. In such cases the hypodermics should be stopped for a few days, and an ice-bag may be applied to the painful part.

Notwithstanding the objections to this method brought forward by some authorities, we still strongly recommend it, as we have found it to be most successful in intractable cases, and have never so far seen any untoward symptoms. We advise that the hypodermic syringe and needle should be sterilized by rinsing with 1 in 20 carbolic acid after boiling, as the carbolic acid does not interfere with the action of the quinine, and has an unfavourable influence upon any tetanus spores which may by any chance be present. Care should be taken that not too much carbolic lotion is left in the syringe and needle; otherwise a precipitate will form

Intravenous Injection.—In cases of pernicious infection with subtertian parasites, no delay should be made in giving the patient an intravenous injection, but the effect of quinine on the circulation must be remembered, and if the pulse is bad, it is advisable to give an intramuscular injection of ether as a preliminary. The same vials and apparatus should be used in the intravenous as in the intramuscular injection.

The injection should be made using a 5 c.c. or 10 c.c. syringe, into the median basilic or median cephalic veins, and not less than 1 gramme (15 grains) of the bihydrochloride dissolved in five or ten cubic centimetres of sterile physiological salt solution should be injected at a time. The skin over the selected vein should be rendered thoroughly aseptic by soap and water and carbolic lotion, or by tr. iodi. and then a bandage tied round the arm, so as to retard the flow of venous blood and make the selected vein stand out. Then the needle should be inserted into the vein (care being taken that there is no air in needle or syringe) in a sloping direction, with the point towards the heart, so that the injection can flow with the circulation. The point of the needle should be felt to be loose (*i.e.*, in the vein). The bandage must now be loosened and the injection made *slowly*, the effect on the pulse being noted. The needle is now withdrawn, and an aseptic pad fixed in position by a bandage.

DURATION OF TREATMENT.--When the fever has subsided and the patient is feeling better, the administration of quinine must not be discontinued, because there is the fear of a relapse, caused by parasites which have not yet been destroyed, and which may be living in the spleen; or, again, there is the fear of the parthenogenesis of the macrogametocyte. In order that the treatment may be successful, the quinine must be continued for a long time. Our routine practice has been to continue with 10 grains three times a day for a month after the cessation of the fever, 5 grains three times a day during the second month, then 5 grains twice a day during the third month. In some cases when the fever has ceased it is advisable to associate some iron and arsenic with the quinine, but these drugs should not be administered during the febrile attack.

Symptomatic Treatment.--The symptomatic treatment may be considered under the following headings:--

1. Symptomatic treatment of acute malaria.
Diet in acute malaria.
Treatment of symptoms and special condit
Treatment of convalescence.
Treatment of chronic malaria.
Treatment of malarial cachexia.

SYMPTOMATIC TREATMENT OF ACUTE MALARIA.--The practitioner who works in the tropics must often be prepared to do the nursing as well as the medical treatment. When the attack begins, the patient must go to bed, and in the cold stage wrap up well with blankets. At the same time arrangements must be made in case of sickness or diarrhœa. The treatment of this and the warm stage must be to encourage perspiration, by warm lime-drinks, hot tea, etc., in order that the toxins may be passed out as quickly as possible. Ziemann recommends hot-air baths to bring on the perspiration. We have tried this method a few times, but have not been greatly impressed with the advantages.

The headache may be relieved by cold applications, and where there is no ice, dissolve some salt and juice of fresh limes or lemons, together with some vinegar or weak acetic acid and Florida water or eau-de-Cologne, in a small basin of water, and, after soaking handkerchiefs in this mixture, apply them one after the other, changing as they get warmed, to the patient's forehead.

A little stimulation of the auricular branch of the pneumogastric by applying some of this cool lotion to the lobule and behind the ear is most refreshing to the patient.

Another method of relieving the headache and pains about the body is to give phenacetin and caffein. Phenacetin or antipyrin should only be given in small doses (gr. ii.-iii.), and not to debilitated patients.

When the sweating begins, the patient usually feels much better, but care must be taken to change the damp clothing, and when this stage is drawing to a close a sponge over with tepid water is most refreshing, after which he will probably go to sleep and wake feeling much better.

DIET IN ACUTE MALARIA.—During the attack the strength must be maintained by light food, such as Brand's essence or chicken-broth, and stimulants, in the form of brandy or champagne, may be required. Milk or whey may also be given, and in cases of stomach irritation albumen water.

During remissions broths and clear soups and milk-puddings should be allowed. In the intermission of a quartan or tertian, and during convalescence, regular meals of good plain food may be given.

TREATMENT OF SYMPTOMS AND SPECIAL CONDITIONS.—*Vomiting* is often distressing, and can be relieved by sips of iced soda-water or champagne. When there is no ice, cover the bottle with a thin layer of flannel soaked in water, and hang in the breeze. If these simple remedies fail, and the symptom is really urgent, apply a mustard-leaf to the pit of the stomach, or give a mixture containing chloroform or a hypodermic of morphine. If, despite all this treatment, the vomiting still continues, the stomach may be washed out with slightly alkaline water.

Hiccough is not often present, and would be a most unpleasant sign. It can be checked by the mustard-leaf, by codein, or by a hypodermic of morphia (gr. ¼).

Cough not infrequently worries the patient. It may be sharp and dry, and is best treated by codein or morphia in some form, *e.g.*:—

Codeinæ	gr. ¼.
Syrupi tolutanæ	ʒi.
Aquæ chloroformi	ad ℥i.

administered every four hours.

Constipation must not be allowed, and should be promptly relieved by a dose of calomel (1 to 3 grains), if necessary, followed by a saline. Ziemann strongly recommends washing out the rectum with warm normal saline solution as a routine practice, but though we have used this in bad cases, we have no experience of it as a routine practice.

Diarrhœa is at first useful in ridding the body of excess of bile and other waste products. Prolonged diarrhœa must be treated with astringents (bismuthi subnitratis or salol gr. x. every four hours). Meanwhile it should be borne in mind that though quinine is absorbed by the stomach, still, with much diarrhœa there is often gastric disturbance, and therefore, if the drug is given by the mouth in these conditions, its utility may be small.

Splenic pain and liver pain are not, as a rule, severe enough to make special treatment needful, but occasionally the splenic pain may be severe (due to perisplenitis), when hot fomentations will relieve it, if it is thought necessary to use them.

Hyperpyrexia must be treated by cold sponging—if possible, with ice; if not, with the mixture mentioned above, or by cold packs, cold baths, and cold enemata.

Cerebral Malaria.—Give large hypodermic saline infusions to wash out the toxins (*vide* Algidity).

Algidity requires special treatment with hypodermic saline injections and warm applications to the body, and especially to the region of the heart. The saline injections consist of sterile normal saline solution, and are injected by gravity from the ordinary glass reservoir via a long piece of indiarubber tubing and a stout hollow needle, such as those in the Potain's aspirator-case. The usual sites for the injection are the sides of the chest, just below the armpit, and the outer aspect of the thighs. At least a pint should be injected in one place. Oxygen inhalations, if available, may also be used.

Diaphoretic pernicious fever requires stimulants, hypodermics of atropine, and ether or strychnine, and treatment as for algidity.

Hæmorrhagic perniciosa may be treated with calcium chloride, and with local applications or injections of adrenalin.

Scarlatiniform perniciosa obviously calls for dilution of the toxins by saline injections.

In *pernicious cases*, when the patient becomes *delirious* or comatose, the practitioner must be careful that the attendants in whose charge he is left are really trustworthy, as unfortunate accidents have been known to happen. Particularly we warn the practitioner to make sure that the bladder has been emptied, especially in delirious patients, not by mere causal inquiry, but by percussion of the abdomen.

In choleraic perniciosa the treatment for cholera should be adopted in addition to quinine. In *dysenteric perniciosa* the treatment must be that suggested for mild dysentery, and, in addition, quinine, while the *pseudo-Addison's* disease is best treated in our experience by 10 minims of adrenalin, given twice daily in addition to quinine.

Treatment of Convalescence.—The important point to be remembered in convalescence is to continue the quinine in smaller doses for at least three months after the attack. The patient should be placed on a tonic with iron and arsenic in some form, and if he has been seriously ill he must have a change to a colder climate. The patient must be impressed with the fact that he must not discontinue the quinine on arriving in a cooler climate, as an attack of fever will surely take place if he does so.

TREATMENT OF CHRONIC MALARIA.—If a person is constantly suffering from attacks of malarial fever, he should be sent, whenever possible, for a change to a cooler climate in the hills or to the temperate zone, but should, of course, continue the quinine treatment. If he cannot afford a change of climate, he must be placed in bed and given rest from work, and a course of quinine therapy by intramuscular injections carried through. Arsenic is useful.

TREATMENT OF MALARIAL CACHEXIA.—The most important feature, in addition to quinine treatment, is to send the malarial cachectic for a change of climate, as mentioned above, and treat the anæmia with iron and arsenic. A course of injections of cacodylate of quinine is often useful.

Theoretical Considerations.—There are a number of theoretical considerations with regard to the treatment which may perhaps interest the reader, and these may be divided into:—

1. Quinine.
2. Effects on man.
3. Effects upon malarial parasites.
4. Immunity of parasite.
5. Prophylactic use.
6. Other drugs.

QUININE.—The aim of the treatment of malaria is to kill the parasites and to aid the excretion of the toxins and relieve the symptoms of the patient.

Fortunately, since the days of the Countess del Chinchon, the world has known the value of cinchona bark in malaria, and later it learnt that this important action was due to an alkaloid, quinine, which exists in the bark in the form of a hydrate. In 1807 Binz showed that quinine killed infusoria, and he believed that this action was due to its checking oxidation.

Quinine is usually sold in the form of the sulphate, $[(C_{20}H_{24}N_2O_2)_2.H_2SO_4]_2.15H_2O$, which is only soluble 1 in 800 of cold water, but is readily soluble in water acidulated with a mineral acid. The solution gives a bluish fluorescence.

It must be remembered, however, that it may not be pure, and may contain lime, chalk, magnesia, starch, etc. It is also important to remember that it is incompatible with alkali, alkaline carbonates, and astringent infusions.

Quinine sulphate is by no means the best preparation, for the hydrochloride, $(C_{20}H_{24}N_2O_2).HCl.2H_2O$, is soluble 1 in 40 of water; but better than this are the acid salts of the sulphate, called the 'bisulphate,' $(C_{20}H_{24}N_2O_2)H_2SO_4.7H_2O$, which is soluble 1 in 11 parts of water, and of the hydrochloride, called the 'bihydrochloride,' $(C_{20}H_{24}N_2O_2)2HCl$, which is soluble 1 in 1 of water. Numerous other preparations are on the market, of which quinine bihydrobromide is recommended in persons who suffer from deafness, and quinine valerianate in those who are very nervous; while quinine tannate, which is not nearly so bitter as the other compounds, especially when made up with chocolate, has been used by Celli in quinine prophylaxis for children and in cases of hæmoglobinuria.

Euquinine, which is quinine ethylcarbonate, $C_2H_5O\text{--}CO\text{--}OC_{20}H_{23}N_2O$, is also not so bitter as the ordinary preparations, and is therefore suitable for administration to women and children, but it has the disadvantage of being expensive and very insoluble in water, and must be given in cachets or dissolved in acidulated water. It has not such deleterious effects on the stomach and nervous system.

Another remedy which contains quinine sulphate, and which was much vaunted in days gone by, is Warburg's tincture, which is said to be prepared by macerating for seven days the following ingredients—

	Grains.
Aloes socotrinæ	240
Rhei	80
Fructi archangelicæ officinalis	80
Radicis inulæ helenii	40
Croci	40
Fructi fœniculi	10
Cretæ preparatæ	40
Radicis gentianæ	20
Radicis curcumæ zedoariæ	20
Cubebæ	20
Myrrhæ	20
Polypori officinalis	20
Opii	2½
Piperis nigræ	4
Cinnamonis	3
Zingiberis	8

in a pint of 60 per cent. alcohol for a week; then pressing, filtering, and dissolving in the filtrate: –

	Grains.
Quininæ sulphatis	175
Camphoris	20

and after three days' filtering, making up to the pint with alcohol. The dose of this mixture is 1 to 4 drachms.

Other preparations can hardly be said to have any particular interest.

In order, however, to bring these various preparations into line with one another, it is necessary to have some arbitrary standard, and this is generally taken as quinine sulphate, which is reckoned as equal to 1. The hydrochloride will then be 0·9, the bisulphate 1·24, the bihydrochloride 1·02, the bihydrobromide 1·23, the valerianate 1·01, the tannate 3·67, euquinine 1·0, and Warburg's tincture 1·09

New Salts of Quinine.—Dihydroquinine hydrochloride (0·6 gramme = 1·0 gramme quinine hydrochloride) is said to be have a specific antimalarial action, but aurochin, chitenin, and tetrahydro-quinine are not satisfactory.

Cinchonin Salts.—Various cinchonin salts have been used in the treatment of malaria, and Sir Leonard Rogers has recently recommended intramuscular injections of cinchonin bihydrochloride.

Effects on Man.—When taken by the mouth, quinine should be dissolved in the acid gastric juice, converted into the bihydrochloride, and absorbed completely into the blood from the stomach, especially if food is taken at the same time. If this does not happen, then such a salt as the sulphate may not be absorbed at all, as it will be precipitated in the alkaline intestinal contents. When given in large or frequent doses, it is apt to irritate the stomach. As to what happens to it in the blood, there are two distinct views—one pointing to rapid elimination, and the other to the fact that it undergoes changes in the tissues. It would appear to be retained longer in the body if absorbed together with food.

It can also be administered by intramuscular injections, when it is said to be largely precipitated at the site of the injection. We have no knowledge personally of this precipitation, and our experience is that intramuscular injections have been most satisfactory, though it must be admitted that there are observers who think that administration *per os* is more valuable than that by intramuscular injections. It may also be given intravenously, as will be explained later.

Quinine in small doses is a vascular tonic, but in large doses it is a cardiac depressant, producing a fall in the arterial pressure, with decrease in the pulse-rate and strength. This is an important matter, to be remembered in administering the drug to the old and the feeble, especially by intravenous or intramuscular injections. On the nervous system it acts as a stimulant, and also increases the flow of blood to the brain. In the tissues it is partly destroyed by oxidation, and therefore the whole quantity administered is hardly likely to be obtained in the urine. Excretion takes place by the kidney almost entirely in the form of quinine dihydroxyl. It can be recovered from urine by acidulating with sulphuric acid, treating with solid picric acid, filtering until clear, digesting with 3 per cent. caustic soda solution, and extracting with chloroform, from which the quinine can be obtained by evaporation. Ramsden and Lipkin have described a new process for isolating quinine from urine (*Annals of Tropical Medicine and Parasitology*, May, 1918).

When given in large doses, the cerebral congestion which it produces causes buzzing in the ears, deafness, due to congestion of the middle ear, and headache, both of which can be treated by bromides, with or without a little ergot. It may also cause erythematous, erythemato-papular, vesicular, and urticarial eruptions.

Quinine Hæmoglobinuria. In persons who have suffered from malaria there is no doubt that quinine can cause hæmoglobinuria, but the way in which it acts is doubtful. Stephens believes that the hæmoglobinuria stands in no relationship to the dose of quinine, and, further, that a second dose may not produce the result, and that it is the blood condition of the malarial patient which is the determining factor. Our experience has tended to show that there is a direct relationship between the quinine and the hæmoglobinuria. Quinine acts in this way by causing hæmolysis of the red corpuscles. Stephens and Christophers found that 0·001 to 0·00082 gramme of quinine hæmolyzed 1 c.c. of a suspension of normal human red cells at 37° C. The hæmolytic action naturally increases the quantity of bile produced. For further remarks on this subject, see the next chapter, on Tropical Hæmoglobinurias (p. 1211).

Quinine Amblyopia.—Amblyopia may result as the effect of large doses of quinine, and appears to be due to constriction of the retinal arteries in temporary cases, and to degeneration of the retinal ganglion cells and their processes in permanent cases (see also p. 2007).

Quinine Fever.—In latent malaria a small dose of quinine may occasionally provoke a febrile paroxysm. This has been compared to the action of a small dose of salvarsan in provoking an exacerbation of symptoms in latent syphilis (Herxheimer's reaction).

Action on the Uterus.—Quinine appears to act upon the uterus, and may therefore produce an unpleasant effect in pregnancy, though whether this is really due to the quinine or to the malaria, or to the two combined, is doubtful.

EFFECT UPON MALARIAL PARASITES.—Quinine appears to particularly affect the merozoites, trophozoites and schizonts, and to act much less vigorously, if at all, upon the gametocytes.

It appears to act most vigorously upon the merozoites, perhaps because they are free in the plasma; next upon the young trophozoites, whose cytoplasm is broken up, and finally it and the nucleus destroyed, but it has much less effect upon the fully grown schizont, not preventing sporulation.

With regard to the gametocytes, it probably has a deleterious action upon the young forms, but certainly not upon the fully grown micro- and macrogametocytes. It is thought probable that it may act upon the very old form of microgametocyte, but this cannot take place, as a rule, with regard to the ordinary fully grown microgametocyte, for anophelines can be infected by the blood of persons containing the two kinds of gametocytes even when treated vigorously with quinine. On the macrogametocyte, particularly that of ***Laverania malariæ***, it appears to have no action. Hence, to get the full effect of quinine on the parasites it must be present in the blood at the time of sporulation, in order that it may kill the merozoites, young sporonts, and schizonts. In order to produce this effect, it is judged that the quinine must be present in the blood in a strength of at least *1* in 20,000. According to Thomson, though quinine has no direct destructive action upon the crescents, it reduces their numbers to less than one per cubic millimetre of blood if given daily in doses of 20 to 30 grains for three weeks; this action is believed to be due to cutting off the source of supply by killing the asexual forms. Methylene blue in doses of 12 grains daily is said by Thomson to reduce the number of crescents, probably by some direct destructive action. Quinine-resisting forms of the parasite have often been reported from South America, and have also been studied by Ross and Thomson, who have found a true parasitic relapse during thorough quinine treatment. In these cases the quinine dosage must be increased. We have administered 2 grammes by intramuscular injection and 1 gramme by the mouth after a few hours as a single dose in such a case with very beneficial results.

Immunity of the Parasite.—The immunity of the malarial parasite against quinine has as yet been but little studied, but this is a subject of the greatest importance at the present time, when quinine prophylaxis is being extensively employed. It has, however, been commonly noticed that the doses of quinine have often to be increased in order to cure an attack of fever in the individuals who have taken quinine more or less irregularly, and that persons who have taken quinine regularly when in an endemic area may have an attack of malarial fever after leaving this area and ceasing the drug.

Prophylactic Use.—This will be discussed in the section on Prophylaxis.

Other Drugs.—It is almost a work of supererogation to mention other drugs in the treatment of malaria, such as cuprein, mercury, atoxyl, and treatment by the serum of immune animals, and by violet light or in the dark. Methylene blue, however, has been used by several authors in the dose of 2 grains every four hours. In our experience its efficacy cannot be compared to that of quinine.

Surveyor has recommended the administration of 2 grains of picric acid twice or three times a day by the mouth as a method of destruction for the crescents of *L. malariæ*. The drug can also be administered by injections of sodium picrate. Nicolle and Conseil and more recently Falconer, Anderson, Micheli, Quarelli and others have tried salvarsan in malaria, with only moderate results. If used, it must be combined with quinine. Neosalvarsan has been found to be useless in subtertian fevers, but it and salvarsan may act upon *Plasmodium vivax* intravenously or intramuscularly. For dosage see p. 1313.

Tartar emetic has been used by Rogers, but the researches by Low and others have shown that when administered alone it has no effect upon the malaria parasites. Röntgen therapy is useless, though the spleen may get smaller.

PROPHYLAXIS.

The very great success which has followed every serious attempt at prophylaxis undertaken during the last few years has made it the urgent duty of each community to scientifically apply a well thought out scheme of a not too expensive nature to its district with the view of reducing the malaria endemic therein.

In order that a disease may be scientifically prevented, a thorough knowledge of its ætiology must be acquired and disseminated not merely among medical men, but also among the public. We know that malaria depends upon—

1. The presence of numerous human beings infected with male and female gametocytes.
2. The presence of numerous anophelines in which the gametocytes are capable of developing into sporozoites.
3. Free access of these anophelines to the infected human beings.

4. Air-temperatures suitable for the development of the malarial parasite in man and anophelines.
5. Free access of infected anophelines to non-immune human beings.

To summarize, there are three factors: (1) Man; (2) the anopheline; (3) the air-temperature.

In the tropics this third factor is in favour of malaria, and it cannot be altered; therefore methods of prophylaxis must be devoted to the human being and the anopheline.

Man.—The preliminary step with regard to man is to ask his intelligent assistance, and for this purpose education with regard to disease in general and malaria in particular is required. First of all it was necessary to bring the medical profession into touch with the discoveries made by Laveran, Manson, Ross, and Grassi, and this has been done. Secondly, it was and is necessary, by lantern lectures, illustrated pamphlets, etc., to convince the educated public of the tropics of the monetary loss caused to the Government, the planter, the merchant—*i.e.*, to the employer of labour—by malaria. Unless this can be done, the money necessary for the effective prophylaxis will not be forthcoming. No one will deny that malaria is the greatest cause of sickness in the tropics, though there may be places where its mortality is low and places where it is high, but that which people fail to recognize is the financial loss caused by this sickness.

Therefore we quote the well-known example of the Adriatic Railway Company, which, according to Ricchi, used to spend on account of malaria among 6,416 workmen living in malarious areas no less than 1,050,000 francs per annum.

But a serious attempt should be made to impress the uneducated masses of the tropics with some sort of knowledge about the disease. This can best be done by simple kindergarten-like instruction, with demonstration of actual living specimens of *anopheles* and their eggs, larvæ, and pupæ, together with the presence of a young child with a huge spleen and of a person suffering from malarial cachexia, and then, at the close of the lecture, to distribute illustrative pamphlets in the vernacular, written in simple language, reviewing the subject of the lecture, together with, if possible, the demonstration of the larvæ in a neighbouring stream or pool.

This attempt to instruct the poorer classes of the tropics may not be productive of much immediate good, but it may bring home to them that malaria is a potent factor in causing illness and death among their infants and young children, and that it is caused by the bite of a particular kind of insect, and can be to a great extent prevented by proper treatment with quinine.

Another method employed is to give the teachers of the elementary vernacular schools a course of instruction in elementary hygiene, including, of course, malaria, so that they may be able to give their pupils elementary instruction in these matters.

In such instruction no pamphlet or book should be used, otherwise there is a danger of the knowledge being acquired by rote. The only way, however, to bring about any result by this method is to award a special grant to the school, based upon the knowledge of the scholars.

All these methods have actually been and are being carried out, but in any case they are only preliminaries, and any good which may result therefrom will not be immediate.

Another preliminary matter is to use the knowledge acquired concerning the life-history of the anophelines, and not to build houses, coolie-lines, etc., in ravines and valleys, or on the margin of water likely to be a breeding-ground for these insects. Place the buildings on high ground, and, bearing in mind the fact that native children harbour gametocytes, build the houses for Europeans away from the native town or village.

Quinine. Leaving now these preliminaries, we come to the actual question of prophylaxis by reducing the malaria in man by quinine administration, as recommended by Koch, Celli, Plehn, Lustig, Negri, and others.

Koch's method consists in taking a large dose (15 grains) of quinine on two consecutive days every eight or ten days for three months, while Celli's method consists in taking about 6 grains (0·40 gramme) of quinine daily; Plehn's, in taking 8 grains of quinine every fourth day. Our own method is to give 5 grains daily, and, in addition, a double dose (10 grains) once a week; and in order to enable the patient to remember the routine, we advise him to take the double dose on a Sunday. For children 1 grain of quinine may be given for every three years of age, or euquinine may be used with advantage in doses of 2 to 5 grains daily. It is not very bitter, and may be given with a little sweetened condensed milk, as advised by Watson, or chocolates of tannate of quinine (2 to 5 grains), as advised by Celli, may be administered.

In very malarious zones such as certain tropical countries and the Balkans, the doses mentioned are not sufficient and should be increased.

All these methods, if properly carried out, give fairly good results, but it must be remembered that unpleasant symptoms may arise after a long use of quinine, of which the most frequent in our experience is a tremor of the hands; but various other nervous symptoms may appear—*e.g.*, irritability.

The advantages of quinine prophylaxis are, however, in excess of its disadvantages, and we strongly recommend its use. In Italy special laws have been passed, due to the efforts of Celli, which render quinine prophylaxis practicable among the poorer classes. The quinine is manufactured by the State and distributed gratis to the poor, while employers of labour are compelled to supply it to their work-people. Governments, municipalities, etc., can also help in this way by giving free quinine to the populace.

The systematic free distribution of quinine powders, tinted if necessary, and enclosed in papers, with a vernacular label informing the recipient that there is no charge, is also useful among the native population, as is the distribution of quinine to children in the schools by the teachers. The distribution must be carried out by itinerary dispensers, for the native will not travel far to obtain quinine. It is, however, necessary to see that the quinine is actually taken, and the use of Tanret's reagent will be found useful in detecting individuals who do not take quinine. Tanret's reagent is prepared by dissolving 1·35 grammes of mercuric perchloride in 75 c.c. of water, and 5 grammes of potassium iodide in 20 c.c. of water in a 100 c.c. measuring flask. The mercuric solution is poured into the iodide solution under agitation and water added to the mark. A few drops of this reagent are added to about 5 c.c. of urine. If no distinct turbidity appears, it means, as a rule, that quinine has not been taken. Turbidity indicates presence of quinine in the urine, but may indicate also presence of various other substances.

By this method Koch freed Stephansort, in New Guinea, from malaria, but there is a doubt as to whether the disease will not recur if this method alone is used. It must be remembered that free quinine distribution on a large scale is very costly.

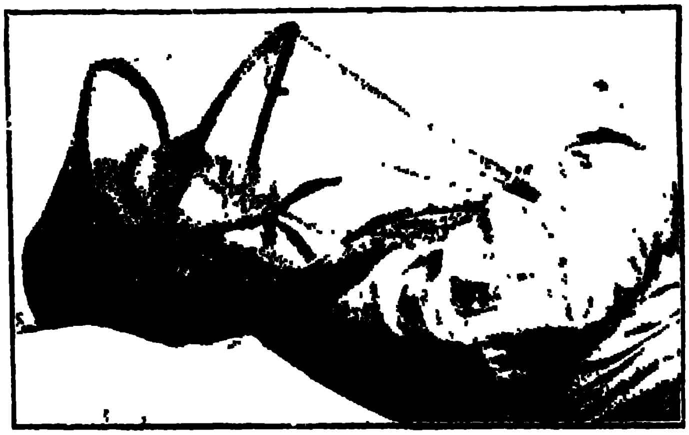

FIG. 627.—THE SIMPSONETTE DESIGNED TO PROTECT THE WEARER FROM MOSQUITO BITES. (From a photograph given us by Mrs. Mary Simpson.)

Bite Prevention. — The next method is to prevent man from being bitten by anophelines. This may be effected by the constant and intelligent use of the mosquito-curtain; by rendering the dwelling, or certain portions of it, gnat-proof; or by the application of chemicals which will keep the mosquitoes away. It is also advised not to go out after sunset, and to protect the whole body against bites.

Firstly, with regard to the mosquito-curtain, the mesh must be suitable—*i.e.*, twenty to twenty-four meshes to the square inch. The lower part of the net should be tightly tucked in under the mattress: on no consideration whatever must it be allowed to hang loosely or to fall on to the ground. It should be in position in the early afternoon, and must be in good repair, for if it is torn it is worse than useless, becoming a mosquito-trap. It must be kept clean, especially at the top, which is apt to accumulate all sorts of queer things from the roof. Never travel into a malarious region without your own net, as the condition of those in rest-houses may be far from good. The *Simpsonette* anti-mosquito and fly protective, non-inflammable headgear, designed by Mrs. Mary Simpson is most useful, as it can be worn under or over the helmet or hat as well as when lying down or sleeping.

Secondly, with regard to gnat-proof rooms or houses, these can be easily constructed at but slight cost by using wire-netting of twenty to twenty-four meshes to the inch, preferably the latter. Rooms and verandas enclosed in this way are a great convenience, preventing molestation from mosquitoes and other insects.

The Irrigation Department of Ceylon possesses movable mosquito-proof rooms, which its engineers can take with them as their work requires. These are constructed of a wooden framework, supporting the gauze, and have a double door. They are only 12 feet by 12 feet by 8 feet, and can therefore be erected inside the room of a native house if desired, or on a veranda. The cost is small.

Hospital wards ought certainly to be rendered gnat-proof in malarious districts, as persons are often found in the wards with their blood teeming with gametocytes. Hence, if there are any suitable anophelines in the hospital, the chance of future patients suffering from other diseases becoming infected is considerable.

With regard to coolies, the third method has been tried to a certain extent with success—viz., that of rubbing all over the body an oil composed of 1½ parts of citronella oil, 1 part of kerosene, and 2 parts of cocoanut oil, to which 1 per cent. of carbolic acid is added. Coolies seem to like this mixture, which is called the 'bamber-green oil.' Menthol, cinnamon oil, eucalyptol, camphor ointments or powders, may be used.

Electric fans and punkahs are secondary methods of preventing anophelines from biting human beings.

Sulphur.—According to some authorities, mosquitoes and flies will not bite persons who take small doses of sulphur regularly, but this is not so in our experience.

The healthy may also be segregated as far from sources of infection as possible. This may be temporary or permanent, according to local conditions.

The Anophelines.—It has already been indicated that it is not necessary to exterminate the anophelines in order to prevent malaria, but that all that is needful is to reduce their numbers. The objection has been raised to anopheline destruction that as fast as they are destroyed in a given area others will immigrate into that place from surrounding areas.

Ross has rather aptly answered that objection by pointing out that if the human birth-rate in a place was suppressed without attracting special immigration, the population would soon decrease, and Professor Pearson, on conjectural bases, has shown that if mosquito propagation is suppressed within the circular area of a mile, the mosquito density at the centre will be 3 per cent., a quarter of a mile from the centre 18 per cent., and at the periphery 75 per cent.

of the density surrounding that area. A square one mile wide will have a central density of 2 per cent., at a quarter of a mile from the boundary 11 per cent., and at the boundary 50 per cent. of the surrounding density. No experiments have, however, been carried out to determine whether these assumptions are correct.

There is, however, no doubt that anopheline reduction leads to the reduction of malaria. The work done under Ross's direction at Ismailia proves this, for the cases of malaria were reduced from 1,551 in 1902 to 37 in 1905, and these latter were all relapses.. The cost of this is given as 50,000 francs for drainage and filling up of pools, with a yearly expenditure of 18,300 francs, which worked out at 2·3 francs per head of population.

Travers and Watson at Klang and Port Swettenham, in the Malay States, by similar methods reduced the cases of malaria admitted into the hospitals from 610 in 1901 to 23 in 1905, while the cases from the surrounding district in which no antimalarial methods were employed were 197 in 1901 and 353 in 1905. The children found infected in the two towns in 1905 amounted to 0·5 per cent. of those examined, while in the surrounding district they were more than 23 per cent. The financial saving is also shown by the fact that Government employés in 1901 obtained 236 sick certificates, amounting to 1,026 days' leave, and in 1905 only 4, amounting to 30 days' leave. The cost to the end of 1905 was £10,100, with a yearly expenditure of £410. The cost up to the end of 1905 worked out at £1 4s. per head of the population.

Similar work has been done in Hong Kong by Dr. Thompson.

In Panama, under American rule, the measures taken are very elaborate and systematic, because the sanitarian is given a free hand, and economy is not considered where health is in question, with the result that malaria and yellow fever have disappeared. There can therefore be no doubt that the destruction of anophelines will lead to the diminution of malaria.

The Insect.—The measures which are used may be classified into those directed against the insect and those against the larvæ. With regard to the insects, fumigation with some substance such as sulphur (2 pounds to be burnt for every 1,000 cubic feet of space) or pyrethrum will stupefy them and cause them to fall to the ground, when they can be swept up and burnt. This is useful in dealing with individual houses prior to residing therein. The insects may also be destroyed in houses by the use of the hand-net as advocated by Ross and Gorgas, while the use of a hand-fan is also recommended. Mosquito traps have also been used and Giemsa's pyrethrum sprays.

Spraying is specially useful for outhouses, stables, etc., and in addition to the pyrethrum spray weak formalin may be used.

The Larva.—It is, however, against the larvæ that measures are most easily taken, and these include:—

A. *Engineering works intended to eliminate breeding places:*—

1. Draining swamps.
2. Draining roads.
3. Filling in hollows.
4. Training streams.
5. Making continuous drains along ravines, etc.
6. Planting trees at intervals, not close together (this is both ornamental and useful), or the thinning down of dense plantations until the trees are at intervals, and the removal of trees with rot-holes, which, however, may be filled.
7. Segregation either of the whole community, by altering the residences from some very infected area or partial segregation of a chosen portion of the community from the worse infected portion. Simpson recommends that at least a zone of 300 yards in width, preferably 400 yards, should separate the residential European quarters from the Native town. Since segregation has been introduced in West Africa, a considerable improvement in the health of the European community has taken place.
8. Efficient drainage to keep down subsoil water-level.

B. *Sanitary works:*

1. *Removal* of small collections of water. Regular inspection of compounds and careful collection and disposal of household utensils likely to harbour mosquito larvæ. Repair of house gutters.
2. *Oiling* collections of water with kerosene (crude petroleum) by means of sprays every ten days, 1 gallon being allowed for 1,000 square yards.
3. *Larvicides.*—Measure the length and breadth of the area of water and add 1 in 20,000 to 1 in 50,000 sanitas okol or 1 in 40,000 izo-izal, or the Panama disinfectant.

Wise and Minnett have recommended that 1 ounce of crude carbolic acid be added to every 16 cubic feet of water, thus giving a dilution of 1 in 16,000, which they maintain will kill the larvæ without injuring any animal which might happen to drink the water.

4. *Screening* wells, cisterns, cesspits, etc., with wire gauze.
5. *Removal* of plants likely to contain water and act as breeding-places (the following may be specially noted bamboos, pineapple plants, travellers' palms, fibre plants). Water-weeds in streams should also be removed, as the larvæ are often found to be protected by these against their natural enemies. Water-weeds should be removed before oiling. Brush and grass should be cut.
6. *Introduction of fish*, especially 'millions,' into collections of water.

It is always easy to find some local fish which will eat larvæ readily. Thus, in Bengal the larvæ-eating fish are: *Haplochilus panchax, H. melastigma, Ambassis nama, A. ranga, Anabas scandens, Barbus ticto,* and several species of *Trichogaster.* Tadpoles and water-boatmen also eat mosquito larvæ.

7. *Growth of weed* in water, especially *Lemna,* the duckweed.
8. *Attention* to the non-stagnation of water in gutters.

Summary.—Every district must be considered separately, and a systematic malarial survey having been made, those methods should be applied which seem most adapted for success. A combination of methods must be better than any one individual method. In any case, a definite scheme should be devised, and thoroughly and continuously carried out. But a word of caution is necessary. Having made the survey and estimated the cost, firstly, leave a good margin for contingencies, and, secondly, insist upon an adequate supply of money being provided: but it is not necessary to embark upon an expensive scheme, as a great improvement can be effected with but little expenditure. It is, however, important to make a beginning, and to attempt to gain the confidence of the public, as to-day there is no difficulty with the authorities, who are usually very willing to help.

The methods mentioned above may be summarized as follows:—

Reduction of Bites.—Mosquito-net, screening the house, use of fans, use of hand-net, use of protective oils.

Mosquito Reduction.—Insects may be killed by hand-net, by culicides, by natural enemies, or inconvenienced by diminution of dense vegetation.

Larvæ may be attacked by removing, oiling, or screening collections of water, natural or in plants, by introducing fish or beetles into water, or by the engineering works mentioned above.

The smaller methods are usually carried out by gangs of workmen—mosquito brigades—under trained supervisors.

Case Reduction.—By quinine prophylaxis and by segregation.

Relative Values.—The relative merits of protection against mosquitoes and quinine prophylaxis have been investigated by Celli, whose results are embodied in the following table:—

Relative Values of Quinine Prophylaxis and Antimosquito Protection.

Method of Prophylaxis.	*None.*	*Quinine Prophylaxis alone.*	*Anti-mosquito Protection alone.*	*Quinine Prophylaxis plus Antimosquito Protection.*
Percentage of infections ..	33%	20%	2·5%	1·75%

Results.—In British Guiana the cases treated in hospitals have been reduced from 33,748 in 1906-07 to 7,384 in 1912-13. In the

Panama Canal Zone the death-rate from malaria in 1881 was 20·5 per 1,000; in 1911 0·96 per 1,000. The malaria cases in 1906 were 821 per 1,000, and in 1911 184 per 1,000. In Ismailia in 1900 there were 2,284 cases; in 1906-08 not a case. In Kuala Lumpur the death-rate was 9·7 per 1,000 in 1907, and 3·9 per 1,000 in 1914. These figures speak for themselves.

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CHAPTER XLI

THE TROPICAL HÆMOGLOBINURIAS

General remarks—Malarial hæmoglobinuria—Quinine hæmoglobinuria—Blackwater fever—References.

GENERAL REMARKS.

HÆMOGLOBINURIA or the presence of more or less altered hæmoglobin in the urine, is found in a number of conditions which may be approximately classified into:

1. **The Symptomatic Hæmoglobinurias,** which occasionally occur in the course of such diseases as malaria, Raynaud's disease, the acute specific fevers, and after severe burns.

2. **The Toxic Hæmoglobinurias,** which are brought about by the action of a number of drugs, as, for example, quinine and its salts, chlorate of potash, antipyrin, carbolic acid, and naphthol, and by certain vegetables used as food, as, for example, certain beans (Favism, *vide* p. 201).

3. **The Specific Hæmoglobinurias,** which are specific diseases, such as blackwater fever and paroxysmal hæmoglobinuria.

In the tropics we are concerned with one entity in each of these groups—viz.:—

1. Malarial hæmoglobinuria.
2. Quinine hæmoglobinuria.
3. Specific blackwater fever.

1. MALARIAL HÆMOGLOBINURIA.

Definition.—Malarial hæmoglobinuria is simply a hæmoglobinuria caused by *Laverania malariæ* Grassi and Feletti, 1890.

History.—This form of hæmoglobinuria has been much confused with quinine hæmoglobinuria and with blackwater fever. It is simply a hæmoglobinuria occurring in the course of atypical subtertian malaria, and caused by the malarial parasites. Stephens has seen it associated with quartan parasites.

Ætiology.—The ætiological factor is *L. malariæ* Grassi and Feletti 1890, together with some other factor, which inhibits the production of antihæmolysins.

Climatology.—The distribution is coextensive with the distribution of the more severe forms of malaria, and is therefore most evident in the tropics and subtropics.

Pathology.—As has been shown by de Blasi, Brem, and Zeiler, the malarial parasites give rise to a hæmolysin which probably varies in quantity and quality with different strains of parasites, but is kept in check by the action of antihæmolysin, which is formed in the body, but which under certain circumstances—*e.g.*, exposure to the weather, etc.—may fail to be produced in sufficient quantities, and hæmoglobinæmia with hæmoglobinuria may occur. Brem found that three parts of a hæmolysin extract from a case of pernicious malaria completely destroyed (hæmolyzed) one part of a 5 per cent. suspension of erythrocytes in twenty minutes. This hæmolysin is thermolabile. Zeiler and Brem have also demonstrated the presence of antihæmolysin in the serum of normal individuals as well as in that of persons suffering from pernicious malaria. It would therefore appear as though the presence or absence of hæmoglobin in an attack of pernicious malaria depends upon the relationship between the quantity of hæmolysin produced, and the amount of antihæmolysin also produced.

Bijon considers that the resistance of the red corpuscles to lysin is diminished, and Gasbarrini believes that the lysin lies inside the red cells.

Symptomatology.—The symptoms are those of an attack of pernicious malaria, in which the main feature is the presence of hæmoglobinuria, the other symptoms being high fever, shivering, vomiting, great prostration, and rapid anæmia.

Diagnosis.—The diagnosis is to be made by first demonstrating the presence of *L. malariæ* in the blood, and then by the rarity of severe jaundice.

Treatment.—This is the same as for other forms of atypical subtertian malaria (p. 1188)—viz., quinine in large doses, before which calcium lactate in 5 to 10 grain doses may be given with advantage.

Prophylaxis.—The prophylaxis is the same as for malaria. This has been exemplified in Robertville, an Algerian village which was highly malarious and where the malarial fevers were associated with pyrexial hæmoglobinuria. After 1910, when preventive measures were instituted, according to Ciavaldini, the malaria decreased and the hæmoglobinuria disappeared.

2. QUININE HÆMOGLOBINURIA.

Definition.—An acute non-contagious fever caused by the administration of any of the ordinary salts of quinine in certain cases of malarial cachexia and chronic malaria, and characterized by hæmoglobinæmia and hæmoglobinuria.

Remarks.—Sir Patrick Manson has pointed out that an attack of hæmoglobinuria can be produced in certain cases by the ingestion of a single small dose of quinine. Ross and Low have reported such a case, under the care of Sir Patrick Manson, where the administration of a 9-grain dose of quinine was followed by hæmoglobinuria in a few hours. Ketchen has recorded a case of seven consecutive hæmoglobinurias in the same individual in whom each attack was the sequel to a dose of quinine. We have met with similar cases, but our maximum is six attacks in one year.

History.—Veratas in Greece, in 1858, was the first to draw attention to this form of fever, and to definitely ascribe the hæmoglobinuria to quinine, and he was followed and supported by Tomaselli, Grocco, and many other Italian and Grecian observers. Later Plehn, Koch, and others, have strongly advocated this theory, but these last observers have applied this one hypothesis for the explanation of all the conditions included under the term 'blackwater fever.'

Climatology.—The attack can take place anywhere for the first time, provided that the individual is suffering from chronic malaria, etc., and the unknown factor or factors to be mentioned below, and has taken the requisite dose of quinine.

Ætiology.—The causation of this condition is the administration of quinine in cases of malarial cachexia and chronic malaria, but this is not the entire ætiology, otherwise the condition would be more commonly met with than at present, and also it is quite safe to administer quinine to the majority of cases of chronic malaria and malarial cachexia without causing hæmoglobinuria. Moreover, the administration of a dose of a salt of calcium prior to the quinine will prevent the hæmoglobinuria, which in the same individual has occurred after such administration.

From one observation which we have made we would throw out the suggestion that one of the other factors in quinine hæmoglobinuria may be the condition of the kidney, and that the site of the hæmolysis may be in that organ.

Pathology.—The pathology of quinine hæmoglobinuria is but little understood, but it has been very ably studied by Barratt and Yorke, who demonstrated the action of quinine in alkaloidal form, and as the bihydrochloride as well as hydrochloric acid and sodium hydrate upon healthy red blood cells, and found that:—

1. All the above-mentioned agents produced hæmolysis.
2. In equimolecular concentration the hæmolytic power is nearly the same.
3. The hæmolysis produced by quinine (alkaloid) resembled a catalytic action, and took place at a monomolecular rate.
4. During life it is not possible to reach a percentage of quinine in the blood sufficient to cause hæmolysis, owing to the toxicity of the drug.

With regard to the action of the quinine, some observers believe that it produces the hæmolysis by lowering the osmotic pressure of the blood plasma.

Morbid Anatomy.—We are not acquainted with any direct observations on this subject, but the appearance of the kidney in people who have died from pernicious malarial fever in which large doses of quinine have been administered without success resembles both macroscopically and to some extent microscopically the kidney seen in blackwater fever.

Symptomatology.—The general symptoms resemble those of an attack of blackwater fever, but are not so severe, and the jaundice is slight or absent.

Diagnosis.—The history of the attack following the administration of quinine in persons suffering from malaria cachexia or chronic malaria may give a clue.

It is suggested that the rate of hæmolysis of the erythrocytes, when treated with quinine, may be compared with that for normal erythrocytes similarly treated. The method adopted to test hæmolysis is to allow 1 c.c. of blood from the pricked finger to fall drop by drop into a 1 per cent. solution of potassium oxalate, which also contains 0·5 per cent. of sodium chloride, until a proportion of four parts of blood to one part of the oxalate is reached. Then the mixture is added to 10 c.c. of a 0·9 per cent. solution of sodium chloride, and centrifugalized until the red cells are completely precipitated, when the supernatant fluid is pipetted off, and then sufficient 0·9 per cent. solution of sodium chloride is added to make a 2·5 per cent. emulsion of red cells. This emulsion is then placed in a series of test-tubes containing various strengths of an isotonic solution of quinine made up with 0·9 per cent. sodium chloride when necessary. The tubes are incubated for three hours at 37° C., and stirred with a glass rod every fifteen minutes, and the result noted at the end of the time.

Prognosis.—This is usually good.

Treatment.—Quinine administration should be stopped, and calcium lactate administered, and the ordinary treatment for blackwater fever as indicated below should be carried out.

Prophylaxis.—Europeans about to visit or reside in the tropics should be given a test dose of 10 or 15 grains of quinine by the mouth, in order to exclude idiosyncrasy. In cases of chronic malaria or malarial cachexia, in which this condition may appear, calcium lactate in 10 grain doses should be given before each dose of quinine.

3. SPECIFIC BLACKWATER FEVER.

Synonyms.—Malarial Hæmoglobinuric fever, Bilious Hæmoglobinuric fever, Bilious Remittent fever, Malignant Bilious fever, Hæmorrhagic Malarial fever, Melanuric fever. *French*: Fièvre Bilieuse Hématurique, Fièvre Bilieuse Hémoglobinurique, Fièvre Bilieuse Grave, Fièvre Bilieuse Mélanurique, Fièvre Jaune des Créoles ou des Acclimatés. *Italian:* Febbre emoglobinurica. *German* : Gallenfieber, Schwarzwasserfieber.

Definition.—Blackwater fever *sensu stricto* is an acute specific fever of unknown causation, characterized by the severity of the symptoms, great blood destruction, jaundice, and hæmoglobinuria.

History.—The knowledge of this fever is recent, for it does not appear to have been noted by Torti, the celebrated writer on pernicious fevers, nor by his predecessors, and the first information of its existence appears to have been given by the French naval surgeons Lebeau, Daullé, and Le Roy de Méricourt in 1850-53, who drew attention to the disease in Madagascar and Nossi-Bé, after which it is mentioned as occurring in Senegal, Cayenne, and the Antilles. In 1858 Veratas described its occurrence in Greece, and in 1859 Cummings met with it in America.

The clinical signs were carefully described by Dutroulau in 1858; by Corre in 1861, who showed that the colour of the urine was due to hæmoglobin, and not to bile or blood, as had been thought; by Barthélemy and Benoît in 1865; Bérenger-Féraud in 1874 (in which year Tomaselli first described it in Italy); Pellarin in 1876; and O'Neill in 1882. Kelsch and Kiener in 1889 gave an excellent description, together with a history of the disease up to that date. In 1890 Schilling met with it in Kaiser Wilhelm's Land, and Grocco and Cardarelli in Italy, after which a series of papers by Mahly, Easmon, Eyles, and Papafio appeared on the disease as seen on the Gold Coast, where it is called 'attridi assara,' which means 'bilious fever.' The name 'blackwater fever,' now universally adopted, was, as far as we know, first used by Easmon.

Researches have been made as to its nature and treatment by Koch, Plehn, Crosse, Prout, Stephens, Christophers, Bentley, Barratt, Yorke, Cardamatis, Leishman, Low and Wenyon, Balfour, and others.

With regard to the parasitic *ætiology* Mache notes that in these cases the cytoplasm of the malarial parasites is apt to stain badly, and therefore, as they are difficult to see, they may often be missed.

Laloir thinks that the peculiar organism which he has described as a malarial parasite in the red corpuscles and nuclei of the mononuclears and in the salivary glands of *Anopheles listoni* var. *albo-apicalis* may be a causal agent.

With regard to *chemical ætiology*, Lahille has shown that there is no deficiency of salts in the blood, and Burkitt has drawn attention to the high acidity of the urine and the diminished alkalinity of the blood

As regards *records* Stephens has drawn up a valuable routine form, which, modified in some particulars, has been utilized in the Sudan for some time.

In regard to *clinical features*, under the term *Icteroidela paludica* Salvin has described a sort of bilious remittent fever as a prehæmoglobinuric fever in Venezuela, and Plehn has classified blackwater into: -

1. *Simple Attack.*- Temperature falls to normal on the second to third day, and even albumen has disappeared from the urine by the third, fourth or fifth day. The only danger is anuria on the third day.
2. *Intermittent Attacks.*—The hæmoglobinuria is intermittent, with very slight icterus, progressive anæmia, and death on fourth to fifth day. Anuria is rare.
3. *Fulminating Type.*—Very slight icterus, anuria, coma; death in twenty-four hours.
4. *Hæmorrhagic Type.*—This appears to us to be the hæmorrhagic type of atypical subtertian fever.
5. *Abortive Ambulant Type.*— This appears to us to be our quinine hæmoglobinuria, as it commences after a small prophylactic dose of quinine.

It seems to us that until tropical practitioners accustom themselves to differentiate from specific blackwater fever the hæmoglobinurias due to quinine and to malaria no real progress will be made with the knowledge of this serious illness.

Climatology.—The disease occurs most commonly in tropical Africa and in certain localities in India, but it has also been reported from many parts of the tropics.

In Europe it is found in South Italy, Sicily, Sardinia, Macedonia, Greece, and Southern Russia. In Africa it occurs in Algeria, and through the whole of the tropical area of West, Central, and East Africa. In Asia it is well known in India, especially in the Duars, the Terai, Assam, the Jeypore district of Madras, and the Canara district of Bombay. It is also found in China, Cochin China, and Farther India. In America cases have been recorded in the southern regions of the United States, in Central and South America—especially Brazil—and the West Indies. It occurs in the Anglo-Egyptian Sudan, but there are many other parts of the tropics from which it has not been reported. Too much trust must not be placed upon this distribution, as confusion exists between the mild attacks of quinine hæmoglobinuria, as well as the atypical subtertian malarial form. True blackwater fever can exist in epidemic form, and is a very fatal infection.

Ætiology.—The causation of blackwater fever has been much complicated by the confusion arising from the non-recognition of quinine and malarial hæmoglobinurias, but when these conditions are admitted there is still the serious disease, 'blackwater fever,' to be explained, and its causation appears to us to be some protozoal parasite as yet unknown.

The various theories which have been advanced to explain the ætiology of blackwater fever are:—

1. The malarial fever.
2. The theory of malaria, together with some other factor.
3. Malarial anaphylaxis theory.
4. An unknown agent theory.
5. Bite of an unknown arthropod.

1. *The Malarial Theory.*—All the old writers on the ætiology of blackwater fever attributed its cause to malaria, in much the same way as they classed most tropical fevers under the same term.

When these fevers came to be differentiated, blackwater fever was assigned to the action of *Laverania malariæ*; but of late years cases have occurred in which this parasite has not been found, but only *Plasmodium malariæ* or *P. vivax*, because these parasites are very commonly met with in the tropics.

The older writers maintained that blackwater fever existed wherever there was severe malaria, and that it was not found where this was absent, and they instanced Southern Italy, where malaria causes a mortality of 7 to 10 per 1,000, as a region where blackwater fever is common, and compared it with North Italy, where the malarial mortality is only 1 per 1,000, and where blackwater fever is rare. Further, it was pointed out that the people attacked with blackwater fever had always previously suffered from malarial fever, and had generally had several attacks. This view may be said to have been supported by Stephens, who states that the blood of persons examined during the day preceding the hæmoglobinuria contained parasites in 95·6 per cent. of cases, while during the day of the attack these parasites were found in only 61·9 per cent., and during the day after the attack in only 17·1 per cent. Stephens and Christophers point out that, though they only found malarial parasites in 12·5 per cent. of all their cases, still they found evidence of malarial infection, as exemplified by the presence of pigment in the leucocytes or by an increase in the percentage of the large mononuclear cells, in no less than

93·8 per cent. Further, the presence of a hæmolysin in malaria has been demonstrated by de Blasi and others.

The reply to these points is that the geographical distribution of blackwater fever is only known in a very general way, and even this superficial knowledge is against the theory that it is due to malaria. Incidentally, we may mention that no one has attempted, as far as we know, to make a spot-map of a district where there is much blackwater fever, showing as far as possible where the disease was really contracted, and to compare this with a similar map made for the cases of malaria in that district. Nor, as far as we know, has anyone attempted to show whether the epidemiological phenomena of blackwater fever coincide with those of malaria. The West Coast of Africa would appear to be a suitable place for these inquiries.

The malarial theory is disposed of, in our opinion, in that it has many times been recorded as occurring in persons who have never suffered from malaria; indeed, according to Craig, it has occurred in people who have not only never been known to suffer from malaria, but in whom neither before, during, nor after an attack have the parasites been found, and, finally, in whom a post-mortem examination failed to reveal any evidence of malaria. Our opinion is more or less confirmed by the fact that an attack of blackwater fever is uninfluenced by quinine. However, at the present time, there are few advocates of the theory that it is simply a malarial infection. Here, perhaps, may be mentioned the fact that Donovan considers that it is malaria, but due to a species of *Laverania* as yet unrecognized. Lalor's parasite requires confirmation, and is in our opinion of doubtful value.

2. *Malaria, together with Some Other Factor.*—As malaria by itself has proved rather weak ætiologically, some other factor has been brought in to support it. Thus Corre suggested chills, Bérenger-Féraud mercury, and others acute and chronic alcoholism, syphilis, severe muscular exertion, mental excitement, and change of climate; but of all theories, that connecting malaria with quinine has been the most popular.

Malaria and Quinine.—Stephens has supported the theory that the disease is partly of malarial origin, aided by a second factor—viz., quinine. In his article in Osler's 'System of Medicine,' Stephens sums up his view: 'Blackwater is not a disease *per se*, but rather a condition of blood in which quinine, other drugs, cold, or even exertion, may produce a sudden destruction of red cells. The condition is produced only by malaria, and generally by repeated slight attacks, insufficiently combated by quinine. In such cases of chronic malaria—*i.e.*, in those suffering from anæmia, with repeated attacks of fever and repeated doses of quinine blackwater fever sooner or later almost certainly supervenes—at least, in tropical climates.'

These statements are too sweeping if genuine blackwater fever is meant, otherwise the home of the disease would be Ceylon, whereas it is so rare that we have never heard of a genuine non-imported case; for in this island there are Europeans and natives with just the conditions required by Stephens, and yet they do not develop blackwater fever, because the only two cases which we have met with or heard of in Ceylon in twelve years were most probably cases of quinine hæmoglobinuria. On the other hand, Stephens's remarks are correct if applied to quinine hæmoglobinuria.

Stephens accounts for the difference between India and Africa as regards the prevalence of blackwater fever by the common malarial parasite being the tertian in India and the subtertian in Africa. Certainly the tertian is very common in Ceylon, though the subtertian is also frequently found. Another point which is difficult to explain is the frequency of the disease in Assam, and the less frequent occurrence in other parts of India where malaria is common.

According to McCay, who has carefully investigated the action of quinine in causing hæmoglobinuria, sulphuric acid and the sulphates cause a decrease in the total inorganic salts of the plasma, which he thinks implies a decrease in its osmotic tension. Water, therefore, passes into the red cells, causing them to swell up, and, if the decrease in osmotic tension of the plasma is sufficient, to burst.

He considers that the causation of blackwater fever is threefold:—

(1) Injury to the stroma of the red cell by the malarial parasite. (2) The action of the malarial hæmolysin. (3) The administration of sulphates.

He thinks that, though the first and second causes may bring about the disease, still quinine sulphate or any other sulphate, by its action on the plasma, is the exciting cause if the former are ineffectual. On the other hand, he finds that chlorides cause an increase of the resisting power of the erythrocytes to hæmolysis. Quinine hydrochloride, especially when combined with sodium chloride and dilute hydrochloric acid, causes usually a marked rise in the resistance. Therefore, according to him, it is not the quinine, but the sulphuric acid in the form of quinine sulphate, which produces the hæmolytic action. In addition to sulphates, McCay found that alkaline carbonates, compounds of alkalis with vegetal acids and potassium salts, diminished the inorganic molecules of the plasma, thus tending to help hæmolysis. We have, however, seen hæmoglobinuria following the administration of euquinine, the hydrochloride, and even the tannate of quinine. We have already referred to Barratt and Yorke's experiments on this subject (see p. 1215).

Malaria, Quinine, or Depressing Influence.—Deeks and James maintain, from the study of 230 cases of blackwater fever in Panama, that it is a manifestation of malarial toxicity usually induced by repeated attacks, but also appearing coincidentally with an acute attack, and may be determined by any depressing influence or quinine.

This is really a malarial toxicity and other factor theory. In order to produce the requisite conditions, they maintain that there must be a population non-immune to malaria, of which infection there must be a large portion due to *L. malariæ*, and malaria must be in such quantity as to produce an almost continuous infection, and this must be associated with a neglect of a thorough administration of quinine, especially in primary attacks.

Against the view that it is caused by malaria treated with insufficient dosage of quinine, followed by a large dose of quinine, we may quote the fact that we are personally acquainted with a case of malaria associated with depressing influences in which the infection was *L. malariæ*, which had remained latent for a considerable period, and which for some weeks was treated by quite inadequate doses taken by the mouth, and after severe fever varying from 104° to 105·8° F., and lasting for two days, 1 gramme of the bihydrochloride of quinine was administered by the mouth, and 2 grammes given at the same time by intramuscular injection, with the result of a quick and lasting cure of the malaria without any signs of blackwater fever. This case appears to us to answer every point required by the supporters of the malaria quinine theory of blackwater fever, and it may further be stated that the original infection with *L. malariæ* was in West Africa in one of the endemic regions of blackwater fever.

Matko gives great importance to a disturbance in the phosphate metabolism as an ætiological factor According to his researches the secondary and tertiary phosphates, whether of sodium or potassium, protect against quinine hæmolysis, while the primary salts do not.

3. ***Anaphylaxis.***—In 1909 Cleland advanced the theory that the disease might be an expression of anaphylaxis to the malarial parasite brought about by the presence in the serum of a foreign protein in the shape of disintegrated merozoites. But this is open to serious objections, though recently supported by Cardamatis, who considers that quinine might be able, when converted into the albuminate, in certain unknown conditions to act as an antigen, which, when combined with the malarial toxin, might produce antibodies, which might provoke a sensitiveness to quinine in the person suffering from malaria, when a further dose of the drug would produce anaphylaxis, perhaps because it combines with the antibodies, or perhaps by its transformation into a hypertoxic substance.

4. *Unknown Agent.*—Sir Patrick Manson, in 1893, first promulgated the theory that blackwater fever was a disease distinct from malaria, and supported this by the peculiar distribution of the disease, which is widespread in tropical Africa, and very local in India.

Sambon, in 1898, having in mind the hæmoglobinuric fevers of animals, brought forward the theory that human blackwater fever would probably be found to be a piroplasmosis, and has informed us that on one occasion Sir Patrick Manson and he saw one body in a red blood-corpuscle of a case of blackwater fever which very closely resembled the bacillary form of Theileria, but it is possible that this was merely a peculiar form of *Laverania malariæ*.

The parasites which have been described are becoming numerous. There is a bacillus by Yersin in the renal epithelium, which has since been shown to be a strain of *Bacillus coli communis;* while the other parasites suggested as possible ætiological factors are a blood parasite by F. Plehn, which he now identifies with the subtertian malarial parasite; and a double-contoured parasite in the red corpuscles by Fisch, which has not been confirmed. A body resembling a *Piroplasma* has been described by Forau, but has been criticized by Stephens, as resembling the fragmentation and flagellation of erythrocytes commonly seen in malarial anæmia in the tropics. Leishman has described cell inclusions varying from 1 to 5 μ in diameter, and usually found in large mononuclear cells of endothelial origin. These inclusions are either structureless, homogeneous, circular forms, or ring forms. They are embedded in the cytoplasm of the cell, and usually assume a chromatin colour with Romanowsky's stain. As a rule, several inclusions are found together in the same cell; more rarely they are solitary. Leishman considers that possibly they are Chlamydozoa. These bodies have been adversely criticized by several observers, especially by von Schilling-Torgau, who considers them to be plasmosomata, and Low has found similar bodies in other diseases. Balfour has seen these inclusions in a case of blackwater fever and in a case of malaria. Schüfner has tentatively suggested that a form of the disease may be of spirochætic origin.

5. *Bite of an unknown Arthropod.*—Balfour suggests that the disease is not of parasitic origin, but due to the injection of some powerful hæmolysin introduced by the bite of some unknown insect or arachnid.

In our opinion blackwater fever is a disease of its own, though we freely admit the existence of hæmoglobinuria from quinine as well as from other drugs, such as chlorate of potash, of which we know of a case at first diagnosed as blackwater fever.

Predisposing Causes.—The predisposing causes of blackwater fever appear to be first racial, second bodily. With regard to the first, the immigrant European suffers more than the native, though the disease also attacks natives and half-castes. This racial distinction is, therefore, probably due to some acquired or inherited immunity. It is said that a person is usually not attacked until after residence for at least a year in the endemic area.

The second series of predisposing causes appears to be anything which lowers the vitality of the body—cold, change of climate, another disease—*e.g.*, malaria, syphilis—or certain drugs.

Pathology.—As the ætiology of the disease is uncertain, the pathogenesis is also little understood.

Christophers and Bentley have brought forward an explanation of the pathology. Their views may be summarized as follows:—*Laverania malariæ*, the subtertian parasite, acts upon the endothelial cells of the blood capillaries of various organs, but especially upon those of the spleen and liver, stimulating them to excessive destruction (erythrokatalysis) of red blood cells by phagocytosis. This phagocytosis results in the production of an auto-hæmolysin of the nature of a hæmolytic amboceptor, which is retained in the endothelial cells until set free by some exciting cause, which may be a chill, overexertion, etc. The result of this excitation is to suddenly set free in quantity this hæmolysin, which destroys the red cells by solution in the plasma (lysæmia), principally in the blood of the liver and kidney, and to a less extent in that of the spleen. The lysæmia produces hæmoglobinæmia, which is best demonstrated by receiving the blood into hypertonic citrate solution and then centrifugalizing, when the serum is observed to be of an orange, rarely of a reddish, colour The amount of hæmoglobin present in this condition was estimated by Christophers and Bentley to be from 1 to 3·75 per cent. of that present in normal blood. This hæmoglobin quickly appears in the urine as oxyhæmoglobin, which may become methæmoglobin on standing. All the hæmoglobin probably does not escape by the kidney, for there is evidence of increased production of bile, and it is possible that only such quantity as the liver is incapable of converting into bile appears in the urine. It is, however, by no means certain whether the pigment escapes only by the glomeruli or through the tubules, or by both, and it is also uncertain whether the hæmoglobin can pass through the cells of a normal kidney.

Barratt and Yorke, on the other hand, find that the hæmoglobinuria is not dependent upon hæmolysinæmia, but that it is due to a hæmoglobinæmia the origin of which they were unable to determine.

They, supported by de Haan, consider that the suppression of urine is due to a mechanical blocking of the renal tubes by the formation of large, firm, coarsely granular casts in the ducts of Bertini. Plehn, however, ascribes this suppression to a nervous inhibition of the glomerular secretion. Many authors ascribe the suppression to nephritis caused by the disease. Recently the subject has been reinvestigated by Yorke and Nauss, who support the mechanical theory, and find that it is considerably facilitated by any factor which tends to lower the blood-pressure, and by that means the secretion of water by the glomeruli, but that if the blood-pressure is kept up by the injection of saline solutions, the tendency to suppression is decreased. This is of importance in guiding the treatment of the condition.

Morbid Anatomy.—There are three cardinal features in the morbid anatomy of a case which has died during blackwater fever, and these are: (1) *Jaundice of the tissues*. (2) *Non-coagulated blood*; (3) *Swollen congested kidneys*. In addition, there may be the signs of acute or chronic malaria in the liver, spleen, and bone-marrow.

On making the post-mortem, the yellow staining of the skin and organs is most marked. The kidneys are enlarged, dark red to black in colour, while microscopically they show degeneration of the epithelium of the convoluted and other tubules, the lumen of which is filled with granular material, while the glomeruli may contain granular material, and show desquamated capsular cells.

The liver is enlarged, and the gall-bladder full of inspissated bile. Microscopically, areas of necrosis, with thrombi in the sublobular veins and quantities of hæmosiderin in the cells, many of which may be in a state of fatty degeneration, are to be seen.

The stomach and small intestine are often hyperæmic, and the bone-marrow is yellowish, and either fluid or gelatinous.

The Blood.—The blood is thin and watery, and there may be hæmoglobinæmia and cholæmia, with lessened tonicity. The red cells and hæmoglobin are greatly reduced, and the former may include shadow cells and small fragments of cells, and deep staining round cells (spherocytes) in the early stages, and later may show degenerative changes such as polychromatophilia and basophilia, while megaloblasts and normoblasts are present. Malarial parasites or pigment may be seen. During the fever there is marked leucocytosis, with polymorphonuclear and mononuclear increase, but when the fever disappears there is leucopenia, with a mononuclear increase.

The Urine.—The urine is dark red to brownish-yellow in colour, becoming sometimes black, like stout, the reddish tinge not being seen until it is diluted, when it shows with the spectroscope the absorption bands of oxy- or methæmoglobin—the latter only if the urine has stood some time. The reaction is faintly alkaline, and the specific gravity is often less than normal. A considerable amount of sediment falls when the urine is left to stand. This sediment is composed of dark brown granular material, which is the débris of the broken-down red cells, very few of which remain intact. Hæmatoidin crystals are sometimes met with. On boiling the urine, and then allowing it to stand for some time, a bright purple colour develops (Plehn's reaction). If some of the urine is made alkaline with potash and then boiled, a purple colour, due to hæmochromogen, is produced (Stephens and Christophers' reaction). The urine resists decomposition for some time.

The presence of urobilin can be detected by acidulating with a little acetic acid, extracting with amyl alcohol, and examining with a spectroscope, when a broad band to the red side of F will be seen. Bile pigments are seldom present, and may be recognized by Gmelin's or Maréchal's reactions. There is a considerable amount of albumen present in the form of serum albumen, serum globulin, and nucleo-albumen. Phosphates are said to be diminished. The hæmosozic value is higher than that of the red corpuscles of the blood.

Symptomatology.—Usually the patient has resided six months or longer in one of the regions mentioned above, and naturally has had attacks of malarial fever, and has taken quinine.

Prodromata.—Prodromata may be almost entirely absent, but usually the patient complains of lassitude, pains all over the body, loss of appetite, restlessness at night, and an entire lack of energy during the day, and a yellowish tinge may be noted in the conjunctivæ or skin for a day or so.

Attack.—Suddenly the patient feels chilly, and shivering fits may occur, accompanied by headache, severe pains in the back and legs, and an intense feeling of weakness and nausea, which, as a rule, quickly ends in retching and then vomiting, first of food, and then of green bile. The tongue is coated with a dirty-yellowish fur, and there is much thirst and constipation, the fæces at first being dark-coloured, and often scybalous.

The liver and spleen are enlarged and tender; the skin is hot and dry, and if not already tinged yellow, rapidly becomes so, deepening in tint as time goes on. It is said that itching is sometimes felt, but we have never noted this. The conjunctivæ are tinged yellow, like the skin. The temperature rises quickly to 103° or 104° F., and the pulse is regular, rapid, small, and compressible. At first the urine may appear normal, but sooner or later the characteristic stout-like colour appears, with pains in the back and burning sensations in the urethra. On the other hand, this may be the first feature of the attack, and causes the patient to send at once for the doctor, though he may not at the time feel ill, or it may occur at the height of the fever, as Kelsch points out.

The mind may be clear or the patient may be brought to the hospital quite unconscious, and may remain so for days, or delirium may set in. After a few hours perspiration appears, and the temperature remits to about 100° F., the urine clears, and a mild case may recover, while in a severe case, instead of the remission, hyperpyrexia, coma, and death may ensue.

Usually, however, after the remission the temperature again rises (post-hæmoglobinuric fever), and the shiverings, vomitings, and pains return, while diarrhœa, with motions full of bile, and sometimes also with blood or hæmoglobin, comes on. A motion with hæmoglobin may present a most striking appearance, being mainly green in colour, with a reddish deposit on the surface.

This second paroxysm may be the last, or it may be succeeded by several others, after which the patient may recover. On the other hand, he may die during these attacks from exhaustion, or from hyperpyrexia and coma, or from anuria and uræmia.

Convalescence.—After the attacks the patient is exceedingly weak, and convalescence is protracted, and is liable to be complicated at any time with anuria, leading to fatal uræmia.

Varieties.—Kelsch and Kiener recognize two distinct types—a mild and a severe, of which the latter is subdivided into three—viz., the ordinary severe, the fulminating with a rapidly fatal issue, and the uræmic type.

Complications.—The most usual complication is the passage of hæmoglobin or blood *per anum*, giving rise to 'dysenteric motions,' as they are often called. Muco-pus is, however, generally absent. Inflammation of the tonsils and salivary glands has been noted.

Sequelæ.—There is nearly always grave anæmia and much weakness as the result of an attack, with often stomach and intestinal derangements, but of all, the most serious is nephritis, leading to uræmia.

Diagnosis.—Blackwater fever is easily recognized, as a rule, the diagnosis being based on the *hæmoglobinuria with high fever and jaundice,* and the severity of the symptoms.

The differential diagnosis has to be made from yellow fever, in which, however, there is never hæmoglobinuria. Acute yellow atrophy of the liver and Weil's disease are easily distinguished by the urine, which does not contain hæmoglobin, and by the presence of the peculiar spirochæte in the blood and urine of the latter disease.

Quinine hæmoglobinuria is not a serious disease, and can be readily prevented and cured, and, moreover, is directly associated with a dose of quinine. Malarial hæmoglobinuria closely resembles blackwater fever, but is definitely associated with subtertian parasites as a rule, and much more rarely with other forms of malarial parasites.

Prognosis.—The mortality in our experience varies greatly, being very high in some epidemics and low in others. The mortalities given by Skelton are as follows: F. Plehn, 4 per cent.; A. Plehn, 6·8 per cent.; Stendel, 16 to 17 per cent.; Koch, 21 per cent.; Bérenger-Féraud, 23 to 24 per cent.; Schellong, 42 per cent.: Reynolds, 50 per cent.

Bad signs are:—

1. Persistent vomiting.
2. Hiccough.
3. Profuse diarrhœa.
4. High fever.
5. Sudden decrease in the tension and increase in the frequency of the pulse.
6. Diminution or cessation of urine.
7. Coma.

Good signs are:—

1. Little gastro-intestinal disturbance.
2. Low temperature.
3. Good pulse.
4. Clear mind.

It is usually said that a person should not return to the tropics after suffering from blackwater fever, but many people do return, and appear to remain in excellent health. Of course, there is the great risk of further attacks.

Treatment.—This may be considered under the following:—

1. During the attack.
2. After the attack.
3. Remarks.

1. During the Attack.—The treatment during the attack may be considered under the headings (*a*) Recommended Therapy, (*b*) General Treatment, (*c*) Diet, (*d*) Symptomatic Treatment.

Therapy Recommended.—We recommend the Sternberg-Hearsey treatment in cases of true blackwater fever, as distinguished from quinine hæmoglobinuria and malarial hæmoglobinuria.

This treatment consists in administering

Liquor hydrargyri perchloridi	30 minims.
Sodium bicarbonate	10 grains.
Water	to 1 ounce.

every two to four hours during the first twenty-four hours, and then every three hours until the urine clears. (For details as to the Sternberg method see Chapter XLII.)

General Treatment.—In treating the disease, the important features to be remembered are that the patients are often infected with malaria; that they suffer from a great blood destruction, and therefore from great weakness; that, as a result of the blood destruction, a severe strain is thrown on the liver and kidneys, and that the latter are apt to be damaged by the hæmoglobin. In fact, some people think that the hæmolysis takes place in the kidney, but in any case there is danger of blocking of the renal tubules, of nephritis, anuria, and uræmia. Lastly, the disease is apt to relapse.

From the very commencement, the patient must be put to rest in bed, and have careful nursing. A most important matter is to flush out the kidneys, and this should be done by introducing water into the body in some way. If the patient can take liquids by the mouth, use soda-water, albumen-water, whey, cold or warm tea, barley-water, or toast-water, in quantity. If vomiting is such that liquids cannot be retained by the stomach, use rectal enemata of warm physiological saline solution (0·9 per cent. of common salt in water) or *sterile* subcutaneous injections (temperature 98·4° F. or 37° C.) of a mixture such as the following:—

Calcium chloride	4–5 grammes.
Sodium chloride	10 grammes.
Distilled water	1,000 c.c.

One hundred to two hundred cubic centimetres of this mixture, ***properly sterilized,*** may be used two or three times a day as a subcutaneous injection in bad cases.

Adam Patrick recommends the intravenous injection of a 1 per cent sterile sodium chloride solution. He has injected as much as 3 pints at one time. Bayliss' Solution, containing 6 per cent gum acacia and 0·9 per cent sodium chloride, may also be used.

Diet.—The diet must be fluid, preferably in the form of whey, milk, chicken-broth, albumen-water, and Benger's food; but strong meat-extracts should be avoided.

If the vomiting is troublesome, and there is no diarrhœa, rectal feeding might be tried. Plenty of aerated water should be allowed.

The condition of the stomach, liver, and kidneys may counter-indicate stimulants at times, but there is no doubt of the value of champagne and brandy when they can be administered.

Symptomatic Treatment.—*Vomiting* may be relieved by sips of iced or cooled soda-water or champagne. If these simple remedies fail, apply a mustard-leaf to the pit of the stomach. Tincture of iodine in a strength of 1 to 2 drops in an ounce of cinnamon water, and administered orally several times a day, may be useful. If this fails, hypodermics of morphine must be tried, but it must be admitted that we do not like to administer this drug in blackwater fever unless compelled, and prefer to combine atropine with it, and even then to give as little as possible. *Constipation* may be combated by means of calomel in repeated small doses, helped if necessary by enemata. *Diarrhœa* should not be too rapidly stopped, but if it is a pressing symptom, weakening and disturbing the patient, then tannic acid in 15 grain doses, tannalbin in 15 grain doses, or bismuth subnitrate in 10-20 grain doses, may be administered by the mouth, or enemata of tannic acid given by the rectum if there is also much vomiting.

The *heart's action* should be carefully watched, and may require support by hypodermic injections of digitalin or caffeine. Calcium lactate, having a tonic effect upon the heart, and being also useful for other reasons in this disease, may be given in 10 grain doses twice or three times a day, or in the form of the injection mentioned above. Extract of the pituitary gland has been recommended in cases of cardiac failure.

Malarial parasites, when present in the blood, require treatment by intramuscular injections of *quinine bihydrochloride* (p. 1188), preceded by a dose or two of calcium lactate, but the sulphate or bisulphate of quinine are contraindicated, and should not be employed.

Pain in the back should be treated by hot fomentations, and if these fail and the symptoms be urgent, by morphine given subcutaneously.

Anuria must be met by vapour baths, before which a hypodermic injection of pilocarpine may be given. If this fails, dry or wet cupping of the lumbar renal area must be tried, and must be helped by oxygen inhalations if available and by free purgation.

Headache may be relieved by cool applications to the head, but special drugs must not be given.

2. AFTER THE ATTACK.—If the patient survive the attack of true blackwater fever, which is often fatal, he should be allowed a long convalescence, with a change to a temperate climate if possible. During this time he will require good, wholesome, nourishing food and slowly graduated exercise.

One attack of 'blackwater fever' *per se* should not necessarily lead to the permanent invaliding of the patient from the tropics, though he should be warned that he returns thereto at his own risk. If, however, permanent damage to any organ is also present, this should be the deciding factor in stating that a return will be dangerous.

3. REMARKS.—Such is the outline of the treatment which we advise, but other authors have different views, and one or two of these may be briefly mentioned:—

Dr. O'Sullivan-Beare strongly recommends the decoction or the fluid extract of the root of *Cassia beareana* Holmes; the latter can be obtained from T. Christy and Sons, Old Swan Lane, Upper Thames Street, London, and should be administered in 1 fluid drachm, well diluted with water, every two hours at first, and afterwards at longer intervals. We have no experience of this drug, but its introducer praises it highly, stating that it relieves all the symptoms quickly. Skelton says he has never seen it do any good, but that it does no harm. So well is the disease known in West Africa that several native remedies exist. With regard to other drugs, atoxyl is said to be useless. Cantlie has used turpentine in mild attacks. Nightingale recommends sodium dimethylarsenate administered in 1-grain doses thrice daily until the temperature is below normal for twenty-four hours. It is stated to soothe the gastric irritation and to clear the urine. Cholesterin in doses of 1 gramme has been given at intervals of four hours until two to three or four doses have been administered. It is given in suspension in thick milk, or as intramuscular injections in olive oil, and has been advocated on account of its antihæmolytic action.

Prophylaxis.—Very little can be said with regard to the prophylaxis, as the knowledge of the ætiology is incomplete. As blackwater fever generally develops in persons who have suffered from malaria, quinine prophylaxis should be carried out in the manner already described in the chapter on Malaria (Chapter XL., p. 1204), attacks of malaria being treated by quinine tannate in small repeated doses, or the drug should be preceded by a dose of calcium lactate.

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CHAPTER XLII

YELLOW FEVER

Synonyms—History—Climatology—Ætiology—Pathology—Symptomatology —Diagnosis—Prognosis—Treatment—Prophylaxis—References.

Synonyms.—Bilious Remittent fever, Acclimatizing fever, Inflammatory fever, Febris Flava, Pestis Americana, Typhus Icteroides. *French :* Fièvre Jaune. *Italian :* Febbre Gialla, Febbre Amarilla. *German :* Gelbfieber. In addition, there are a large number of local names, such as Bulam fever (Grenada); Kendal's disease (Barbados); Pest of Havana (Cuba); Maladie de Siam (Martinique); Febre remittente biliosa dos bezos quentes (Brazil); Febre amarello dos acclimatados (Brazil); Magdalena fever (Columbia).

Definition.—An acute specific non-contagious fever of unknown causation characterized usually by two paroxysms of fever, separated by a remission or intermission, and accompanied with albuminuria, jaundice, and hæmorrhages, with usually a normal number of leucocytes and polymorphonuclear leucocytes. It is spread by the agency of *Stegomyia calopus* Meigen, 1818 (synonym, *S. fasciata* Fabricius, 1805, *non* O. F. Müller, 1764).

History.—Yellow fever is believed to have originally been a disease of the Antilles, and to have attacked the troops of Christopher Columbus in 1495 in the Isle of Spain (St. Domingo), from which it was carried by the Spaniards to the mainland of America. The endemic home of the disease at the present time is the east coast of Mexico, where it was reported in 1509 at Vera Cruz, and Central America from Cape Tampies to Cape Gracias à Dios, and the Greater and Lesser Antilles. From this area it can spread by ships to various parts of the world, where it may become epidemic.

The first clearly written description of yellow fever is that by P. du Tertre, in Guadeloupe, in 1635, but it soon became well known from the epidemic in Cuba in 1648-49: Jamaica, 1655; San Domingo, 1656; Martinique, 1688; and Vera Cruz, 1690. In 1698 it was recognized that the disease was being carried from place to place by ships, and a quarantine ordinance was brought into force, which lasted from 1709 till 1790, when the extensive wars of the period caused it to be ineffective, with the result that between 1791 and 1815 most extensive epidemics took place, and gave ample opportunity for the study of the disease. In 1794 Drysdale, of Baltimore, in 1797 and 1805 Rush, in Philadelphia, and in 1802 Vaughan, in Wilmington, drew attention to the large numbers of mosquitoes and other insects which abounded in their respective towns during yellow-fever epidemics, though rare in preceding years. With regard to bilious remittent fever, a good account of this disease was given in 1842 by Burton in the first volume of the *British Medical Journal* (then called the *Provincial Medical Journal*). In 1848 Nott, of Mobile, accused some insect or mosquito of being the possible carrier of yellow fever. In 1876 Dowell, of Galveston, showed that mosquitoes and yellow fever obeyed the same natural laws, and in 1878 it was demonstrated in Mobile that quarantine of the patients, together with sulphur fumigation, could control the epidemic. But it was not till 1881 that Charles Finlay, of Havana, directly attributed the spread of the disease to the mosquito. In 1882 Gererd, having caused a mosquito to suck the blood of a patient on the fourth day of the fever, then allowed it at once to bite his hand, with the result that he developed in due course a mild attack of yellow fever. The credit of having supported the mosquito theory for many years in numerous publications belongs to Finlay.

In 1883 Freire, of Rio de Janeiro, thought that he had discovered the cause of the disease in the shape of a micrococcus, and later C. Valle, C. Finlay, and Gibier each described specific bacteria. Sternberg studied the disease for years, but could find no definite bacterial or other cause. He, however, in a certain number of cases, came across a bacillus, which he called ' X.' In 1897 Sanarelli announced that he had found a bacterium (*Bacillus icteroides*) which he believed to be the cause of the disease, and, further, he prepared a serum for its treatment. Sanarelli's findings were at first confirmed by a large number of observers.

In 1900 Reed and Carroll announced that *Bacillus X* belonged to the colon group of bacteria, and *B. icteroides* to the hog-cholera group, and was probably identical with *B. choleræ suis*. In our experience *B. icteroides* is not identical with *B. choleræ suis*, but is a distinct species, although it plays no part in the ætiology of the malady, and is merely the cause of a secondary infection. In the same year Reed, Carroll, Agramonte, and Lazear proved that the disease could be produced by the subcutaneous injection of infected blood into a non-immune person; that the disease was not contagious, and was only spread by the bites of *Stegomyia calopus*. The agency of the mosquito was speedily confirmed by Guiteras, Ribas and Lutz, Marchoux, Salimbeni and Simond, Parker, Beyer and Pothier, and later by Rosenau, Parker, Francis and Beyer.

In 1903 Parker, Beyer, and Pothier concluded that the ætiological cause was *Myxococcidium stegomyiæ*, found in infected mosquitoes, which they believed to be an animal parasite closely resembling a *Coccidium*. Carroll, however, refuted this, as did Marchoux, Salimbeni, and Simond, and finally Rosenau, Parker, Francis, and Beyer clearly proved that *M. stegomyiæ* was a yeast normally found in mosquitoes.

In 1905 Rosenau, Francis and Beyer showed that the disease could be communicated by the inoculation of infected blood filtered through the closest-grained Pasteur-Chamberland B filter which they could obtain, and therefore came to the conclusion that the causal agent of the disease must be of ultramicroscopic size.

In 1909 Seidelin described the presence of minute bodies (*Paraplasma flavigenum*) in the red cells of persons suffering from yellow fever, but these are not believed to have anything to do with yellow fever. Low and Wenyon have shown that Seidelin's bodies are common in the blood of young guinea-pigs.

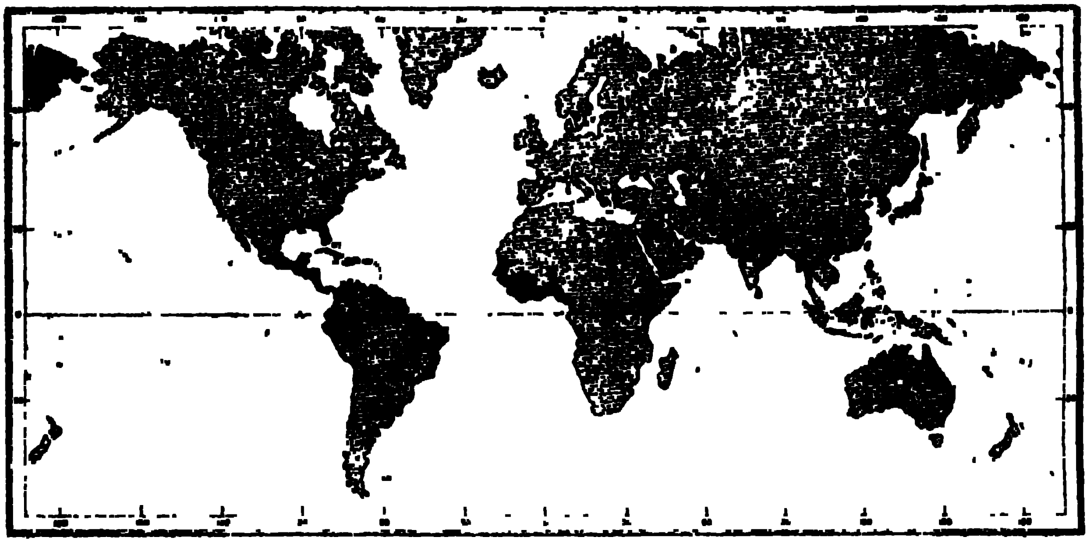

FIG. 628.—MAP OF THE DISTRIBUTION OF YELLOW FEVER. (After Newstead.)

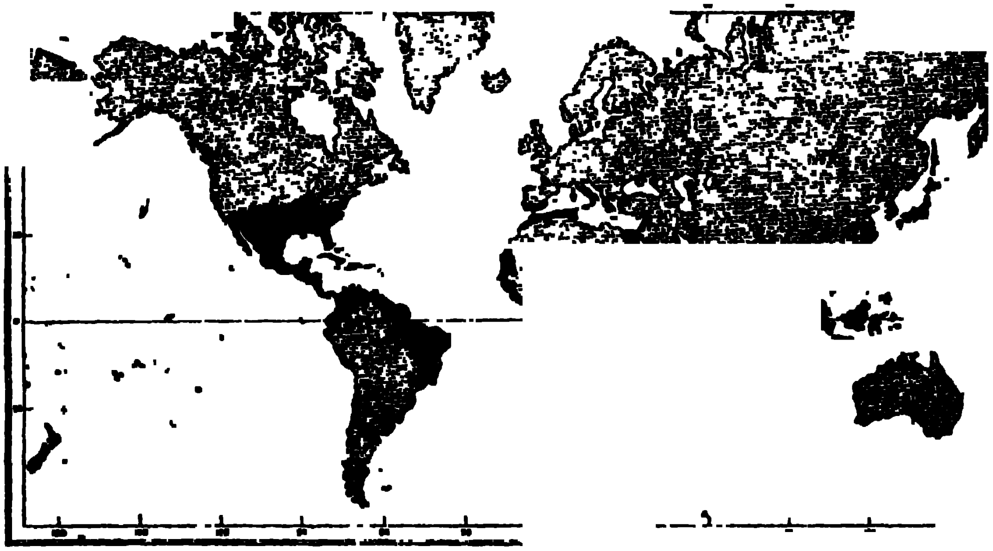

FIG. 629.—THE DISTRIBUTION OF *Stegomyia calopus*. (After Newstead.)

The theory of the propagation of the disease by *Stegomyia calopus* has been put to the practical test of prophylaxis with most excellent results in Havana, Texas, Mexico, and New Orleans, and in the works of the Panama Canal. The late Sir Rubert Boyce did excellent work in drawing attention to the yellow fever of West Africa, where it is extremely deadly at times, and which is probably a secondary endemic centre.

It is impossible to close this history without drawing the reader's attention to the great benefit conferred upon mankind by the labours of Reed, Carroll, Agramonte, and Lazcar, the last named dying from yellow fever following an experimental bite of an infected mosquito.

Climatology.—As already stated, the endemic area includes a portion of the Atlantic coasts of Mexico and Central and South America, as well as the Antilles. Some of the more important endemic centres at the present time are Guatemala, Spanish Honduras, Nicaragua, Costa Rica, Salvador, French Guiana, Dutch Guiana, along the Rivers Magdalena, Orinoco, and Amazon, and in Ecuador. There is evidence that the Cape Verde Islands were infected in 1510-15, and that the Gulf of Benin received its yellow fever from this source in 1520, and it is possible that it has been endemic on the West Coast of Africa from that date. Boyce was of the opinion that it has been a disease of Africa from time immemorable, but, though these early historical points cannot satisfactorily be settled, there is more evidence that the true home is Central America, and that Africa is a secondary endemic area, in which very serious outbreaks have been recorded in the past, and where the disease is at times epidemic.

From the endemic centre the disease can spread by the agency of ships until it reaches 46° 56′ N. (Quebec) and 34° 54′ S. (Monte Video), which correspond to the isotherm of 60° F. (16° C.) for the mean temperature of the hottest month of the year. At its northern limits the disease is generally very mild, but at its southern limits it may be very severe.

The areas most usually affected are the Atlantic coasts of North America, as far north as Charleston (32° 46′ N.), and of South America as far south as Rio de Janeiro (22° 54′ S.). Another region commonly affected is the West Coast of Africa from Senegambia to Saint Paul de Loando.

Europe has frequently been attacked—*e.g.*, England (Swansea) in 1865, France in 1861, Spain and Portugal in the eighteenth and nineteenth centuries, the last infection being in Madrid in 1878, and Italy (Leghorn) in 1804.

The disease has apparently more than once reached the Pacific, for it spread in 1740 to Guayaquil, in Ecuador, and in 1854 to Peru.

The distribution corresponds with that of *Stegomyia calopus*, and the fact that the disease is endemic in warm climates and more marked in the hot season, while it disappears in the winter of temperate climates, reappearing in the summer, coincides with the habits of the mosquito. Further, the facts that it is carried by infected ships and that it may affect low-lying regions near the coast, particularly ports, in which the dwelling-houses are especially attacked, are explicable by its mosquito transmission.

It appears to us that the fever associated with black vomit, found among children in 'Grande terre,' Guadeloupe, must either be a form of yellow fever or closely allied to it, though possibly some cases may be confused with the

vomiting sickness of Jamaica, in which black vomit is absent (p. 1695). At the same time it is interesting to note the general similarity between pappataci fever, dengue, and yellow fever, which appear to form a group of closely allied diseases.

Yellow fever has been recorded by Hudellet at Dinguira, Mahina, Ouida, between Kayes and the Niger in the Sudan, while cases have been recorded in Java.

Ætiology.—The causal agent exists in the blood of an infected person, as can be proved by the fact that the subcutaneous inoculation of 0·1 c.c. of the infected blood into non-immune persons produces attacks of the disease, but it cannot be spread to man by post mortem wounds. This causal agent appears to be, at least in one of its stages, of exceedingly small size, for diluted blood filtered through a Pasteur Chamberland B bougie can still cause the disease if inoculated intravenously into a non immune.

According to Seidelin it is a small protozoon (*Paraplasma flavigenum* Seidelin, 1909) found in the red blood cells, but the parasitic forms described by the author are now considered to be artefacts.

It is obviously a living organism, and not a chemical substance, because of the time it takes to develop in man and the mosquito, for the incubation period in man is usually three days. The mosquito, in order to become infected, must bite a patient during the first three days of his illness, and then fourteen days must elapse before the infected mosquito can transmit the disease.

The proof of the transmission of the disease by *Stegomyia calopus* was worked out by Reed, Carroll, Agramonte, and Lazear, by constructing a gnat-proof building divided into two gnat-proof compartments, into the first of which infected mosquitoes were liberated and allowed to bite a non immune, while other non-immunes slept in the second compartment. The man in the first compartment developed an attack of yellow fever, while the others did not.

Non immunes living in gnat proof houses, with articles of clothing and bedding soiled with urine, faeces, black vomit, etc., from cases of yellow fever, did not contract the disease, though after this experiment was finished some were infected by means of the bites of infected mosquitoes, thus proving that they were not immune.

Marchoux and Simond extended this knowledge by showing that a *Stegomyia* can live for some thirty days, and lay seven batches of eggs. Those laid after the twelve days' incubation by an infected mosquito are also infected, and can transmit the contagium vivum to a second generation of mosquitoes, but these cannot infect non-immunes until fourteen days after hatching as imagines.

The new generation of *Stegomyia* were fed upon glucose, and were made to bite a recent non-immune arrival in Brazil, but no infection followed. A week later the same mosquito was allowed to bite the same person, who then developed a typical attack of yellow fever, from which he subsequently recovered and was found to be immune.

This is believed to indicate that a mosquito requires a feed of blood before it can produce infection.

It is also stated that before a stegomyia can lay eggs she must have a feed of blood, the eggs being laid three days later, after which she is said to feed only at night, while before this she feeds during the day and during the night.

From this it is argued that any stegomyia which bites in the day-time can have only immature parasites, and therefore cannot produce an infection.

A mosquito can produce yellow fever some fifty-seven days after infection, which appears to become more virulent the longer it remains in the insect, especially if the air temperature is 27° to 28° C.

Further, the contagium vivum can apparently only exist in man and *Stegomyia calopus*, though it is true that a chimpanzee, after an incubation of three days, suffered from a typical attack of yellow fever, induced by experimental mosquito-bites, as was shown by Thomas in 1907. No other mosquito so far has been proved to carry the infection. It appears, also, that the development in the mosquito depends to some extent upon the air temperature, as in the case of the malarial parasite.

Thomas has succeeded in producing a reaction in a chimpanzee five days after infection by the bite of an infected *Stegomyia*, and in guinea-pigs from four and a half to thirteen days after being bitten by infected *Stegomyia*. It must be remembered that in yellow fever epidemics it is stated that dogs and fowls are supposed to be ill but from what cause is unknown. Manson has suggested that the disease may be kept up by animals.

The ætiology may therefore be summarized by saying that the causation is an animal parasite, living in the blood stream of man and in the body of *Stegomyia calopus* Meigen, 1818 (*S. fasciata* Fabricius, 1805, *non* O. F. Muller, 1764), by the bites of which it can be transmitted to man and the chimpanzee. The blood of the infected man is transmissive only during the first three to four days. *Stegomyia calopus* begins to be infective fourteen days after the transmissive feed, and remains infective for at least another forty-three days, and it has been claimed that it can pass on the infection to its young, which require a feed of blood before the virus becomes infective. During this non-infective period they bite during the daytime, but do not after their first feed and the deposition of their first eggs. It is possible that other species of *Stegomyia*, in the future, may be found to be carriers as well as *S. calopus*.

Unfortunately, according to Theobald, it is necessary to change the old name *Stegomyia fasciata* Fabricius, 1805, to *S. frater* Desvoidy, 1827, or to *S. calopus* Meigen 1818 though there is some doubt as to whether the latter, which is, of course, the older term, really applies to the insect we know as *S. fasciata*. The reason for this change is because the term *fasciata* was used by O. F. Müller in 1764 (not by de Villers, often wrongly spelt Villiers) for a *Culex* distinct from *S. fasciata* Fabricius, 1805. More recently there seems to be some doubt as to the correctness of the new term—that is, *S. calopus*—and a return to the old term, *S. fasciata*, may be necessary.

Spirochæte.—In 1909 Stimson, reported the presence of a spirochæte in yellow fever (*S. interrogans* Stimson, 1909), but no importance was given to this observation. Recently Noguchi has cultivated from the blood of several cases a spirochæte somewhat similar to *S. icterohæmorrhagiæ*, and has named it *Leptospira icteroides*.

Pathology.—In yellow fever the cells of the liver swell, and, pressing upon the bile capillaries, obstruct the flow of bile and cause a hepatogenous jaundice, characterized by yellow staining of the skin and tissues, and by the presence of bile in the urine. Further, the swelling blocks the intralobular capillaries, causing congestion of all the viscera drained by the portal vein, but especially of the pyloric end of the stomach and the duodenum, because of the arrangement of the veins from those parts. This stagnation of the blood may allow a secondary bacterial infection to take place, which shows its effect on the intestine and spleen.

The liver cells degenerate so extensively in bad cases as to cause the urea function to be considerably lessened in activity, and thereby a condition of ammonæmia comes about, which produces most serious toxic effects upon the brain and other organs. In addition, the disease in some way seriously affects the endothelial lining of the blood capillaries, producing hæmorrhages in various parts of the body. If these leading features of the pathology are borne in mind, the post-mortem appearances and the symptomatology will be easily understood.

An attack generally confers a lasting immunity upon a person, and second attacks are rare, and it appears that the so-called racial immunity of people living in endemic regions is really an acquired immunity, due to mild attacks in childhood. Relative immunity can be acquired by inoculation of infected blood heated to 55° C. for five minutes. Further, it is found that the serum of a convalescent has some protective power.

The Blood.—There is no marked alteration in the numbers or appearance of the erythrocytes, even in fatal cases. A few normoblasts are said to be present at times. On the other hand, there is a decided loss of hæmoglobin, though this is rarely much reduced in the first three or four days; and hæmoglobinæmia is said to occur in fatal cases before death. But this does not appear to coincide with the fall of specific gravity, which may be present without loss of hæmoglobin.

The leucocytes do not appear to be distinctly increased in numbers, varying from 3,200 to 20,000 per cubic millimetre, the increase, when present, being largely caused by polymorphonuclear leucocytes. The coagulation of the blood is diminished, and ammoniæmia is thought to be present in bad cases.

The Urine.—Albumen appears early—as a rule, on the second day—and increases in quantity remarkably, especially in severe cases. During convalescence it may disappear, or may last for months. Bile is present about the fifth or sixth day, and red blood cells may also occur, though leucocytes are rather rare. Casts are present—first hyaline, then granular, and finally epithelial. Urea is diminished in bad cases, and the diazo-reaction is believed to be absent in uncomplicated cases.

The Vomit.—The vomit is often distinguished as white, red, and black. The white is acid, colourless or bile-stained, and is composed largely of mucus. The red vomit contains bright blood, while the black is acid, containing hydrochloric acid, epithelial cells, red corpuscles, fat, débris, and micro-organisms, its colour being due to the presence of hæmoglobin, turned to acid hæmatin by the hydrochloric acid.

Morbid Anatomy.—The skin is yellow from bile-pigment, and blotched with post-mortem lividity and hæmorrhages. The mucosa of the tongue is fissured, and the mouth may be covered with blood. The liver is yellowish or brownish in colour, marked by hæmorrhages. The cells are swollen and in a state of advanced fatty degeneration. The gall-bladder contains inspissated bile, sometimes mixed with blood. The spleen is normal in size, but may be congested and soft. The stomach and intestines may be full of blood, usually in the form of a black homogeneous tarry fluid containing black particles, and the mucosa of the stomach, especially that of the pylorus and duodenum, is usually much swollen, and the mesenteric glands may sometimes be enlarged. The kidneys are, as a rule, normal in size, and show signs of some congestion. Bowman's capsules are said to be dilated, but this is not constant. The cells of the tubules show fatty degeneration, and the lumen may contain granular débris. The suprarenal capsules may be hyperæmic or show fatty degeneration, but neither of these is constant, and hyperæmia or fatty degeneration of the pituitary body and the thyroid gland have been described, but are not important. The bladder is usually empty. The heart shows ecchymoses, and effusions may be found in the pericardium. The lungs may be congested, and hæmorrhages may be found beneath the pleura. The uterine mucosa is congested, and there may be blood in the cavity. The meninges of the brain are congested, and hæmorrhagic spots may be seen.

Symptomatology *Incubation.* An exact knowledge of the length of the incubation period is of the utmost importance from a prophylactic point of view. Calculated from experimental mosquito bites, it varies from two days twenty-two hours to seven days five hours, but the latter figure was in a man who had had a mild attack. With regard to the former period, it is the shortest actual record, but some more doubtful figures, as low as two days one hour, are given. Excluding the man with the slight attack, the incubation period, as generally given by American observers, would be from two days twenty-two hours to six days two hours. Marchoux, Salimbeni, and Simond consider that the incubation may be as long as twelve days, and draw this conclusion from inoculation of modified blood serum, and also from natural infection. Carter's careful clinical records, however, give the incubation period as varying from three to five and three quarter days.

The average time appears to be about five days, but to be on the safe side at least six to seven days must be allowed.

The Fever.—The fever is divisible into two paroxysms, separated by a remission or intermission. The first attack is characterized by headache, pale, then flushed, face, injected eyes, and pains in the body, and after the second day albuminuria: while the second attack shows the jaundice from which the disease obtains its name, and the hæmorrhages, of which black vomit and black motions form such ominous signs.

Onset.—Prodromata are usually absent, but general malaise may be felt for some little time previously. The attack begins with a sensation of coldness, with or without rigors, and with severe frontal headache, pains in the back and limbs, while the face, at first pale, becomes flushed and painful, the skin congested, the eyes brilliant and injected, and photophobia is often present The temperature rapidly rises to 103° F. or more: the respiration quickens and is laboured: the pulse is quick, full, and bounding, reaching to 100 or 120 per minute. The appetite is lost, and there is usually vomiting, associated with pain and tenderness in the region of the pylorus, and usually constipation. The urine is generally diminished, acid in reaction, with a high specific gravity, and albumen is present from the first or second day. Its passage may cause a sensation of burning. During this stage there is often insomnia.

Intermission.—On the second to fourth day the remission sets in, the temperature either dropping with a crisis, accompanied by sweating, to normal, or remitting to about 100° F., the flush and pains disappearing. In the former case the disease ends and convalescence begins. More usually, however, after a few hours' remission, during which the patient feels much better and sleeps well, the temperature again rises to 104° or 105° F.: but a most characteristic feature, called 'Faget's sign,' now shows itself, in that the pulse does not increase in rapidity as the temperature rises. On the contrary, as days go on, the pulse-rate tends to become slower and slower, without regard to the temperature. This sign depends upon the severity of the case, being most noticeable in severe types, in which it may be only 70 to 60 per minute, though associated with a high temperature.

Second Attack.—During the second attack all the symptoms of the first paroxysm return, but the congestion of the skin is not so marked, and the yellow tint of jaundice appears for the first time, and deepens as the illness proceeds. The vomiting and tenderness in the stomach return, and are associated now with much thirst and prostration. The tongue is dry and furred, with red tip and edges. Hæmorrhages may now occur from the nose, mouth, or uterus, and the bad signs of black vomit and melæna may appear. The urine diminishes in quantity, and the albumen increases. In bad cases its excretion may totally cease. There is generally much restlessness, and often delirium.

Terminations.—Two courses are now possible. The first is that after three to four days' illness the temperature may decline, the urine increase in amount, the albumen diminish, and the vomiting gradually cease: while sweating may occur, and the patient, passing into a deep sleep, awakens on the road to convalescence. The second is that the temperature does not decline, the jaundice deepens, hæmorrhages appear under the skin, and from the regions indicated above, hiccough, subsultus tendinum, clammy sweats, anuria, coma, and convulsions lead to death, which may, however, take place before the full development of these symptoms by cardiac or respiratory failure.

Varieties.—Three varieties may be recognized, though some authors describe more. These are the mild, the severe, and the malignant. The mild type consists of simply the first paroxysm, in which the temperature does not rise above 102° F., the urine contains albumen, and the fever ceases by crisis on the second or third day. The severe type shows the characters given above as typical for the disease. The malignant type begins with high fever, 105° to 107° F., with violent vomiting and the early appearance of black vomit and melæna, when the patient quickly becomes delirious, and dies in the initial fever.

Complications.—Any pre-existing pathological condition is serious in yellow fever, but renal and cardiac affections are perhaps the worst. Gangrene, abscesses, congestion of the lungs, and intussusception are possible complications arising in the course of the disease.

Sequelæ.—Boils and abscesses, dysentery and hepatitis, are the common sequels, but usually convalescence is not complicated or protracted.

Prognosis.—The mortality is very variously given, usually 10 to 25 per cent. for the United States and Europe, and 45 to 80 per cent. for the endemic area and West Africa. The extremes are 0·5 to 94·5 per cent.

All cases of yellow fever must be considered serious, especially if complicated with pre-existing disease, and constant care must be taken to measure the daily quantity of urine passed, and to estimate the amount of albumen; for marked diminution of the urine, especially anuria, is a grave sign. High temperatures, black vomit, melæna and other hæmorrhages, and marked disturbance of the nervous system, are all bad omens.

According to Sternberg, if the temperature does not rise over 103° F. the prognosis is usually good.

Diagnosis.—The typical symptoms in an epidemic will hardly be mistaken for any other disease, but the mild early case is very difficult to recognize. The best signs for a positive diagnosis are the early albuminuria, the epigastric tenderness, and, later, the jaundice, with Faget's sign, and the black vomit.

Differential Diagnosis.—The most important diseases to differentiate in the first stage are dengue, subtertian malaria, blackwater fever, and relapsing fever. Dengue may be recognized by the absence of albuminuria, the preliminary rash, and leucopenia; subtertian malaria by the parasites in the blood, and in some cases the typical four-hourly temperature chart; blackwater fever by the hæmoglobin in the urine and the mononuclear increase; relapsing fever by the parasites in the blood and the leucocytosis.

Treatment.—There is no specific remedy known for yellow fever. The usual treatment, if the patient is seen on the first or second day, is to give repeated small doses of calomel until 3-5 grains have been administered, and then a draught of magnesium sulphate and sodium sulphate. Then employ Sternberg's mixture, which is:—

Sodium bicarbonate	150 grains.
Perchloride of mercury	⅓ grain.
Water	60 ounces.

This is given in three tablespoonful doses every hour.

General Treatment.—As the cause of the disease is unknown, the treatment must aim at the prevention of the spread of the infection, the rapid elimination of the toxins, and the alleviation of the symptoms. To prevent the spread of the disease, the patient's bedroom must be rendered gnat-proof. The excretion of the toxins must take place by the bowels, skin, and kidneys, and therefore it is necessary to encourage the action of all three. The action of the bowels can be maintained by enemata of 1 tablespoonful of sodium sulphate dissolved in a pint of warm water, and given morning and night.

When there is severe headache a hot mustard foot-bath may be given, which [illegible] relieve the head. After this the patient is warmly wrapped up in blankets, care must be taken that he is not oppressed by the clothing, for only those who have been seriously ill can appreciate how embarrassing the weight of heavy blankets is to the heart. It is hoped that by these means the action of the skin will be stimulated.

In order to dilute the toxins, and at the same time to stimulate the action of the kidneys, an alkaline treatment, with plenty of fluid, is required. This can be effected by administering 2 to 4 quarts of iced Célestins variety of Vichy water in the twenty-four hours, or the same quantity of any alkaline mineral water, to each pint of which 30 grains of sodium bicarbonate have been added; or by Sternberg's mixture as recommended above; or an effervescing drink can be made up of sodium bicarbonate and fresh lime-juice, but care should be taken that this is mixed in such quantities as to be neutral, and it may, if necessary, be combined with sodium sulphate. If this alkaline treatment cannot be given by the mouth, then the bicarbonate of soda must be administered as warm enemata.

Symptomatic Treatment.—As regards symptoms, if there is great pain, this can be relieved by a small dose of phenacetin, while severe lumbar pain may be relieved by hot fomentations; but if no urine is passing, the warm mustard bath will be better.

Vomiting is treated by sips of iced Vichy, iced champagne, a blister to the pit of the stomach, a dose of a mixture containing chloroform, or a hypodermic injection of morphia. If there is much fever, this must be treated by cool sponging and cool applications to the head.

Black vomit should be treated by the application of the ice-bag to the pit of the stomach, and hæmorrhages in general should be met with doses of calcium chloride or hypodermic injections of adrenalin or ergotin.

In these bad cases it is advised by some authors to rub olive oil into the skin in quantity, with a view of ladening the endothelial cells of the blood capillaries with fatty particles, and so protecting them against the action of the toxins.

Anuria requires treatment by hot fomentations to the loins, or cupping and hot-air baths and Carroll recommends the injection of 15 grains of urea, either hypodermically or by the rectum, with a view to stimulating renal activity, on the ground that in these bad cases the production of urea by the liver is not sufficient for that purpose.

Cardiac failure requires hypodermic injections of strychnine, camphor dissolved in ether or oil, or simply ether.

Diet.- No food should be given for two or three days, but only the alkaline drinks, and champagne if necessary, the idea being to relieve the stomach and prevent the accumulation of waste products in the system, and so to save the kidney from too much work

After this time, or if the temperature is below 102 F., milk and lime-water, toast water, and barley water may be given. With a view to saving tissue waste and getting fat into the circulation, pure frozen cream, cold white wine-jelly or lemon jelly, should be given, or olive oil administered by the mouth or rubbed into the skin, as indicated above.

After the temperature has been normal for some three days, chicken-broth, custard-pudding, blanc mange etc., can be tried, and a few days later the diet can be gradually increased.

Strong beef extracts and strong alcoholic stimulants should be avoided, the best stimulant being iced champagne in tablespoonful doses.

Prophylaxis.- Yellow fever is generally conveyed from one place to another by ships, but in order to produce an epidemic several factors are necessary viz., cases of the disease from which *Stegomyia calopus* may become infected, together with conditions of temperature, moisture, etc., suitable for the development of the germ in the mosquito, and also for the propagation of the mosquito itself, together with the presence of non-immune people for the mosquito to infect. It is also necessary to bear in mind that the incubation period is usually from three to six days, and therefore quarantine must be of at least five days, or, to be on the safe side, of six or seven days' duration. In order that the mosquito may become infected it must bite a patient during the first three days of the illness, and another fourteen days must elapse before it is able to infect non-immunes. Therefore an infected ship must be anchored at least a quarter of a mile from the shore and from other ships. The sick must be placed in mosquito-proof rooms, the crew quarantined for at least six to seven days, and the whole ship disinfected by a Clayton's disinfector, preferably between 9 a.m. and 3 p.m., while the mosquitoes are quiescent.

Dock-labourers working on suspected or disinfected ships should live in special gnat-proof buildings, and be under medical supervision.

With regard to an infected area, it must be remembered that *Stegomyia calopus* is essentially domestic in its habits, that it is active from 2 p.m. till early morning, but that it is quiescent between the hours of 9 a.m. and 2 p.m., when, therefore, visits can be made to infected areas without risk. Further, the mosquito is known to bite dead bodies and suck the blood, but this will seldom infect it, as a patient generally lives longer than the three days during which the disease can be communicated to the mosquito Lastly, it can pass through a screen with fifteen meshes, but not through one with twenty meshes to the inch.

The mosquito does not die after laying its eggs, but lives until it has laid seven batches *i.e.*, some thirty days. The eggs laid twelve days after infection are capable of carrying the infection into the second generation, which can spread the disease fourteen days after becoming imagines As the mosquito is believed to be non infective when it bites in the daytime, non immunes may visit an endemic area in the day with impunity, but must not stay late in the afternoon

When a person is moved from an infected room, disinfection should be begun at once. All cracks, openings, etc., should be closed with paper, and fumigation carried out, preferably by means of sulphur dioxide gas, or if there is an objection to this because of the damage it causes, pyrethrum may be used, but must be burned in the proportion of 1 pound to 1,000 cubic feet of air-space if the mosquitoes are to be merely stupefied, and 2 pounds if they are to be killed: or tobacco, 1 pound per 1,000 cubic feet, may be used.

In addition, if an epidemic is to be eradicated, cases must be at once notified to the central authority, and patients must be strictly treated in mosquito-proof rooms, and every person, immune or non immune, must use mosquito-curtains, while an anti-mosquito scheme on the lines mentioned under Malaria must be undertaken. Special care must, however, be taken to eradicate, after a careful survey, all the breeding-places, not forgetting those in old tins, cocoanut-shells, gutters, small pools, etc. In endemic areas, houses and public buildings should be rendered gnat proof Lastly, when an epidemic breaks out in any place, it may be taken for granted that the importation took place at least two to three weeks prior to the discovery, for this is the time required for the incubation of the germ in the mosquito and in man; and it may also be assumed that mild cases are probably being treated for influenza or malaria. Therefore a house-to-house visitation is almost necessary, in order to find out the extent of the outbreak.

Given a free hand and plenty of money, there should be no difficulty in dealing with a threatened epidemic, but the public must be won over to assist, and offenders must be fined for transgressions against sanitation, as is done by the Americans in Panama, the offences being the presence of mosquito larvæ, imperfect screening of the house, accumulation of water, etc.

The prophylactic measures may be summarized as follows:—

A. Where there is reason to believe that yellow fever is endemic.
(1) Segregation of non-immunes, partial or complete, town planning.
(2) Screening:—
  (*a*) The bed.
  (*b*) The veranda.
  (*c*) The house
(3) Systematic mosquito destruction:—
  (*a*) Removal of breeding places.
  (*b*) Screening of water cisterns.
  (*c*) Oiling.
  (*d*) Drainage.
  (*e*) Bush clearing.
(4) Education. Infliction of fines for transgressions
(5) Quarantine administration.
(6) Non-immunes only to visit endemic area in the daytime.

B. Where yellow fever has broken out.
(1) Removal of all non-immunes outside the infected area, and deflection of the traffic outside the infected area.
(2) Isolation of cases and suspected cases.
(3) Provision for isolation of contacts.
(4) Early notification.
(5) Fumigation.
(6) Emergency mosquito measures:—
  (*a*) Removal of receptacles.
  (*b*) Oiling.
  (*c*) Screening.
  (*d*) Drainage.
(7) Education:—
  (*a*) Lectures.
  (*b*) Meetings.
  (*c*) Pamphlets.
(8) General organization of the medical forces.

No anxiety need now be felt as to the spread of yellow fever to Asia though the Panama Canal has been opened, for it appears as though not merely yellow fever, but all infectious and contagious fevers are bound to be eradicated from the Canal zone under the able American rule.

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CHAPTER XLIII

DENGUE AND ALLIED FEVERS

Dengue—Seven days' fever—Dengue-like fevers—References.

DENGUE.

Synonyms.—Febris Endemica cum Roseola, Exanthesis Athrosia, Knokkelkoorts Arthrodyme, Fièvre Rouge, and probably the 'seven days' fever.'

There are upwards of one hundred known synonyms for this fever, many of which refer to it as a form of rheumatism, or give it fanciful terms, such as 'breakbone' or 'breakheart,' 'broken wing' or 'giraffe fever.' It is sometimes called 'three days' fever,' a term by which pappataci fever is also known.

The word 'dengue' is said by Vambery to be of Arabic origin, and to mean weakness, but it might equally be of East African, Indian, or Spanish origin.

Definition. Dengue is a term covering one or more acute specific non-contagious fevers of unknown origin, but caused by a virus contained in the blood. It is characterized by two febrile paroxysms, separated by an intermission or remission, without jaundice, albuminuria, or hæmorrhages, and with a marked leucopenia, and a pulse which varies directly with the temperature. It is spread by the agency of *Stegomyia calopus* Meigen, 1818, and probably by *Culex fatigans* Wiedemann, 1828.

History.—It appears to have been first recognized at Batavia, in Java, in the year 1779, by Bylon, though it may have been noted by Pazzio previous to this in 1764-68 in an epidemic in Seville. It was soon discovered in other places, being found from 1779 to 1780 in Egypt, Arabia, Persia, and North America, and in 1784 in Spain, to which it appears to have come from the West Indies, and in 1818 in Peru. In 1824-28 it occurred all over the tropical and subtropical zones, and in 1830-70 it formed a series of large and small epidemics in the same regions. From 1871-73 there was an epidemic implicating East Africa, Egypt, Arabia, India, Burma, Indo-China, and China, and spreading later to America and North and West Africa—*i.e.*, practically to all the tropical regions. In 1876-88 it was epidemic in Hong Kong, Egypt, Syria, and the Mediterranean, and in the Fiji Islands in 1885, to which it was conveyed by a European suffering from the complaint. In 1889 it was especially prevalent in Asia Minor, Turkey, and Greece. From 1890 to 1895 there were outbreaks in Senegambia and Hong Kong, and in 1894 it was introduced into North Queensland. From 1895-96 there were epidemics in Bombay and in Charleston. In

1897-98 it was epidemic in Georgia, Florida, and Texas. In 1901 it occurred in Penang and Asia Minor; in 1902 in Hong Kong, Singapore, Madras, Rangoon, and Upper Burma. In 1906 it occurred in Saigong on a French warship, and recently it has been prevalent in Singapore, West Australia, and Ceylon. Manson says that an epidemic or pandemic takes place about once in twenty years.

The discovery of the disease, therefore, appears to have been first made by Pazzio and Bylon, and the first full clinical description given by Dickson in 1828.

The first attempt to find a causation for the disease was by McLaughlin in 1886, who found micrococci in the blood, but this was disproved by Klein, Wright, Crookshank, and Macfadyen. In 1903 Graham stated that he had observed small hyaline, unstainable rods or dots in the red blood corpuscles, which he considered to be protozoal parasites of the nature of Plasmodia. This discovery has been refuted by Carpenter and Sutton, Guiteras, Agramonte, Kiewiet de Jonge and Hahn, Still and Ashburn, and Craig. Graham fed *Culex fatigans* Wiedemann on patients suffering from dengue, and claimed to have found his parasites in these mosquitoes up to the fifth day after feeding. He did not find any oökinetes or oocysts, but he says he found spores in the cells of the salivary glands of the mosquitoes from forty eight hours to one month after they had fed on infected blood. Further, he states that he caused a typical attack of dengue by injecting subcutaneously a solution, in normal saline, of the salivary glands of a mosquito which had bitten a dengue fever patient twenty four hours previously. He only performed one experiment, because the illness caused was very severe, but he succeeded, after an incubation of four to six days, in infecting healthy people by the bites of mosquitoes (*Culex fatigans*) fed on dengue fever patients

Though Ashburn and Craig (in 1907) have not supported Graham by finding the parasite, they have supported him by proving that a typical attack of dengue can be produced by the intravenous inoculation of filtered and unfiltered blood from an infected patient, and that the disease can be, and usually is, transmitted by the bite of *Culex fatigans* Wiedemann.

In 1912 and 1913 Laloir drew attention to *Stegomyia calopus* as the carrier of dengue. Cleland, Bradley, and McDonald demonstrated that the virus of dengue fever was carried by *Stegomyia calopus*, in which it underwent development Archibald found that the same insect was the only possible carrier in certain parts of the Sudan. These observations support Legendre's earlier views with reference to Hanoi. The leucocytic formula has been carefully studied by Ashburn and Craig and by Archibald.

Climatology.—The history of the disease indicates roughly its geography, which lies mostly in the tropics, but can extend to the subtropical zones. Cases have been reported from Southern Europe. Its usual boundaries are 32° 47′ N. and 23° 23′ S., but during warm weather it may spread to 36° 10′ N., and even to

42° N. and 28° S. in exceptional cases. It is, therefore, a disease of tropical climates, and of warm weather in other climates. It appears to be favoured by low-lying lands near the sea, well supplied with water, and not to be found at high altitudes; but there are exceptions to this. It occurs in Australia, where it has appeared since 1885, and is common in the Anglo-Egyptian Sudan and along the Red Sea.

When the distribution of dengue is compared with that known for *Culex fatigans*, it will be seen that the two coincide most remarkably. In fact, at the present time it appears as though the geographical distribution depends upon the distribution of that insect, together with the importation or presence of infected persons.

Ætiology.—We are indebted to Graham and Ashburn and Craig, and to Cleland, Bradley, and McDonald, for our knowledge of the ætiology of this disease.

There appears to be no doubt that dengue fever is caused by some unknown living organism which requires over two days to increase so as to produce the symptoms of the disease when inoculated into human beings, and generally five to nine and a half days when produced by bites of an infected stegomyia.

Both Graham and Ardate have observed small bodies in the red blood-corpuscles, which are described as small, usually round, but sometimes elongated, bodies about one-fifth to one-third of the size of a red corpuscle. They divide up into minute granules, which become extra-corpuscular.

This organism exists in the blood, as can be shown by the intravenous injection of 20 c.c. of dengue fever blood producing typical attacks of the disease, the incubation usually being two to three days; but it is so small that it will pass through the pores of a filter which will retain *Micrococcus melitensis*, which is only 0·4 μ in diameter, as is demonstrated by the production of the disease by intravenous injections of filtered dengue fever blood, the incubation being two or three days, as before. It may also be present in the lymphatic glands, the gland juice being at times infective, as proved by experiments.

Blood is infective from two to eight days, but not after the fourteenth day, and the virus is said to be transmitted by the bites of *Culex fatigans*, which is thought to be an agent in the spread of the disease, but Cleland, Bradley, and McDonald's experiments have thrown considerable doubt on this. There may, however, be two distinct diseases, one caused by a stegomyia and one by a culex, the incubation period being about three days sixteen hours. It can also be transmitted by the bites of *Stegomyia calopus*, when, further, there is a natural immunity against the disease in some people, and also some degree of acquired immunity of unknown duration obtained by an attack.

The points in the ætiology which require further research are the nature of the organism and its chemical products; the changes, if any, which the parasite undergoes in the mosquito; the length of time during which the mosquito can carry the infection; whether any mosquito other than *Culex fatigans* and *Stegomyia calopus* can spread the disease; and how long the acquired immunity lasts in man. In conclusion, it may be said that there is no evidence of infection other than by the bite of mosquitoes, and there is no evidence that a monkey can be infected by inoculation.

Pathology.—There is but little that can be written on this subject, as the cause of the disease is unknown, and therefore, of course, its action cannot be explained.

Morbid Anatomy.—This appears restricted to the description of the complication which killed the person—viz., peritonitis or pleuritis.

Symptomatology.—The *incubation* period, judging from experimental infection by mosquito-bites, varies from three to six days in the case of culex, and five to nine and a half days in the case of stegomyia. Prodromata are usually absent, but general malaise may be felt during a period not exceeding three days before the onset.

The *attack* is usually sudden, and introduced by severe pain in some part of the body, or merely by the sensation of extreme fatigue, or by chilliness and shivering, or by deep flushing of the face. In children convulsions or delirium may usher in the illness. In any case the temperature rapidly rises, the pulse quickens, and the skin and mucosæ become markedly congested, especially about the face, mouth, and throat. The conjunctivæ are injected, the eyes watery, and sometimes vomiting and purging are also present. The disease now progresses for one, two, or three days, after which there is, as a rule, a remission or an intermission.

Course.—During this period the temperature rises to 103° to 106° F., and the pulse increases proportionately with the temperature to 90 to 120 per minute. Severe pains in the head, and especially in the eyeballs, are experienced, and, in addition, pains in different parts of the body, especially in the lumbar region and the legs. Often the joints are painful, usually without any sign of redness or swelling. This pain in the joints appears really to be due to the muscles in the neighbourhood, as the joint can often be passively moved without pain, while active movement induces almost agony. There are, however, rare cases in which the joints are affected, as is shown by redness and swelling. As regards the alimentary canal, the tongue is moist, but becomes covered with a white-creamy fur. There is no appetite, nausea and vomiting are not uncommon, and constipation or diarrhœa may be present. Enlargement of the cervical and axillary glands is present to the extent of 30 per cent. to 70 per cent. of the cases of some epidemics. The glands remain enlarged for some time, and may be tender on pressure. The juice of these glands has reproduced the disease in two out of three cases. The circulatory system is not affected, except that fainting occurs at times, while a sensation of præcordial discomfort or of suffocation may be complained of. Insomnia and delirium are not infrequent, but meningitis and neuritis must be uncommon if they occur at all, though hyperæsthesia of the skin may be observed. The skin shows the congestion already mentioned, which is not always present, being at times replaced by the opposite extreme of pallor. Jaundice, if it occurs, is rare. Hæmorrhages are rare, and will be mentioned as a complication. The changes in the blood have been carefully worked out by Ashburn and Craig. The erythrocytes are usually normal in appearance and number, but a few poikilocytes may be seen, while the hæmoglobin and colour-index are also normal. Leucopenia is so constant as to be of diagnostic importance, varying from 4,860 to 1,200, the average being 3,800 per cubic millimetre. The leucocytes are normal in appearance, but there is an increase of the large mononuclears and eosinophiles, and a decrease in the polymorphonuclear leucocytes. The urine appears to be usually quite normal, except that it is high-coloured, but may contain a minute trace of albumen, and in severe cases Guiteras says the diazo-reaction can be obtained.

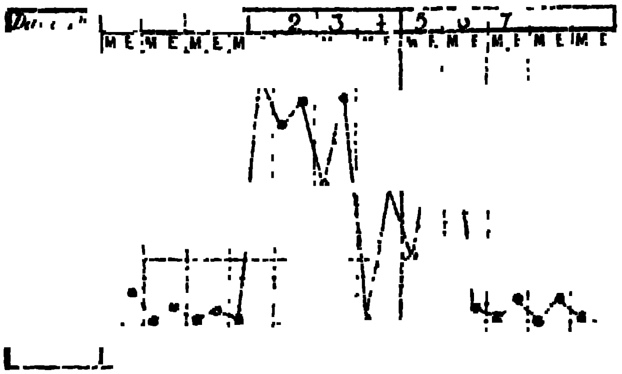

FIG. 630.—TYPICAL TEMPERATURE CHART OF DENGUE FEVER.

Intermission.—On the third day the temperature usually falls, but rarely reaches to normal. This fall may be accompanied by the usual signs of a crisis—namely, profuse perspiration, the passage of much urine, violent diarrhœa, and bleeding from the nose—but in many cases these signs may be absent. The patient now feels better, except for slight pains, and a genuine intermission in the disease is established. In other cases, however, this intermission may be entirely wanting, and the temperature may only remit, remaining at 100° to 102° F.

Second Attack.—The intermission or generally remission lasts until the fifth day of the illness, when the temperature rises to some point usually below 103° F., and at the same time a rash appears on the palms and backs of the hands, and rapidly spreads to the arms, the trunk, and the legs. This rash may be of two types—a measly eruption of small, circular, dark red maculo-papules, which almost entirely disappear on pressure, or a scarlatiniform eruption of close-set bright red points, which may coalesce and form large red patches. Eruptions intermediate in appearance between these two types may, however, be present, and occasionally only an abortive or no eruption at all occurs.

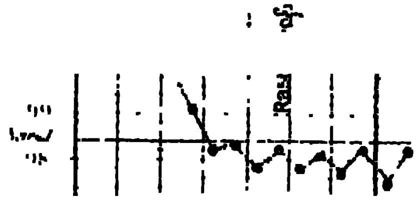

FIG. 631.—THE ATYPICAL TEMPERATURE CHART OF DENGUE FEVER.

This rise of temperature may last from a few hours to a day, and generally declines by crisis, with or without perspiration, on the sixth day. The skin eruption usually lasts from two to eight days, after which occasionally there is a desquamation, which may continue for two to three weeks.

The typical disease shows a first attack, a remission or intermission, and a second attack, though the two attacks may become merged together. The typical rash may be absent, and sometimes the disease is so mild that it ends on the third day with the first crisis.

Convalescence may be quick and permanent, but, on the other hand, it may be protracted and complicated with sequelæ. Immunity is said to be complete twenty-four days after recovery from a typical attack.

Varieties.—It is now generally agreed that seven days' fever is merely a variety of dengue fever, and therefore for comparison we attach a description of it to this chapter.

Megaw distinguishes the following varieties:—

1. *The Evanescent Type*, with only a short slight attack of fever, and corresponds with one variety of the old *febricula*, and cannot be recognized except during an epidemic of dengue fever.

2. *The Interrupted Fever Type.*—This is the three days' fever, followed after one or two days of apyrexia with another attack, and is typical dengue fever. True intermission is, however, rare, a fever of the saddle-back type being much commoner.

3. *The Saddle-Back Type.*—This is the so-called seven days' fever.

4. *The Continued Fever Type.*—This is rare, and is characterized by a lack of the usual remission or intermission of the fever.

Complications.—The rarity of the symptoms of hæmorrhage may perhaps justify its mention as a complication. It takes place from the mucosæ, as already mentioned, of the nose, stomach, intestines, and uterus. Hyperpyrexia may occur as a complication, but is rare, and pleurisy, pericarditis, orchitis, endocarditis, and meningitis sometimes complicate the disease and alter its characteristics. We have seen enteric develop in three typical cases of dengue, and appendicitis in two cases.

Sequelæ.—The most important sequelæ are the pains in the joints and muscles, which worry patients considerably. This polyarthritis affects joints of all kinds, both small and large, and is associated with swellings, so that the condition is like rheumatism, but salicylates are useless. The severe type is rare, but is very distressing, and may last six to eight weeks or longer. It is not uncommon in a milder form, with pain in various joints and slight swelling, and in this condition may last for months.

Relapses are said to take place, but Ashburn and Craig doubt whether any occur a short time after an attack, as the persons who were supposed to relapse, in their experience, really suffered from malarial fever; for, as a matter of fact, there is an acquired immunity for some little time after an attack which prevents such relapses.

Reinfections.—These are not uncommon, and each attack may be quite typical, being associated with the rash.

Diagnosis.—This is based on the sudden onset with extremely severe muscular pain, the remission or intermission in the course of the fever on the third or fourth day, the rash generally appearing on the third to the sixth day. The diseases most likely to be mistaken for dengue are yellow fever, malaria, influenza, scarlet fever, measles, rheumatic fever, smallpox, tonsillitis, typhus, and pappataci fever.

Yellow fever is recognized by its slower pulse, jaundice, albumen in the urine, and hæmatemesis; *malaria* by its blood parasites; *influenza* by the absence, as a rule, of any eruptions and the presence of catarrhal symptoms; *scarlet fever* by the presence of the sore throat with enlarged cervical glands; *measles* by the catarrhal symptoms and the absence of the severe pains; *rheumatic fever* by the swelling of the joints; *smallpox* may be with difficulty recognized until the eruption comes out; and *tonsillitis* may be recognized by examining the throat. In the tropics, where *enteric* is frequently atypical and often begins suddenly, there may be difficulty during the first few days in distinguishing the two diseases. The very severe pains are, however, rare in enteric, and the course of the fever will clear the diagnosis. From *typhus* it may be diagnosed by the leucopenia. From *pappataci fever* it may be distinguished by the presence of the rash and the frequent rise of the temperature on the fourth to fifth day.

Prognosis.—This is quite good, as the mortality is usually nil, but in Australia it caused 1 death in 1,000 cases, especially in those under five and over sixty years of age.

Treatment.—No rational treatment can be given, as we do not know what the nature of the cause will prove to be. Symptoms must, however, be relieved. The fever and headache may be combated with cool sponging and cool applications; the pains by hypodermic injections of morphia or doses of Dover's powder: this will also relieve the nervous symptoms, which otherwise will require bromides. Antipyrin, phenacetin, and aspirin, may be administered with care, and the bowels should be opened by calomel. The diet must be low, and stimulants should not be given.

Prophylaxis.—Protection against mosquitoes, as described under Malaria, excluding, of course, quinine prophylaxis, is the correct method of preventing the disease.

SEVEN DAYS' FEVER.

Remarks.—In our opinion the seven days' fever is dengue or a variety of it. We have come to this conclusion after having had the opportunity of studying epidemics of dengue and of the so called seven days' fever in various countries.

History.—This disease was described by Rogers in 1905-08 as a sporadic fever of Indian seaport towns. It is probably identical with Crombie's simple continued fever, and, according to many observers, including ourselves, is a form of dengue.

Climatology.—So far, in India and Ceylon it has been found in towns in low-lying districts near the sea, and is believed not to spread inland. In Calcutta it occurs from May to September, and is very common in Colombo during the same months.

Ætiology.—Rogers found a motile bacillus related to the coli bacillus in the blood, which he thinks may possibly be the cause of the disease. It resembles the *Bacillus coli communis* in size and shape, and possesses flagella; is decolourized by Gram; produces a diffuse haziness in broth; slowly liquefies gelatine; grows on agar like *B. coli*; does not produce gas in glucose agar; nor gas, nor acid, in dextrose, lævulose, and maltose broths; nor does it ferment arabinose, galactose, saccharose, lactose, inulin, salicin, erythrite, mannite, or dulcite. It is agglutinated in 1 in 20 and 1 in 40 dilutions of the serum of seven days' fever patients. These observations have not been confirmed. Clayton suggests that the disease is carried by mosquitoes. The fever is commonly found among Europeans, and especially among people having to do with shipping, and also in new-comers.

Pathology.—The morbid anatomy is unknown, as the mortality is nil.

Symptomatology.—The incubation period is unknown, and no prodromal symptoms have been recorded. The invasion is sudden, with a rapid rise of temperature to 102° or 105° F., but the pulse is not as quick as it should be, compared with the temperature.

The face is flushed and the palpebral conjunctivæ injected, and some rose-coloured spots may appear on the skin. Pain is felt in the back and, less commonly, in the limbs. After the initial rise there is usually a gradual marked remission of the temperature for two to three days, when the fever again rises, producing the typical saddle-back remission. After the second rise the temperature gradually or quickly falls to normal, and the disease ends about the seventh to eighth day. There is generally frontal headache, and the tongue is furred on the dorsum, while the edges are red. Nausea and vomiting are not common; the bowels are usually normal, though constipation or diarrhœa may occur. The abdomen is often distended, and may be painful. The liver is usually normal, but may in a few cases be slightly enlarged, and the spleen is at times enlarged. The respiratory and circulatory organs are normal, except that the pulse is often slow as compared with the temperature.

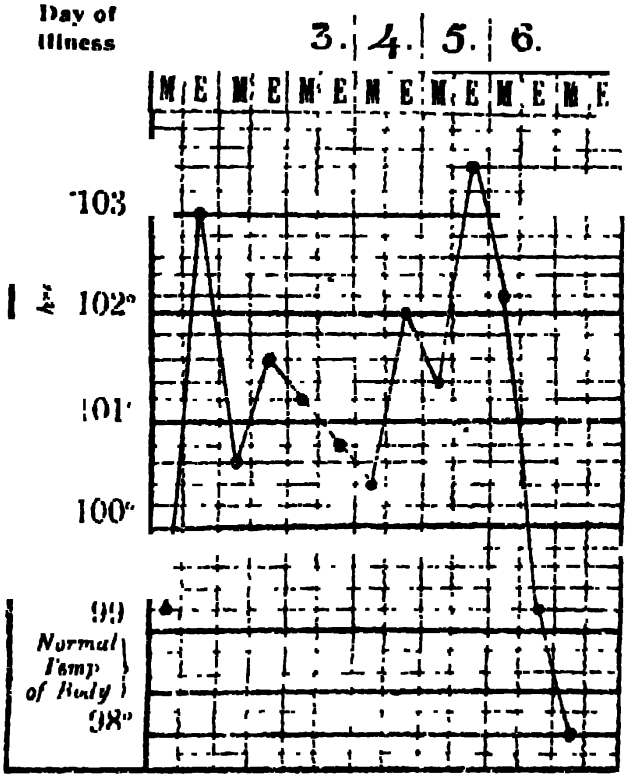

FIG. 632.—TEMPERATURE CHART OF A CASE OF SEVEN DAYS' FEVER.

The blood shows a slight reduction of the erythrocytes and a marked leucopenia—2,000 to 4,000 per c.c. The polymorphonuclear leucocytes are reduced, and the lymphocytes and mononuclears are increased. Nothing abnormal is found in the urine, except the usual appearance of febrile urine.

Rashes are frequent. The most common is a mottling or a diffuse erythema of the extensor surfaces of the forearms on the fourth to sixth day, which may fade before the temperature falls.

There are no complications or sequelæ, and the prognosis is excellent, as the mortality is nil. Mild recurrences in following years may be met with, but relapses in the same year, though rare, do occur, as we have met with such a case. Convalescence is rapid.

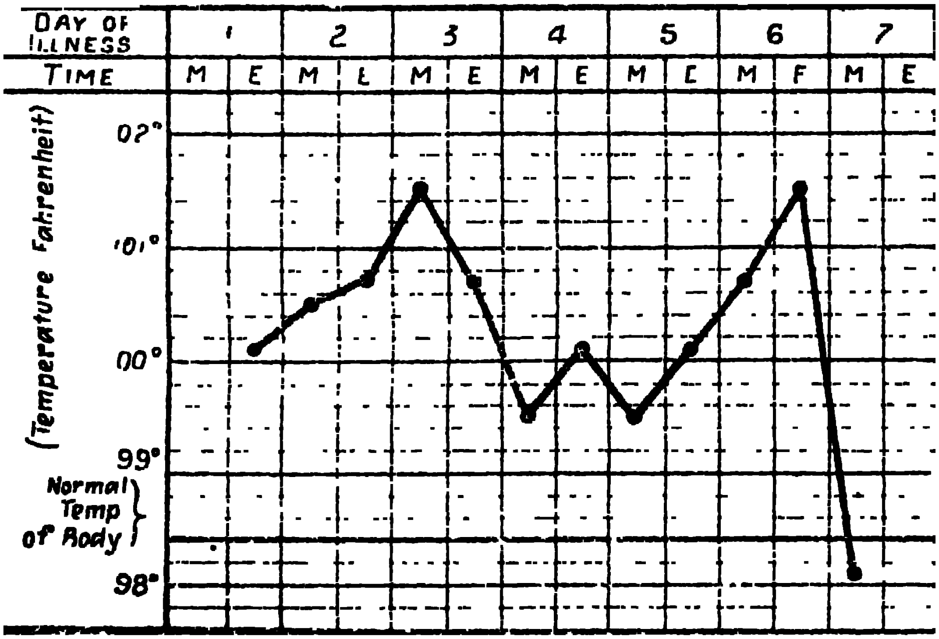

FIG. 633.—TEMPERATURE CHART OF A CASE OF SEVEN DAYS' FEVER.

Diagnosis.—It can be distinguished from malaria by the absence of parasites, and the slow pulse with high fever; from influenza by the absence of respiratory symptoms.

Treatment.—This is purely symptomatic.

DENGUE-LIKE FEVERS.

Synonym.—Climatic fevers.

Under this heading come the fever of the Antilles, the fever of the Red Sea, the six days' fever of Asia, the fever of Massowah, the six to eight days' fever of Aden described by Smith and Loughman, the six days' fever of the Canal zone in Panama described by Deeks, and the pseudo-dengue fever of Cochin China, which are all closely allied to dengue fever, lasting about seven days, and being associated with pains in different parts of the body, and having, in brief, the symptoms described above for seven days' fever or for dengue fever.

VAN DER SCHEER'S FEVER.

Synonym.—Five days' fever.

Definition.—A fever usually lasting for five days, and associated with an eruption of red macules and papules about the size of a pin's head, occurring on the trunk. It may be a form of dengue.

Remarks.—This fever, first described by van der Scheer, has also been investigated by Neeb, but its nature is at present not understood.

Symptomatology.—The illness begins suddenly with severe headache and backache, the temperature rising to 104° to 105° F. in the evening, but remitting considerably in the morning. Sometimes there is bilious vomiting and delirium. On the third day the eruption appears as macules or papules about the size of a pin's head on the chest, which spread to the back and abdomen. After five days' remittent fever the crisis comes on the sixth or seventh day, when the temperature rapidly falls below normal. This fall is accompanied by moderate sweating. In more severe cases the crisis is absent, and, cardiac failure setting in, the patient dies cyanosed.

Some days after the crisis there is a furfuraceous desquamation associated with pruritus on the palms of the hands and soles of the feet, and at the same time there is a considerable loss of hair and a bitter taste in the mouth.

Diagnosis.—It can be distinguished from malaria, relapsing fever, etc., by the absence of parasites in the blood, and from measles by the absence of the catarrhal symptoms, from scarlet fever by the absence of a sore throat, and from typical dengue fever by the temperature tracing.

Treatment.—The treatment is purely symptomatic, but it is recommended that injections of caffeine be administered on the sixth day to prevent a possible attack of cardiac failure.

IM-PYENG.

According to Landis and Matignon, there exists in Corea a fever called by the inhabitants Im-Pyeng. It is most frequently met with in the country districts from February or March to July, when it is most common among the poor, but affects all classes of society. It would appear to us to be allied to dengue fever.

Ætiology.—The causation is unknown, but it is regarded as contagious by the inhabitants of Corea. Matignon considered that it resembled relapsing fever, but was unable to find a *Spiroschaudinnia* in the blood.

Symptomatology.—The disease begins with headache, backache, or vague pains, which may become violent, while the temperature may rise to over 104° F. in the evening, but remits considerably in the morning, rising again in the evening to about 102° F., and again remitting considerably in the morning, and this fever may be accompanied with delirium. The fever continues for some seven to ten days, but usually after the sixth or seventh day the fever declines, and reaches normal in twenty-four to thirty six hours, this decline being associated with a profuse perspiration.

Sequelæ.—The patient is left with both general and cardiac weakness after an attack.

Treatment.—Quinine sulphate in association with antipyrin is the treatment usually adopted.

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CHAPTER XLIV

PAPPATACI FEVER

Synonyms—Definition—History—Climatology—Ætiology—Pathology—Morbid anatomy—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—References.

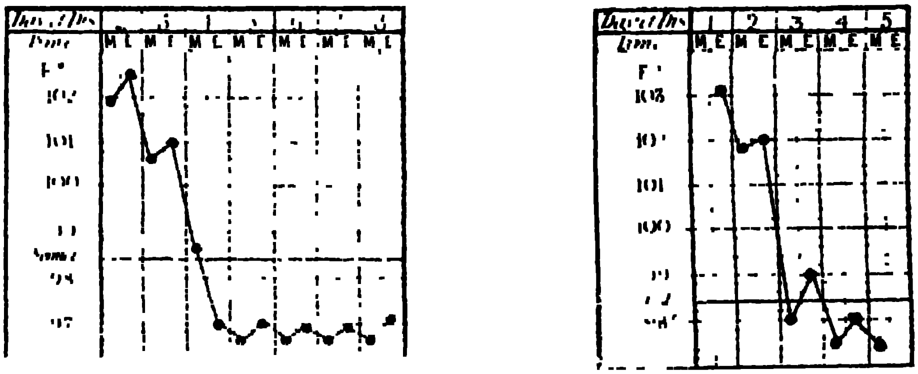
Synonyms.—Three days' fever, Phlebotomus fever, Sandfly fever, Summer fever. *French:* Fièvre des trois jours, Fièvre de Pick, Fièvre de Pym. *Italian:* Febbre gastrica, Febbre estiva, Febbre climatica, Influenza estiva, Influenza malarica, Mal della secca, Febbre dei tre giorni. *German:* Hundskrankheit, Sommerfieber, Endemischer Magenkatarrh. *Latin:* Febricula *pro parte*, Gastro-enteritis endemica, Gastro enteritis climatica.

Definition.—An acute specific fever of unknown causation, lasting three days, and characterized by nervous symptoms, pains in various parts of the body, and gastro intestinal disturbance, and spread by the agency of *Phlebotomus papatasii* Scopoli, 1786.

History.—In 1804 Pym described a fever of three days' duration as occurring in the Mediterranean basin, and this was confirmed by Burnett in 1816. From that time constant references may be found to this complaint in the English Army reports concerning Malta, where it was sometimes called 'summer fever.' In 1855-56 there was a considerable number of cases in that island, due to the passage of the troops *en route* to the Crimea. The fever was also described by Cicoli in 1871-75 in Pola, by Pick in 1887, by Karlinski in 1889, by Taussig, who was the first to suspect *P. papatasii*, in 1905, and in the same year by Panec. In 1903 McCarrison was the first observer to differentiate the disease, which he did in Chitral, when he suspected the sandfly as the causal agent. In 1907 it was noticed that although undulant fever had almost disappeared from Malta there were no less than 340 admissions for 'simple continued fever' into the Army hospitals, and in this year Gerrard and Marratt drew attention to this fever. In 1909 Doerr, Franz, and Taussig published their classical account of the ætiology and symptomatology of the disease, thus placing it upon a sound basis, and in the succeeding year Birt confirmed and extended these discoveries, and in the same year Tiraboschi found it in South America, and Phillips in Cairo. In 1911-12 Miorcec and Laplanchi found it in Crete, Niclot in Oran, Sergent in Biskra, Léger and Séquinaud in Corsica, and Wall described it again in Chitral. In 1915 Castellani found it in Serbia and Macedonia and showed that the so-called Skoplji or Uskub fever is pappataci fever. It occurs in Khartum.

Climatology.—It is found in all the countries bordering on the Mediterranean and Adriatic Seas, and it is known in India, Egypt, South America, and in South Africa (Cairs). It is possible that it may be found to be cosmopolitan in its distribution.

In temperate climates it only occurs in the summer months, and, when studied epidemiologically, it is found to be correlated with the distribution of *Phlebotomus papatasii*. How the infection is maintained during the winter months is not understood, as the imagines do not live through the winter, and as a relapse after a long period is unknown. Doerr believes that the female flies transmit the infection to their progeny, which in turn restart the disease during the succeeding summer. It is, however, by no means certain that the infective agent disappears from the blood when it ceases to be infective on inoculation



Figs. 634 and 635.—Temperature Charts of Pappataci Fever.

Ætiology. The causation of the fever is quite unknown, but the researches of Doerr, fully confirmed by Birt and others, have proved that a virus exists in the blood of patients suffering from the disease; that this virus is infective during the first day, and up to the end of the second day of the fever, but not later; that it is filterable through a Pasteur-Chamberland candle F; that *Phlebotomus papatasii* Scopoli, 1786, is the carrier of the disease, but does not become infective at once after feeding, but, on the contrary, is not infective under a week, after which it can convey the infection. This proves that the organism undergoes development in the fly. How long the fly remains infective is not known with certainty, as it usually dies after ten days' captivity, but it is probable that the disease is transmissible to young broods of flies. The incubation period of the experimental cases varied from three days sixteen hours to seven days, and a few of these cases showed only the gastro-intestinal symptoms, without any sign of fever. Animals have so far not been infected with fever except one small monkey by Tedeschi and Napolitani. Chalmers and O'Farrell have also infected a monkey by intravenous inoculation of human infected blood. It may be noted that phlebotomus can bite in the daytime and not merely at night.

Pathology.—Antibodies appear to be generated during an attack, as Doerr has shown that the serum from convalescents may neutralize infective serum; moreover, this action may be demonstrated during a period varying from one week to two years after an attack. An attack of fever confers a relative immunity, as relapses are seen, but reinfections are believed never to occur, and the natives of an endemic region are believed to be immune, possibly because there has been a previous attack during childhood.

Morbid Anatomy.—In the few post-mortems which have been performed, the signs exhibited have been those of the complication from which the patient died, as the disease *per se* is not fatal.

Symptomatology—*Incubation.*—The incubation varies from three to seven days. Prodromal symptoms in the form of malaise, vague pains, discomfort, and weariness, are generally present in India, but rare in Europe and Africa.

Attack.—The onset is sudden, with a slight rigor or a feeling of chilliness and severe frontal headache, lumbar and body pains. The conjunctivæ are injected and the cheeks slightly flushed. In a fairly large number of cases the flushing of the face and neck is extremely well marked, almost amounting to an erythematous rash. A peculiar feature of this symptom has been described by Castellani—viz., the flushing is persistent, lasting eight to fifteen days after the fever is over, and fades away so slowly that in many cases it is not difficult to diagnose the disease in persons convalescent therefrom. The skin is hot and dry, and the temperature rapidly rises, reaching 104° F., or rarely 105° F., in twenty-four hours. The pulse may reach 100 to 116, but is often unduly slow. The patient is very irritable, and intolerant to sounds. Movements of the eyes are painful, the conjunctivæ are injected, and often show a red band running from the cornea across the sclera. Sleep is impossible at times, but at other times the patient may be very drowsy. The tongue is coated on the dorsum with a white or brown fur, and the edges may be red. The appetite is lost and the sense of taste destroyed, but vomiting is uncommon, though there is pain in the epigastrium and sometimes diarrhœa. The mouth and throat are congested and irritable, and the gums may show a tendency to bleed, and there may be a little bronchitis. The cough is generally dry, with thick, tenacious, muco-purulent expectoration. The tonsils may be enlarged and the uvula congested, but this is not constant. Not only is there the congestion of the tonsils and pharynx, but the mucosa of the soft palate presents a peculiar appearance, showing small hyperæmic roundish spots. The eruption is sharply limited by a line of demarcation between the soft and hard palates. This appearance is not peculiar to the disease, being found in certain cases of relapsing fever, typhus, and malaria. It is rare in typhoid. The liver and spleen are normal. Vertigo and faintness may be present, and pains in the joints, especially in the elbow and knee, as well as in the bones and muscles, and burning sensations in the palms and soles. Cramps are not uncommon. Excitation is frequent, and delirium occasionally seen.

The blood shows a leucopenia—4,000 to 5,000 leucocytes per cubic millimetre—and the differential count is as follows:—

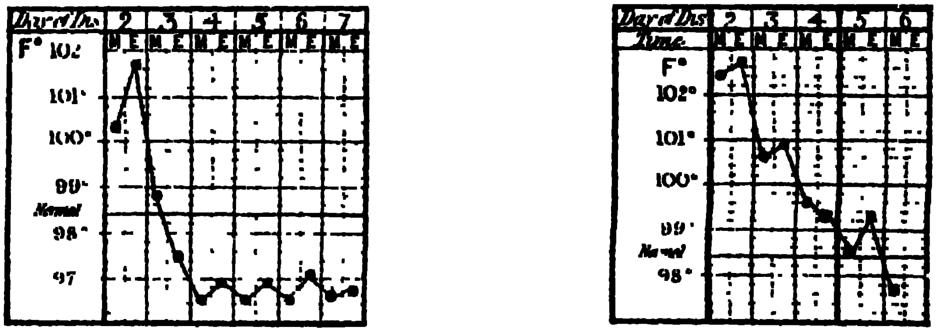
Polymorphonuclears	61·7
Lymphocytes	21·3
Mononuclears	14·0
Eosinophiles	2·7

The blood-pressure is normal during the attack, but somewhat diminished during convalescence.

The urine is diminished in quantity, but is of normal colour, specific gravity, and acid reaction, and does not contain albumen, except rarely, and then only a trace. Ehrlich's diazo-reaction is negative.

The skin is usually dry throughout, but profuse sweating may occur, and erythemata of a morbilliform or a multiform character may be seen, as well as a few roseolæ, but are very rare. A skin change, which starts at the commencement, is a delicate subcuticular mottling of the chest and abdomen, 'Cutis marmorata.'

Course.—In thirty-six to forty-eight hours the temperature falls to normal, but may show a terminal rise. This fall is often accompanied with epistaxis, more rarely with sweating, vomiting, or diarrhœa. When the temperature falls the symptoms abate, but much weakness is felt, the convalescence being prolonged. A post-critical rise is not very rare, and occasionally there may be a low irregular fever lasting for about a week and even longer.



FIGS. 636 AND 637.—TEMPERATURE CHARTS OF PAPPATACI FEVER.

Diagnosis.—In a country where sand-flies exist the disease may be diagnosed by (1) the sudden onset of the fever, ending on the third day without any roseolar-like rash; (2) rheumatoid pains all over the body, very well marked; (3) no enlargement of the spleen; (4) persistent erythematous flushing of face and neck after defervescence in 40-50 per cent. of cases—so-called Castellani's sign. There is, however, no certain sign for diagnosis except human inoculation, and as the incubation is so long the fever will have declared its character before the inoculated person develops the attack. Cuti- and ophthalmo-reactions have failed to be demonstrated. The *differential diagnosis* from malaria can be established by failing to find the parasite in the blood, and by the absence of enlargement of the spleen; from typhoid fever by the sudden onset; from influenza by the absence or mildness of catarrhal symptoms, the relative slowness of the pulse, and the leucopenia, but both diseases may exist together; from sunstroke by the absence of the severe symptoms, nervous symptoms, and the lower temperature; from dengue fever it can only be distinguished by the fever ending the third day, and by the absence of the rash. In countries where pappataci fever and typhus are endemic the diagnosis at the onset between these two fevers may be extremely difficult. Examine the blood: in pappataci there is generally leucopenia; in typhus no leucopenia, frequently leucocytosis.

Varieties.—An afebrile variety, with only headache and body pains, is described, as well as an abortive form lasting two days. Relapses and true reinfections may also occur.

Complications. -The complications are bronchitis and phlebitis.

Sequelæ.- Pains in the bones, neuritis, and a peculiar loss of memory may be sequelæ.

Prognosis.—This is good, as no one has been known to die of the uncomplicated complaint.

Treatment.—The treatment is purely symptomatic, and consists in sending the patient to bed, in administering a saline purgative, and following this by aspirin in 5 to 15 grain doses given three times a day. This treatment is said not merely to relieve the pains, but to render the attack milder. Pyramidon also promptly relieves the pains, while it has been recommended that the phlebotomus bite should be painted with tincture of iodine.

Franz and Kolar recommend the subcutaneous or intravenous injections of colloidal silver, but this hardly appears necessary in such a mild fever. Atoxyl has been found to be useless, and quinine to be harmful.

During convalescence a change of air and an iron tonic may be recommended.

Prophylaxis. - -The only obvious means of prophylaxis consists in isolating the sick and protecting them against the phlebotomus by means of mosquito curtains of a sufficiently fine mesh. It must be remembered that the little fly bites mostly in darkness, and chiefly in houses.

As regards ordinary prophylaxis, a fine mosquito curtain, together with the use of camphor, is to be tried. Fumigation by burning pyrethrum may also be tried.

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CHAPTER XLV

THE AFRICAN TRYPANOSOMIASES

General remarks—The sleeping sicknesses—The trypanosome fevers—References.

GENERAL REMARKS.

THE human African trypanosomiases include two different clinical conditions—viz.—

A. The *sleeping sicknesses* characterized by the fact that we definitely know that the preliminary fever leads to meningo-encephalitis and meningo-myelitis.

B. The *trypanosome fevers* characterized by the fact that we do *not* know that in these cases the disease will end in meningo-encephalitis and meningo-myelitis.

Before Castellani discovered a trypanosome in sleeping sickness, Ford and Dutton had demonstrated that 'Gambia fever' was due to a trypanosome. After this discovery this disease was named 'trypanosome fever,' and was considered to be quite distinct from sleeping sickness. After Castellani had found a trypanosome in sleeping sickness the two diseases, trypanosome fever and sleeping sickness, were at the time judged to be covered by the one name 'sleeping sickness.' Recently, however, *Lanfranchi's laboratory infection* with a trypanosome has lasted for more than seven years, and there is no sign of meningo-encephalitis, as may be judged *inter alia* by the excellent papers which the distinguished professor produces. In fact, judging by the symptoms exhibited by Lanfranchi, which resemble those found in the trypanosomiases of animals, it seems very doubtful whether he will ever show signs of what we clinically call 'sleeping sickness.' Further, the organism with which he is affected appears to be of the *Evansi type*, a form known to be in his laboratory when infection took place.

Under these circumstances, it appears to us to be useful to return to the old name *trypanosome fever* for infections of man and animals with those pathogenic trypanosomes which produce fever and do not end in meningo-myelitis. At present those known in man are the case of Professor Lanfranchi and the infection with a variety of the *Vivax* type described by Macfie, both of which, in our opinion, should remain under this denomination until it is proved that they belong to the sleeping sickness group.

THE SLEEPING SICKNESSES.

Synonyms.—Sleeping dropsy, Negro lethargy, Morbus dormitivus. *French:* Maladie du Sommeil. *Portuguese:* Doença de Sonno. *Italian:* Malattia del Sonno, Letargia dei Negri. *German:* Afrikanische Schlafkrankheit, Trypanosomen Fieber. Native names are very numerous—Lalangola, Láá La-negulo, N'tansi, Mongota, Kónje Márree, Kaodzera, N'dulu, Tula Manugina, Nelavare, Dadane, Toruahebue, etc.

Definition.—The sleeping sicknesses are chronic specific fevers caused by the trypanosomes *Castellanella gambiensis* Dutton, 1902; *Castellanella castellanii* Kruse, 1903, spread by *Glossina palpalis*; and *Castellanella rhodesiensis* Stephens and Fantham, 1910, spread by *Glossina morsitans*, characterized by an inflammatory condition of the lymphatic system leading to a meningo-encephalitis which shows itself as dulness of the intellect, apathy, and lethargy, associated with tremors and a peculiar gait, and unless treated ending fatally.

Remarks.—This chapter should be read in conjunction with Chapter XIX. (p. 380), in which we have outlined a new classification of the trypanosomes with the view of crystallizing the knowledge obtained up to date with regard to these parasites. In so doing we have been compelled to introduce new terms, which we have made as few as possible by utilizing those found in the literature with which we are acquainted. Two of these new terms occur in this chapter, because we have gone more fully into the trypanosomes of man than into those of animals, because this is a work on tropical medicine and not upon trypanosomes, and because those of man are the forms which have been most satisfactorily studied.

Chalmers has introduced the name *Castellanella* as the generic name for the group of trypanosomes which includes the organisms of sleeping sickness, because *Castellanella castellanii* (Kruse, 1903)—synonym, *Trypanosoma castellanii* Kruse, 1903– is the organism upon which practically all the work in connection with sleeping sickness was done prior to the discovery of *C. rhodesiensis*, which is quite distinct from the other two forms.

This is a point not generally recognized, nor is it realized that though *C. castellanii* and *C. gambiensis* are morphologically alike, they may be very different if studied carefully from a pathological and serological point of view, as there is a suspicion that the well-known difference in type between the milder form of the disease as seen in portions of the West Coast of Africa and the severer as seen in Uganda may not be due to acquired partial immunity, but to a difference in the two organisms.

In order to emphasize the necessity for further work with regard to *C. gambiensis*, we have isolated it from *C. castellanii*.

We would also point out that in the few papers in which comparisons have been made with regard to the pathological effects of *C. castellanii* as found in sleeping sickness and *C. gambiensis* as found in trypanosome fever, they both refer to *C. castellanii* obtained from cases in Uganda showing at the time signs of sleeping sickness or simply symptoms of trypanosome fever.

It appears to us that *Castellanella gambiensis* as seen on the West Coast of Africa, and as originally described by Dutton and Todd, requires more study, and we are supported in this by Macfie's work with regard to *C. nigeriensis*, which we believe to be the same organism, and by the observations of Yorke and Blacklock at Sierra Leone.

To summarize, we believe that though *C. gambiensis* and *C. castellanii* are morphologically similar, the clinical difference between the milder form of the disease as seen on the West Coast of Africa and the terribly severe form found in Uganda is such as to demand the separation of these two forms until it is proved that they are really identical from a pathogenicity and serological point of view.

History.—The earliest mention of sleeping sickness so far discovered is by John Atkins, in his little book entitled 'The Navy Surgeon,' published in 1734, in the appendix to which he describes 'the sleeping distemper,' common among the negroes on the Guinea Coast among whom he had travelled in 1721. In 1803 Winterbottom gave an interesting account of the disease as he met with it on the West Coast of Africa near Sierra Leone. His description is quite understandable, and he draws attention to the presence of the enlarged glands of the neck, the association of which with the disease was so well understood that slave-traders would not buy slaves who had enlarged glands.

In 1808 Moreau de Jonnès described the disease in negro slaves in the Antilles. In 1849 Clarke on the Gold Coast, Davis and Daniell on the Guinea Coast, and Ferreira, came across it at St. Thomas. During the next twenty years a number of observers described sleeping sickness, among whom it is important to note that Guérin met with it in 1869 in Martinique in negro slaves who had been imported from Africa. In 1876 Corre gave a good description of the disease as he knew it in Senegal.

In 1891 the first case was brought to London, and was studied by Sir Stephen Mackenzie; and in 1900 two more cases were brought to London, this time under the care of Sir Patrick Manson. The morbid anatomy of these cases was carefully studied by Dr. Mott, who has done so much to clear up the pathology of this disorder.

In 1901 Forde and Dutton found a trypanosome *T. gambiense* (*C. gambiensis*) Dutton, 1902, in the blood of a patient suffering from a peculiar type of fever on the Gambia (Gambia fever, Dutton's disease), which was never thought by them to be connected with sleeping sickness. In 1902-03 Castellani in Uganda found a trypanosome in the cerebro-spinal fluid of persons suffering from sleeping sickness, and in 1903 reported that it was the ætiological basis of the disease. It was named *Trypanosoma castellanii* by Kruse in 1903, and on it most of the work with regard to sleeping sickness has been done prior to the discovery of Stephens and Fantham's organism. Low and Castellani gave a clinical account of the disorder which is largely followed in this chapter, which, therefore, contains a clinical account of the illness produced by *C. castellanii*. Low and Castellani called attention to two constant symptoms which had not been remarked by previous observers, the fever and the peculiar tremors; and Christy published many interesting epidemiological features concerning the disease. In 1903 Sir David Bruce and Nabarro showed that the trypanosome was spread by *Glossina palpalis* Robineau-Desvoidy, a conclusion already reached by Sambon and Brumpt on epidemiological grounds. From 1903-05 much clinical, experimental, and epidemiological work was done by Dutton, Todd, and Christy, the Commissions of the Royal Society and various Governments, and by the members of the Liverpool School of Tropical Medicine. Kleine, in a series of important researches, has experimentally shown that *C. castellanii* undergoes a cycle of development in *G. palpalis*—a fact which has been fully confirmed and extended by Sir David and Lady Bruce, Hamerton and Mackie, and Miss Robertson, as well as Fraser and Duke.

Koch, Laveran, Mesnil, Minchin, Blanchard, Greig, Gray, Tulloch, Kinghorn, Montgomery, Martin, Pittaluga, Lebœuf, and Roubaud, have all studied the disease and its epidemiology, and an International Conference was held in 1907 in London, and a Bureau for the study of the disease founded. This bureau for some time issued monthly bulletins, which are most valuable to the student of the disease: but recently it has become converted into the Bureau of Tropical Diseases.

In 1910 Stephens and Fantham created a new species of trypanosome (*C. rhodesiensis* Stephens and Fantham, 1910) for the parasites found in cases of sleeping sickness in the Luangeva Valley in Rhodesia, because the trophonucleus of a certain percentage of short forms was situate either close to, or even on the aflagellar side of, the kinetonucleus. In 1912 Kinghorn and Yorke showed that this trypanosome was transmissible by *G. morsitans* Westwood, 1850; and in the same year these observers pointed out the importance of the meteorological conditions on the development of the trypanosome in the fly. Further work has been done by Sanderson, Murray, Shircore, and others. As regards the history of the treatment, arsenic was long ago considered beneficial for the trypanosomiases of animals, Livingstone being the first to apply the drug to a horse for the purpose of treating nagana. Since then it has been used for the same purpose by several persons, notably by Lingard (1893) for surra and by Bruce (1896) for nagana, while Laveran and Mesnil introduced sodium arseniate in 1902 for the same disease, E. J. Moore and Chichester advocated the use of hypodermic injections of arsenic, and Thomas and Breinl of the same of sodium arseniate. In the meanwhile Manson had treated several cases of sleeping sickness with arsenic (liquor arsenicalis); and Ehrlich and Shiga had treated various experimental trypanosomiases with colouring compounds belonging to the benzo-purpurin group, of which trypan-red is the best known. Laveran and Mesnil also did some valuable researches on the subject. Thomas, in 1905, first brought the drug 'atoxyl' to the notice of the profession as a means of treatment of experimental trypanosome affections; and Kopke, in 1906, tried it in human beings affected with sleeping sickness.

The beneficial action of atoxyl in sleeping sickness was further confirmed by Broden, van Campenhout, Manson, Koch, and many others. In 1907 Ehrlich and his pupils, Franke and Roehl, discovered the very important fact that trypanosomes may, after a time, become atoxyl-resistant. Ehrlich therefore suggested mixed or alternating treatment with various preparations, and the same suggestion, though based on different grounds, was made by Moore, Nierenstein, and Todd. Plimmer and Thomas introduced tartar emetic, which has been found to be very beneficial, especially if associated with the atoxyl treatment.

Geography and Epidemiology.—The disease was first noticed on the West Coast of Africa at Sierra Leone, but was soon found to extend far southwards, and was also noted to be imported from this endemic area at times to the West Indies, where, however, it soon died out, becoming neither epidemic nor endemic. This fact clearly proved that, though the disease may be introduced by man along channels of intercommunication into a strange country, some other factor is necessary before it can spread from the infected new-comer to the inhabitants. This factor we now know to be a tsetse-fly.

In 1882 the disease had a geographical distribution from Senegal to Loando, and also to the islands of the Gulf of Guinea. Gradually, as civilization spread, it became known that the disease was not confined [illegible] coast but extended far [illegible] in 1898 was known to be at Jebba, on the Upper Niger, and at the Stanley Falls, on the Upper Congo. In the meanwhile Stanley had travelled across Africa with a large number of Congolese followers, and had relieved Emin Pasha and his people at Wadelai, on the Victoria Nile. These followers of Emin Pasha, together with some of Stanley's expedition, who had settled in the country about Kavali, to the west of the Albert Nyanza, were brought by Sir F. Lugard, for political reasons, to Busoga and Uganda. Christy and Hodges believe that the disease was carried from the Congo by Stanley's men, and that they and Emin Pasha's people brought the disease with them into Busoga and Uganda when they were moved from Kavali. But the fact is clear that when, in 1900, the Cooks first noticed the disease in Uganda, it was widespread, and had been there for some time, and it seems probable that Busoga was infected in 1896. Certainly, in 1901, Mengo, the Sese Islands, and the western shores of the Victoria Nyanza, were infected, and the disease spread in 1902 to the eastern shores and to late German East Africa.

In 1904-05 Dutton and Todd found that it had become widely disseminated throughout the Congo Free State, spreading by human agency along trade routes, and expressed the opinion that before long it would pass from the Congo into Eastern Rhodesia. Since then sleeping sickness has been found in that country, though, the trypanosome found in Rhodesia being a different species, it is more probable that the disease has been endemic there, and not recognized for a long time. It appears also to be spreading northwards from Uganda, for Greig, in 1904, found it at Wadelai, on the Victoria Nile, but not as high as Nimuli. It invaded the Lado earlier than 1908, and in 1909 the disease was recognized definitely in the Bahr-el-Ghazal Province of the Sudan.

Therefore the distribution of the disease at the present time may be said to extend along the West Coast of Africa; from St. Louis, in Senegal, to Mossamedes, in Angola; from the coast to Timbuktu on the Niger; through the whole of the Congo into Uganda and Rhodesia; from Uganda and Busoga southwards to late German East Africa; and northwards into the Bahr-el-Ghazal Province. The discovery of the tsetse-fly in Arabia makes it possible that the disease may some day still farther extend its area.

There does not appear to be any seasonal influence.

Ætiology.—From the present state of our knowledge it would appear that from a clinical and ætiological point of view there are three types of sleeping sickness, which may be differentiated as follows:—

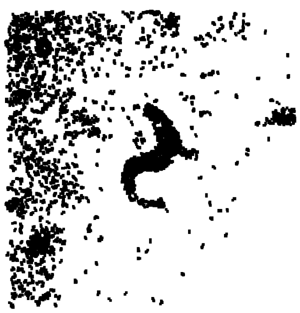


FIG. 638.—TRYPANOSOMA IN CEREBRO-SPINAL FLUID.

Preparation from the cerebro-spinal fluid of a case of sleeping sickness.

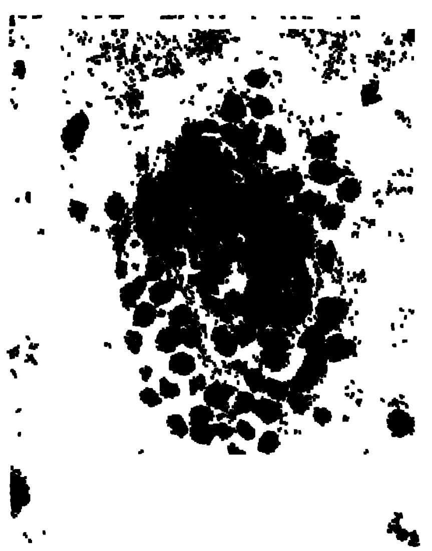


FIG. 638A.—LYMPHOCYTIC ACCUMULATION AROUND A VESSEL IN THE BRAIN.

I. *The Equatorial type*, caused by *Castellanella castellanii* and spread by *Glossina palpalis*.

II. *The Southern type*, caused by *Castellanella rhodesiensis* and spread by *Glossina morsitans*.

III. *The North-Western type*, caused by *Castellanella gambiensis* (synonym, *C. nigeriensis*) and spread by some as yet not clearly differentiated tsetse-fly, which may or may not be *Glossina palpalis*, and which Dutton suggested might possibly be *G. lachinoides*.

For description of the parasites, see p. 417.

Duke's researches made it possible that there is a vertebrate reservoir for *C. castellanii* in the antelope, because he found a trypanosome very like this organism in these animals, and because some boys working on an uninhabited island in Lake Victoria became infected with sleeping sickness. We feel, however, that the proof is not quite absolute with regard to this point.

Yorke and Blacklock with regard to *C. gambiensis* find that man is the principal vertebrate reservoir, with a possible secondary reservoir in domestic cattle.

With regard to *C. rhodesiensis*, as long as the view held that this was identical with *C. brucei* there was no difficulty in believing that the vertebrate reservoir was in such animals as the hartebeest, water-hogs, and domestic dogs; but with the human, crossed immunity, and serological experiments detailed on page 426, it again becomes evident that these two trypanosomes are distinct, and therefore the question as to the existence of *C. rhodesiensis* in game animals must again be considered as *sub judice*. The confusion has arisen by trusting too implicitly to only morphological characters, and ignoring serological tests.

In Chapters XIX., p. 388, and XXXV., p. 878, we have considered the tsetse in relationship to its carriage of these organisms, and in Chapter XXXIII., p. 837, we have described these flies. *C. castellanii* is spread by the agency of *Glossina palpalis* and *C. rhodesiensis* by *Glossina morsitans*, but it is not proved by actual experiment what fly carries *C. gambiensis*. It is *assumed* that it is *Glossina palpalis*, but the subject obviously requires careful study.

The tsetse flies obtain the trypanosomes by sucking infective human blood containing the organisms, which undergo development in the bodies of the flies. In due time (*vide* Chapter XIX.) the young trypanosomes in short form appear in the salivary glands of the tsetse-fly, and from these organs they pass into man when the fly next feeds upon him.

The fly appears to be the definitive host of the trypanosome, but there is no evidence that the infection is passed on to the succeeding generation.

From a practical point of view the bite of the infected tsetse is the most important method of infection, but less important methods, such as sexual intercourse, are possible and must be remembered.

With regard to *predisposing causes*, race, sex, and age have not been proved to have any influence, though the last two have been thought to be predisposing causes.

Occupation, however, has a considerable influence, for persons who live near the shores or work along the shores of lakes and streams, such as fishermen, are more liable than others to contract the disease, because of the habits of the fly, while porters marching through fly-zones are also liable to be attacked.

Pathology.—The trypanosome either enters the lymph-stream directly after the bite of the fly, and is blocked in the lymphatic glands, which it inflames, and through which it passes to the blood-stream and cerebro-spinal fluid, or, less probably, it enters the blood-stream first, and escapes by rupture of a capillary into a lymph-gland. But the polyadenitis is not the only change induced, for the lymphatic tissues of the intestine (solitary or agminated glands) are also inflamed, and the heart and other organs infiltrated with lymphocytes. This stage is marked by fever, but sooner or later, as a result of this lymphatic disease, changes are induced in the membranes and substances of the brain and spinal cord (chronic meningo-encephalitis and meningo-myelitis), especially along the course of the vessels, which result in the proliferation of the neuroglia and in a lymphocytic accumulation around the vessels. These two processes compress the vessels, and lessen the supply of blood to the cells of the brain and spinal cord, in which, as the result of malnutrition, changes ensue, which produce the typical symptoms of the cerebral stage of the disease, which is often called 'sleeping sickness.' The trypanosome apparently cannot pass through the placenta, as infected women give birth to healthy babies.

Towards the end secondary infections with bacteria may take place, the most constant of these being due to streptococci and the pneumococcus, which probably shorten the life of the patient.

Cerebro-Spinal Fluid. - The cerebro-spinal fluid was first studied by Castellani, and it may be noted here that it was during his researches on the leucocytic formula that he discovered trypanosomes for the first time in sleeping sickness. More recent researches are those by Broden and Rodham and others. During the first stage of the disease it is usually of normal appearance and clear, while on centrifugalization there is practically no sediment, though occasionally a few small mononuclear cells may be present, and trypanosomes are, as a rule, absent.

In the sleeping sickness stage it is often slightly turbid, and contains an amount of serum albumen and serum globulin: and on centrifugalization some sediment is obtained, consisting of a few cells, which are mostly mononuclear leucocytes, endothelial-like and vacuolated cells, while trypanosomes are almost constantly present, and also often aflagellate, roundish, or oval forms, with one or two chromatin masses, as described by one of us in 1903. These may probably be compared to the so-called latent forms described in the spleen by Breinl and others, though Laveran and other authorities consider them to be degenerated or fragmented forms.

Morbid Anatomy and Histopathology.- The macroscopical changes found post mortem are principally in the central nervous system and in the lymphatic glands, but pathological changes brought about by complications may also be noted.

The body is usually emaciated and anæmic, rigor mortis is well marked, and the skin may be normal, or dry and desquamating, or may show pustular eruptions on the hands and forearms, or ulcers on the feet which are generally due to jiggers (*Dermatophilus penetrans*). Enlargement of the lymphatic glands of the neck and groins is generally easily seen. On opening the brain-case, it will be noted that the under surface of the scalp is pale, that the dura mater may or may not be adherent to the bone, that the cerebro-spinal fluid is increased in quantity, and the gyri of the brain are often flattened. On careful examination, the pia arachnoid will be found to be thickened in places, and may or may not be adherent to the grey matter. The brain substance, which is generally firmer than normal, but may be soft and œdematous, is usually congested, and the fluid in the ventricles is increased.

With regard to the spinal cord, it will be seen that there is an increase of fluid, which, if examined with the microscope after centrifugalization, generally shows leucocytes and trypanosomes. The cauda equina may be found at times surrounded by gelatinous tissue. The cord itself is often congested, and hæmorrhages have been described.

The lymphatic glands of the submaxillary region, anterior and posterior triangles, around the bronchi, of the mesentery, behind the peritoneum, as well as those of the inguinal and femoral regions, may one or all be enlarged, congested, and even hæmorrhagic. At times abscesses are found in these glands, but they are due to secondary infection. The abdominal cavity often contains some straw-coloured fluid, and the pericardial fluid may also be excessive. There may be some increase in size of the lymph-follicles and Peyer's patches of the small intestine. The lungs may show signs of pneumonia and other complications. The other organs are usually not markedly affected.

The microscopical examination of the organs has been performed with the greatest care by Mott and Breinl and the members of the Portuguese Commission (Bettencourt, Kopke, Rezeide, and Maude).

The utmost care must be taken to distinguish between the lesions due to the trypanosomes and those caused by terminal infections such as the diplococci, streptococci, and colon bacilli; for these infections may give rise to chromatolysis in the nerve cells and degeneration in the nerve fibres of the brain (pons and medulla) and spinal cord (especially in the posterior and lateral columns), and perhaps in the peripheral nerves, which have nothing to do with the disease in question. With this proviso the microscopical examination is characterized by a round-celled infiltration surrounding the vessels of the pia arachnoid of the brain and spinal cord. This infiltration, first described by Mott, is best seen in the membranes, where there is an accumulation of cerebro-spinal fluid, and in the brain, around the vessels of the medulla, pons, cerebellum, and those entering the base. The process appears to begin with a growth in size, and then a proliferation of the neuroglia elements, which has been minutely described by Eisath, and is found, not merely around vessels, which show a small-celled infiltration, but around those which do not. Round cells are found later in the meshes of this proliferated glia.

These cells are (*a*) lymphocytes; (*b*) peculiar cells called the 'plasma cells of Marschalkó,' characterized by the nucleus becoming situated at one end of the cell, and staining blue with methylene blue and eosine, while a clear halo separates it from the cytoplasm, which stains pink; (*c*) 'morula cells of Mott,' which are large round or oval cells with an excentric blue nucleus and a cytoplasm containing a clear eosinophile area; (*d*) a few mononuclear leucocytes; (*e*) a few polymorphonuclear leucocytes. The cells of Marschalkó are considered by Mott to be derived from lymphocytes, and the morula cells to be degenerated cells of Marschalkó. Mott considers that the lymphocytes are probably formed by proliferation of the endothelial cells of the perivascular lymphatic space. According to Breinl, a layer of blood cells may be found external to the round cells, and hæmorrhages may be found in the cord. The ependyma of the lateral ventricle also shows a proliferation and dense fibrous formation at times. With regard to the parenchymatous elements, Mott considers that there may be increase in neuroglial nuclei and lymphocytes in the perineural spaces, while there is atrophy of the dendrons and diminution of the Nissl bodies, and alteration in the nucleus, which becomes large, clear, and excentric. These changes are most marked in the cerebral cortex and medulla, and less so in the spinal cord. The cells of the posterior spinal ganglion, however, show chromatolysis. The central canal of the spinal cord may be dilated, but is more generally occluded by proliferation of the cells of the ependyma. It is interesting to note that Mott did not find any of these changes in the brain and spinal cord of a cured case of trypanosomiasis, who died several years later of cystic disease.

The histological lesions of the encephalitis found in sleeping sickness closely resemble those of general paralysis and encephalitis lethargica (nona).

The next series of characteristic changes are in the lymphatic glands, in which trypanosomes are often found. These changes begin with a conversion of the lymphocytes into cells of Marschalkó, and these, again, into morula cells. The endothelial cells of the lymph sinus proliferate and take on a phagocytic action, containing lymphocytes, red blood cells, and chromatin particles. At the same time the gland becomes intensely congested, and the fibrous tissue of the capsule and septa proliferates, so that they and the walls of the lymph sinuses and of the vessels become thickened.

A lymph nodule therefore appears to be surrounded by a fine connective meshwork, containing few lymphocytes, but many red corpuscles and phagocytes. As time goes on, the inflammation in the gland subsides, and it becomes less vascular, firm, and hard, and full of dense fibrous tissue. Secondary infection, however, may occur with the formation of abscesses.

Microscopically, the lungs may be found to be hyperæmic, even when normal, to the naked eye, while the complication of pneumonia will give rise to the usual appearances. The heart shows small-celled infiltration in all its layers, with sometimes hæmorrhages. Vianna has noted in animals infected with *C. castellanii* cysts in the muscles similar to those of *S. cruzi*, and appears to have found them also in the muscular and nervous tissues from a case of sleeping sickness. The liver and spleen may show thickening of the capsule, while the latter is very congested, and its trabeculæ are increased in thickness. In natives signs of chronic malaria are almost constantly present in the spleen and liver. The bone-marrow may be very cellular, with congested vessels and hæmorrhages.

Stevenson and others have found trypanosomes scattered through the brain substance in no special relation to the capillaries and smaller bloodvessels in animals inoculated with *Castellanella gambiensis* (*nigeriensis*) and other trypanosomes.

Symptomatology.—The course of the disease may be roughly divided into three stages—the incubation, the febrile, called also glandular stage, and the cerebral stage.

Incubation.—The duration of the incubation period is not certainly known in man, but may be considerably shorter than was believed by the old authors: probably in most cases it does not exceed two or three weeks, and, according to Martin and Lebœuf's observations in Europeans, it may be even less than ten days. On the other hand, some infected individuals may not show any sign of disease for months, and, it is said, even five or six years. The bite of the infected *Glossina* gives rise, as a rule, only to very slight local irritation, which quickly subsides, and is often overlooked by the patient.

Febrile or Glandular Stage.—The onset of the disease is characterized by attacks of fever almost constantly associated in Europeans with an erythematous eruption. This fever lasts about a week, and disappears, to recur again later for the same or much longer periods. It is generally of an intermittent or remittent type. During an attack the pulse-rate and the respirations are increased, and there is often enlargement of the liver and spleen, though how much of this may be due to recurrent malaria is not known; the pulse often remain rapid during the apyrexial periods. Neuralgic pains and headache may also be complained of.

FIG. 639.—NEGRO PATIENT IN THE LATE STAGE OF SLEEPING SICKNESS.

An erythematous eruption is often found on Europeans. It begins, as a rule, with badly defined, pinkish patches, which clear in the centre until a ring is produced; if a portion of the ring fades a crescent may be produced. This circinate eruption may appear on any part of the body, but is especially frequent on the trunk; in some cases, instead of rings, solid infiltrated patches, the size of a half-crown or larger, are present. Rubeloid spots and a mottled appearance of the skin are not rare. A vesiculo-papular eruption has also been described, but is rare in our experience. Dermatographia is common in Europeans. In full-blooded negroes the erythematous eruption may not be noticeable; in them very often a dry, scaly condition of the skin is found. These various eruptions are called *Trypanides*. Patches of localized œdema may be seen in some cases.

The most typical sign of the disease in this stage is enlargement of one or more lymphatic glands, especially those of the neck, in the posterior triangle (Winterbottom's sign.) The enlarged glands are in this period generally fusiform, and of rather soft consistency. Another early symptom, noted by Kerandel, is a general, intense, deep hyperæsthesia. As repeated attacks of fever increase, the patient may become anæmic and asthenic, but the febrile condition may last for years, and, indeed, in this stage the disease may be cured.

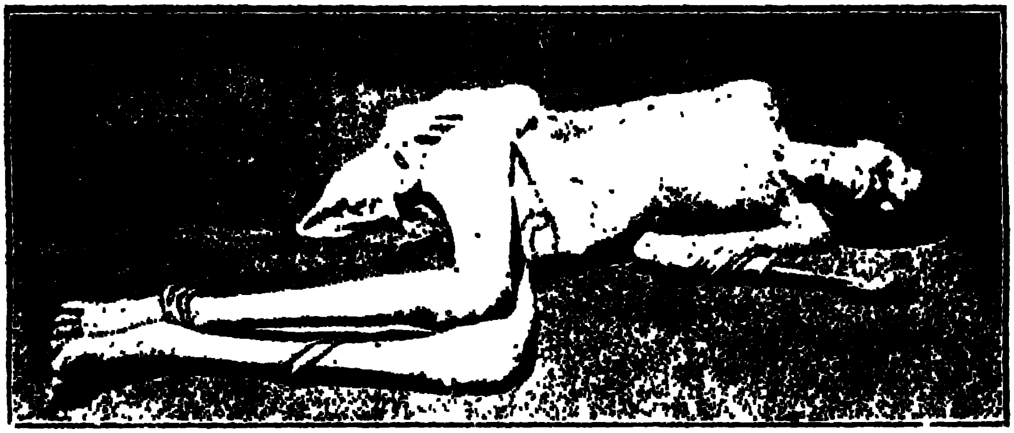


FIG. 640.—SLEEPING SICKNESS, LATE STAGE, IN ANGLO-EGYPTIAN SUDAN. (Photograph kindly lent by Colonel A. Balfour.)

The Cerebral Stage (the So-called Sleeping Sickness).—After the febrile stage has lasted some time (weeks or months), and even years, a change begins to appear in the habits and disposition of the patient. Previously bright, intelligent, and hard-working, he becomes apathetic, dull, with a disinclination for exertion, preferring to sit quietly or to lie down. He also becomes careless in his work and dirty in his habits, and at the same time a difficulty in walking begins to be noticed. In this condition the sleeping sickness stage of the disease may be said to have been properly entered. Typically, the patient is dull and apathetic, but can be easily roused, and answers questions rationally, without difficulty in speech. Sleep may be excessive, but is not the prominent symptom so often described, the condition being more one of lethargy, from which the patient can be easily roused. Fine tremors are noticed in the tongue at first, later in the hands and arms, and sometimes also in the legs, and even in the abdominal muscles. The tremor of the tongue and hands may be a very early symptom and may be present in the febrile stage. These tremors may occasionally be so severe that they cause the whole body to shake, and at times epileptiform fits, general or localized, may be seen. The gait is peculiar, there being apparently a difficulty in raising the feet, so that the patient shuffles along; but there is no paralysis as a rule, and the superficial reflexes are normal; the deep reflexes may be exaggerated and then lost; there is no clonus. There is inco-ordination in some cases, and Romberg's sign may be present. As the disease advances, rigidity appears, especially in the muscles of the neck and legs, which latter may assume the position of flexion of the thighs on the abdomen and the legs on the thighs. Babinski's sign is generally absent. Sensation is at first normal, but there may be hyperæsthesia in the region of the fifth nerve and other nerves, and at times the patient complains of headache. The pupils are equal, moderately contracted, and react to light and accommodation. There is nothing abnormal in the organs of special sense as a rule. There is usually fever, the temperature rising in the evening from 100° to 104° F., and falling to subnormal in the morning: but this may be varied in many ways: thus for a period the temperature may be almost normal or subnormal, while for some days before death it becomes, as a rule, permanently subnormal.

There are no special symptoms, such as rigors or sweating, associated with the rise of temperature. The pulse is quick (90 to 140), but it is independent of the temperature, being quick with a low temperature. It is regular, but small and very low in tension, and generally is imperceptible at the wrist for some time before death. The heart as a rule shows no abnormal symptoms, though systolic inorganic murmurs may be present. The respirations are regular and equal, but are increased in number, especially towards evening, varying from 20 to 30; before death they not uncommonly take on the Cheyne-Stokes type. Congestion and œdema, with patches of pneumonia, are not infrequently met with before death. The appetite is good, and may even be increased; digestion is usually satisfactory, but constipation may be marked, or there may be occasionally diarrhœa. The tongue is frequently flabby and covered with white fur; the fæces of native patients are typical of a vegetable diet, and show the usual parasites of a tropical country. The spleen and liver may be enlarged, which perhaps may partly be due to malaria.

The Blood.—The examination of the blood is complicated, because its condition is bound to be influenced by the secondary infections with other parasites, animal and vegetal.

With this understanding trypanosomiasis causes in a certain number of cases a gradual diminution of the red cells to 2,000,000 or less, with a corresponding decrease in the hæmoglobin; but it is to be noted that, as first observed by Low and Nabarro in several cases, the actual number of erythrocytes may be above normal. The red cells are usually normal in appearance, but normoblasts may be seen. The leucocytes are normal in number, as a rule, with an increase of mononuclear cells, while there may be a terminal polymorphonuclear increase before death.

In fresh preparations the red cells are not evenly distributed, nor do they form rouleaux, being generally clumped into masses. This phenomenon of *auto-agglutination* was first noticed by Kanthack, Durham, and Blandford in the lower animals inoculated with nagana; and in man in cases of sleeping sickness, by Dutton, Todd, and Christy, and may be of diagnostic value. The phenomenon of auto-erythrophagocytosis has occasionally been noted.

The chemical examination of the blood in trypanosome infections of animals has been performed by Takmioff and by Nierenstein, the latter of whom found, by Moore and Wilson's method of testing the alkalinity of the ash, that the acidity of the blood was increased, probably due to the formation of amido-acids, either secreted by the parasites or produced by their action upon the proteids of the serum. The acidity was tested by phenolphthalein and Congo red, and the alkalinity, which remained fairly constant, was tested by dimethyl-amido-azo-benzol.

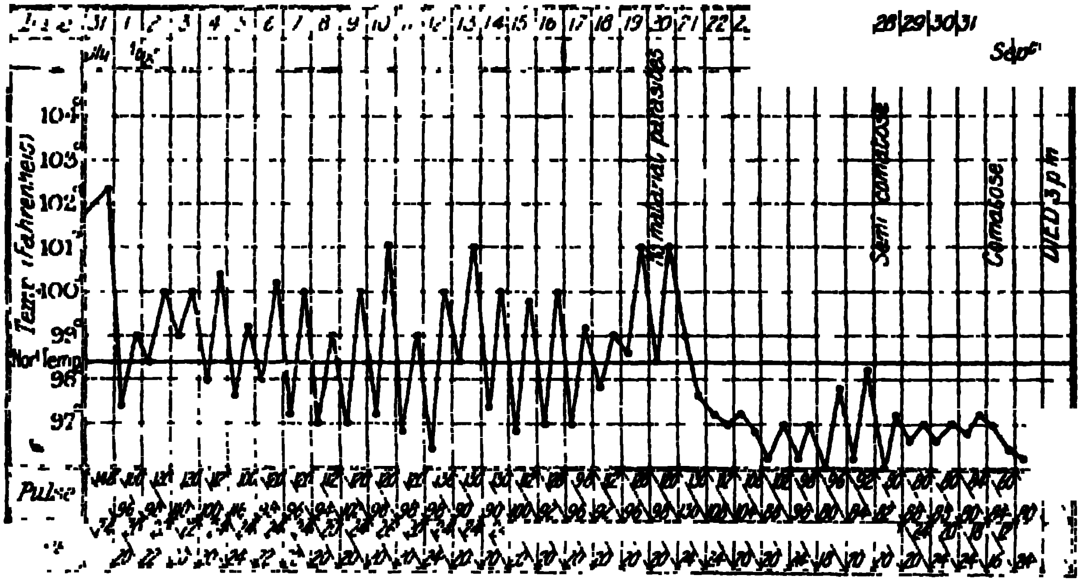


FIG. 641.—TEMPERATURE CHART OF A CASE OF SLEEPING SICKNESS. (From Low and Castellani Reports of the Royal Society on Sleeping Sickness.)

The animals were infected with *T. brucei* and *T. equiperdum*, but so far no observations have been made on human blood.

Urine.—No abnormality is found in the urine, but the reaction, amount of phosphates, etc., of course, varies with the food taken. In native patients it is very often alkaline.

Sexual desire and menstruation are normal at first, but later are lost. The lymphatic glands throughout the body, but especially those of the neck, and more especially those of the posterior triangle, are enlarged. It is to be noted, however, that in the last stages the lymph glands often undergo a process of fibrosis, becoming smaller and harder. The skin becomes dry and rough, but may be perfectly normal, though a papulo-pustular eruption may at times be noted on the backs of the hands and forearms. Nutrition suffers, and the patient generally becomes much emaciated.

As the disease progresses the muscular weakness and emaciation becomes worse and worse, the tremors more pronounced, the saliva dribbles from the mouth, the urine and fæces are passed involuntarily, and bedsores form, while the intelligence becomes more and more affected, and the patient passes into a state of coma, with a permanently subnormal temperature and an absence of pulse at the wrist, and in a short time is liberated from his sufferings by death. The duration of the cerebral or sleeping sickness stage varies from a few weeks to several months. Since the atoxyl treatment has become of general use, Hodges has noted that convulsive and mental symptoms are more prominent, and that death is often sudden, without being preceded by a period of coma.

Varieties.—When the disease is due to *C. rhodesiensis*, it generally runs a more rapid course, seldom exceeding four or five months. Lethargic symptoms may not appear, and the enlarged glands in the posterior triangle of the neck may be absent, while enlargement of the epitrochlear glands seems to be frequent. The disease caused by *C. gambiensis* appears to be of a milder type than that due to *C. castellanii*.

Complications.—The patient is often infected by parasites other than trypanosomes; thus, *Plasmodium* and *Laverania*, *Filaria*, *Schistosoma mansoni*, *Ancylostoma duodenale*, *Ascaris lumbricoides*, *Trichurus trichiura*, *Strongyloides stercoralis*, *Trichomonas intestinalis*, *T. vaginalis*, *Dermatophilus penetrans*, and *Loeschia* may all be found. The commonest complication during the last stage is a cerebro-spinal meningitis, due to streptococci, the pneumococcus, or the meningococcus.

Pneumonia, laryngitis, and œdema of the glottis are not rare, while iritis is seen at times, and symptoms of mania, delirium, and epilepsy may be observed.

Diagnosis.—In the first stage (febrile or glandular stage) the disease may be readily confused with malaria and other fevers, but in endemic areas the true nature of the malady may be often suspected on certain clinical data, the principal of which are the attacks of fever not influenced by quinine, the erythematous eruption in Europeans, the rapid pulse frequently present also during the apyrexial periods, the asthenia, the deep hyperæsthesia (Kerandel's symptom), the fine tremor of the tongue (Low-Castellani's symptom), the cervical polyadenitis (Winterbottom's symptom). During the sleeping sickness stage the clinical diagnosis is based, in addition to the above symptoms, on the drowsiness and apathetic appearance of the patient, on the remarkable wasting and debility, and the more marked, and occasionally generalized, tremors. The long course and, usually, absence of facial paralysis differentiates clinically sleeping sickness from encephalitis lethargica (nona). To make a definite diagnosis, the demonstration of *C. castellanii*, *C. gambiensis*, or *C. rhodesiensis* in the body of the patient is necessary. The following methods should be used:—

1. *Microscopical Examination of the Peripheral Blood from the Finger or Ear.*—This procedure is often a failure, even using thick films.

2. *Scarification of the Erythematous Eruption and Examination of Blood Films.*—This method is more useful than the first, but may fail.

3. *Nabarro's Method.*—Repeated centrifugalization of 10 c.c. of citrated blood, and examination of the third sediment. The results are good.

4. *Dutton-Todd's Method.*—Some citrated blood is centrifugalized in small tubes and the leucocytic layer examined for trypanosomes.

5. *Greig-Grey's Method.*—Aseptic puncture of the enlarged cervical glands with a sterile syringe. The gland-juice is examined for trypanosomes. This, from a practical point of view, is the most valuable method. To Mott belongs the credit of having first suggested the search for trypanosomes in the lymph glands as a diagnostic method. Balfour has devised a 'gland-holder,' which is useful in some cases.

6. *Castellani's Method.*—Centrifugalization for fifteen minutes of 10 c.c. of cerebro-spinal fluid, aseptically removed by means of lumbar puncture. The sediment is examined for trypanosomes by making fresh and stained preparations. The result is almost constantly positive in the sleeping-sickness stage, but negative, as a rule, in the first stage of the malady.

The technique to perform lumbar puncture is as follows: The patient may be given chloroform, but usually a local anæsthetic spray is sufficient. Lay the patient on the right or left side, flex the thighs on the abdomen. Then make the skin of the lumbar region aseptic, and, feeling with the tip of the finger the position of the laminæ, thrust the sterile needle between the laminæ of the third and fourth lumbar vertebræ, ½ inch from the median line, obliquely outwards and forwards into the canal. The fluid will escape, and can be collected in a sterile tube After withdrawing the needle, the area should be covered with an aseptic pad and bandage.

7. *Inoculation of Susceptible Animals.*—Ten c.c. or 20 c.c. of blood are aseptically removed from a vein and inoculated into susceptible animals, or 10 c.c. of cerebro-spinal fluid may be inoculated. The animals most suitable are monkeys, guinea-pigs, and dogs. The most suitable monkeys, according to Thiroux and d'Anfreville, are those of the species *Cercopithecus ruber*, while some other species—*e.g.*, *C. fuliginosus*—are almost refractory.

The following biological phenomena and reactions may sometimes be of diagnostic value:—

1. *Auto-Agglutination.*—In many cases of sleeping sickness, in wet preparations of blood examined microscopically with a low power, the red corpuscles are not evenly distributed, nor are they arranged in rouleaux, but are clumped together 'agglutinated'—in irregular masses. This appearance is not specific of trypanosomiasis, having been found in cases of filariasis, malaria, syphilis, and yaws.

2. *Complement Fixation.*—Levaditi and Muttermilch have applied the Bordet-Gengou reaction to trypanosome infections. According to them, the complement can be fixed by using as antigen an extract of trypanosomes separated from red cells.

3. *Levaditi and Muttermilch's Leucocytic Attachment Reaction.*—Levaditi and Muttermilch have shown that trypanosomes treated with the specific serum (heated at 55° C.) develop a property of becoming attached to leucocytes, and that this phenomenon is specific. The test may be used for identifying a trypanosome or for diagnosis, but, according to Laveran and Mesnil, is not very reliable in the case of *C. castellanii* infections.

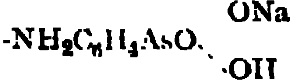
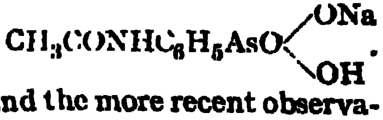
Attempts have been made to evolve agglutination reactions, trypanolytic precipitin, and other biological tests for purposes of the diagnosis of sleeping sickness, but so far with little success.

Prognosis.—The prognosis is serious, but not quite so serious as it was before the introduction of atoxyl and the mixed atoxyl tartar emetic treatment. If the patient is in the early stage, and can be removed from the endemic area and put under good hygienic conditions and atoxyl treatment, the disease may be cured, or at least a marked improvement may be obtained. Great care, however, is necessary before saying that a patient is really cured, and at least two blood injections into susceptible animals should be performed before giving a decided opinion. If, however, the patient is compelled to live in the endemic area, and cannot be treated with atoxyl, the outlook is most hopeless. It is to be noted that there are several strains or varieties of different virulence. The Uganda and French Congo strains caused by *C. castellanii*, as noted by Laveran and Mesnil, cause a more acute type of the disease than the Gambia strain due to *C. gambiensis*, and *C. rhodesiensis* is in laboratory animals more virulent than *C. castellanii*, and the disease caused by it in man runs a more rapid course.

Treatment. - The only medicaments which have been so far found to be of any real value are, first, arsenic in the form of atoxyl, and, in a less degree, antimonium in the form of tartar emetic, the best method of treatment being a combined treatment with the two drugs.

Atoxyl.— We recommend 2 to 3 grains of atoxyl by intramuscular injection every third day for at least two years, or 0·3 gramme every fourth day for the same period, with 0·1 gramme for a child ten years old.

Borden and Rodhain's method is 7½ grains of atoxyl by intramuscular injection every fifth day. Koch recommended the subcutaneous injection of 7½ grains (½ gramme) on two successive days every ten days for two months, when the treatment is to be stopped until further symptoms develop, and when this occurs the treatment should be repeated. The drug can be obtained or imported from any chemist in sterile vials ready for hypodermic medication. The injection of atoxyl is occasionally followed by a febrile reaction, due, according to some observers, to the absorption of products of trypanolysis.

Atoxyl is sodium-*p*-aminophenyl arseniate— $NH_2C_6H_4AsO\begin{matrix}ONa\\OH\end{matrix}$ —and contains from 25·05 to 20·78 per cent. of arsenic, according to the amount of water of crystallization. Mono-acetylated atoxyl is  $CH_3CONHC_6H_5AsO\begin{matrix}ONa\\OH\end{matrix}$.

According to Mesnil and Nicolle's observations, and the more recent observations of Nierenstein, it is not the arsenic in these compounds which is to be looked upon as the effective agent, but the amido-group, which may possibly be the effective agent in trypan red, afridol blue, afridol violet, and parafuchsin, which do not contain arsenic, but possess amido-groups, and affect trypanosomes in a similar manner to atoxyl. According to Ehrlich, Levaditi, and Yamanouchi, atoxyl undergoes a reduction in the animal tissues. Ehrlich has prepared two derivatives of atoxyl, one of which, already mentioned (arseno-phenylglycin), is very effective in mice on atoxyl-resistant trypanosomes. Levaditi and Yamanouchi have also prepared an active derivative of atoxyl, which they call trypanotoxyl Nierenstein thinks that atoxyl is oxydized in the tissues, and it is only in the nascent state that it becomes efficacious

Soamin -Owing to the fact that large doses of atoxyl lead to such unpleasant results as optic atrophy, gastro-intestinal inflammation, and peripheral neuritis, other arsenical preparations have been recommended; and the firm Burroughs and Wellcome has introduced, under the trade name of ***soamin***, a preparation somewhat similar to atoxyl, but said to be less poisonous. It is given in the same doses as atoxyl, but the therapeutic results do not appear to have been very successful. *Soamin*, according to the published formula, is $C_2H_4NH_2AsO(OH)(ONa)5H_2O$.

Arseno-phenylglycin. Ehrlich has prepared a derivative of atoxyl, called ***arseno-phenylglycin***, which is from two to four times less toxic than atoxyl itself

This preparation has been tried by Ehrlich, Mesnil, Kerandel, and others upon lower animals experimentally infected with *C. castellanii*, and has been found to be very effective, being also a prophylactic. It has been used in man by Kleine in the same doses as atoxyl, but has now been abandoned.

Liquor Arsenicalis. -When for special reasons it is impossible to carry out the treatment by injections, arsenic may be given by the mouth in the form of Fowler's solution which must be given, well diluted in water or milk, in 5-minim doses and gradually increased to 15-minim doses.

Löffler and Ruh's neutral solution of arsenious acid (1 c.c. of which contains 1 centigramme of arsenious acid) may be given in doses of 2 c.c daily for three days, and then continued in doses of 1 c.c. per diem for several weeks, after which it must be temporarily discontinued, but must after a time be restarted, and in this manner continued for months, provided no ill-effects are produced.

Salvarsan and Neosalvarsan -Their action is less efficacious than atoxyl.

Atoxylate of Mercury - This preparation, introduced by Uhlenhuth, has given less satisfactory results than atoxyl.

Quinine Derivates - Morgenroth and Halberstaedter have shown that some quinine derivatives, such as hydroquinin, have a preventive and curative effect in certain experimental trypanosomiases.

Ipecacuanha Derivates —The emetine salts might be studied in regard to their possible action on trypanosomes.

Anarcotine. - -The use of this opium alkaloid has been suggested by Johnson.

Combined Therapy. As the result of the important observations of Ehrlich on the phenomenon of chemio-resistancy, which may be acquired by trypanosomes after a long use of the same drug, numerous combined treatments have been suggested. Of these, the most important are: (1) antimony and atoxyl; (2) mercury and atoxyl; (3) orpiment and atoxyl; (4) various dyes and atoxyl.

Antimony and Atoxyl Treatment. - Antimony salts, as well as phosphorus, were first suggested by Mesnil as likely to be of use in trypanosomiasis. To Plimmer and Thomas belongs the credit of having experimentally shown the powerful trypanocide action of antimony. In man the subcutaneous or intramuscular injections of solutions of the various salts of antimony (sodo-tartrate of antimony, sulphide of antimony and soda, etc) are very painful. Plimmer therefore suggests oil emulsions, Manson gives the drug by the mouth or by the rectum, and other authors by intravenous injection. Daniels and

Newham recommend the painless Martindale's injectio antimonii oxidi, 30 minims (= gr. $\frac{1}{20}$ antim. ox.) to be given subcutaneously once or twice daily. Apparently the trypanocide action of antimony is more powerful in the lower animals than in man, in whom the results are inferior to those given by atoxyl. A mixed antimony and atoxyl treatment is, however, of advantage in most cases, an atoxyl injection (3 grains) being given every third day, or 7½ grains every fifth day, and sodio-tartrate of antimony (Plimmer's salt) administered daily- 2 grains dissolved in a large quantity of water (2 pints) by the mouth or by the rectum. Tartar emetic, however, is best given by intravenous injections, using solutions of 1 in 100 or 1 in 1,000. The dose of the drug to be given is 5 to 10 centigrammes per injection. It is important that none of the fluid of the injection should escape into the surrounding tissues, as a violent inflammation may result. These injections should be administered monthly on ten consecutive days for a long period. The injection of salts of antimony may produce a marked fall in the blood-pressure, dyspnœa, and signs of collapse, and therefore Thiroux suggested that subcutaneous injections of caffein should precede ten or fifteen minutes their administration.

Basing his opinions upon the very successful treatment carried out by Captain Simson, R.A.M.C., at the Yei Sleeping Sickness Camp in the Mongalla Province of the Sudan, Captain Spence, R.A.M.C., is treating cases in the Bahr el-Ghazal Province as follows :-

A. Cases in the early stage :-

1. Six intravenous injections each of 6 centigrammes of *antimony* at three-day intervals.
2. Interval one month.
3. Twelve intramuscular injections each of 30 centigrammes of *atoxyl* at three-day intervals.
4. Interval one month.

5 and 6. Repeat 1–4.

7. Three months after last treatment the blood of the patient is inoculated into an animal. If the animal remains uninfected the patient is given a numbered disc and told to report every three months.

Total dosage: Atoxyl, 10·8 grammes in about one year; antimony 1·08 grammes.

B. Relapses and cases first seen in a late stage of the disease :-

1. Nine intramuscular injections each of 1 gramme of *atoxyl* at ten-day intervals.
2. Interval one month.
3. Nine intramuscular injections each of 1 gramme of *atoxyl* at twenty-day intervals.
4. Interval one month.
5. Nine intramuscular injections of *atoxyl* at thirty-day intervals.
6. Interval of three months.
7. Animal is inoculated as above.

Total dosage: 27 grammes of atoxyl in two years.

Cases in which no symptoms are noted and in which animal inoculations are negative are kept under close control for two years, after which they report every six months for two years and the result judged.

Mercury and Atoxyl.- Mercury was first introduced in 1902 for the treatment of sleeping sickness by Low and Castellani, using intravenous injection of Baccelli's sublimate solution (hydrargyri perchloridi, 0·10 gramme; sodii chloridi, 0·50 gramme; aquæ destillatæ, 100·00 c.c.; 1 to 4 c.c. per intravenous injection), in association with arsenic and quinine by the mouth. A fall of the temperature was observed in some cases, but the fatal course of the disease was not influenced. Moore, Nierenstein, and Todd have used mercury and atoxyl in combination or alternation, with the idea that mercury might act upon the latent form of the trypanosome, while atoxyl would influence the active form. In man this combined treatment has apparently not given any better results than atoxyl alone.

Orpiment and Atoxyl.—This combined treatment, consisting of atoxyl and an inorganic salt of arsenic such as orpiment, has been recommended by Laveran and Thiroux, and has been used in man with good results. The orpiment should be given in pills, in the dose of 2 grains of orpiment two or three times daily. The administration of orpiment frequently causes diarrhœa. Thiroux therefore incorporates in the orpiment pills some opium. Thiroux's formula is:—

Orpiment	20 grammes.
Extr. opii	0·40 gramme.
Gumm. Pulv. glyceriz.	q.s.

To be divided into 200 pills.

Various Dyes and Atoxyl.—Combined treatments of Mesnil's afridol and atoxyl, Ehrlich's parafuchsin and atoxyl, picric acid, safranin, trypaflavin and other dyes and atoxyl, have been suggested, but in man the results have not been so successful as in the lower animals.

Treatment of Natives. In the case of natives it is necessary to gather them into special sleeping sickness camps in order that treatment may be efficiently carried out. These camps should be in some fly-free area, and should be provided with a trained medical staff. Patients able to work should be employed to raise crops for their own consumption, to supplement the diet provided by the Government.

Symptomatic Treatment.—In addition to the atoxyl treatment or combined treatments, malaria and the intestinal parasites must be treated if present. The patient should, if possible, be removed from the area of infection and placed under good hygienic conditions and on good food, and no case should be considered to be cured until the injection of the blood, on more than one occasion, into susceptible animals fails to infect them.

Prophylaxis.—At the present time prophylaxis must be undertaken on the assumption that the disease is spread from place to place by man along channels of human intercommunication, and from man to man by *Glossina palpalis* and *G. morsitans*, and that at least in the case of *C. rhodesiensis* there are animals which act as reservoirs of the virus. With regard to these flies, further information is required as to their bionomics, though Bagshawe's and Hodges' researches, as well as those of Zupitza, Sander, Minchin, Kinghorn and Yorke, Carpenter, and others have thrown some light on the subject.

Before enumerating the principal prophylactic measures to be recommended, we wish to draw attention to the fact that these, as pointed out by Bagshawe, will be useless without the co-operation of the natives. This co-operation may be obtained by explaining to them at every possible opportunity the reason for the measure taken. In this missionaries and native chiefs may be of the greatest help. With this proviso we consider the following to be the principal prophylactic measures:—

Public Prophylaxis.—We advocate:—

1. The formation of a Central Executive International Board, with headquarters in either Paris or London.

2. The formation of an Executive Sleeping Sickness Commission in each political division of Africa in which the disease exists.

The different Governments should be invited to co-operate to prevent persons travelling from districts where the disease exists into non-infected regions, and medical posts of inspection should be established for the examination of natives. According to some authorities (Dutton, Todd), all natives presenting enlarged glands should be considered, from a practical point of view, as trypanosome carriers, and prevented from emigrating. This is, perhaps, going a little too far, inasmuch as, in our experience, and in that of Low, Bagshawe, Koch, Hodges, etc., numbers of natives have enlarged glands, though not suffering from trypanosomiasis; and, on the other hand, cases of trypanosomiasis occur in which there is no enlargement of the lymphatic glands. We admit, however, that gland palpation may be of some use in formulating an approximate idea of the extent of the dissemination of the disease.

The sick should be removed from the fly regions and segregated in places where the *Glossina palpalis* and *G. morsitans* are not found, or where the temperature and climatic conditions are unfavourable to the development of trypanosomes in the flies. They should be treated with atoxyl before being moved.

In the regions where the disease is due to *Castellanella castellanii*, which is mostly carried by *Glossina palpalis*, villages should be removed, if possible, from the fly zones: and the occupations carried on in fly zones, such as fishing, should be discouraged. This has been done in certain regions round the Victoria Nyanza Lake, but the result has not been completely successful, as infected flies were found to be plentiful three years after the measures had been carried out. The waste land became full of game and wild animals, some of which are probable reservoirs of the infection. Duke, in fact, has found *C. castellanii* in two marsh antelopes or situtunga (*Tragelaphus spekei*), and believes this observation to be confirmed by the infection of two boys working on an uninhabited island in Lake Victoria.

Clearing of the bush along the water's edge for 100 yards, and round a village for 300 yards, at least, is to be advised.

European bungalows should be segregated from native quarters. Houses should be rendered gnat-proof, and natives bringing water from streams should not be allowed to enter the house, as they are liable to be surrounded by tsetse-flies which have followed them. Indeed, some authorities look upon the bath-room as a source of European infection.

Destruction of the Animals on which the Fly feeds.—Koch recommended the destruction of the crocodiles by poison, and by collecting and destroying their eggs. Unfortunately, the crocodile is not the only animal on which the fly feeds. The blood of many other vertebrate animals is palatable to the fly, and therefore this method of prophylaxis is without much practical importance.

Destruction of the Vertebrate Reservoir.—Many authorities have supported the idea of exterminating the big game, because they may be the vertebrate reservoir, but this requires further proof, and is therefore at present too radical a measure.

Destruction of the Pupæ.—Minchin has suggested the breeding of the jungle-fowl to destroy the pupæ, which, as discovered by Bagshawe, are found in the turf among the roots of banana and other trees. Balfour and others have suggested trapping the adult flies in various ways. Further information, however, is necessary on the enemies of the pupæ and adult tsetse-flies.

Personal Prophylaxis.—Natives in the fly zones should be encouraged to wear suitable clothing, and the reason explained to them. Europeans should be careful not to expose their legs and hands to be bitten. High boots, puttees, or leggings should be worn, and where the flies abound gloves and veils, though very uncomfortable, are of service. White clothes are better than dark ones, as it has been long observed that the tsetse-fly, as well as many other insects, have a preference for black or dark colours. The use of volatile substances such as citronella oil has been advised by some. Unfortunately, the odour of such substances is repellent to many persons.

Morgenroth and Halberstaedter have shown that certain derivates of quinine, in the lower animals, prevent an experimental trypanosome infection, and Bagshawe suggests that a daily dose of quinine may be useful in man.

Vaccination.—Attempts at vaccination have not yet entered a practical stage, as inoculation with dead or attenuated viruses have so far failed in the lower animals.

Summary of Prophylactic Measures.

I. General measures:
  1. Co-operation of various Governments, especially in controlling the movements of non-infected natives.
  2. Formation of medical posts of inspection at suitable places to prevent infected natives entering non-infected areas and *vice versa*.
  3. Segregation of the sick, if possible, in districts free from *Glossinæ*, or where the climatic conditions are unfavourable for the development of the trypanosome in the fly.
  4. Clearing of the bush near villages and along the water's edge, especially at landing-places, fords, and ferries.
  5. In certain cases—especially with regard to *C. rhodesiensis*—the destruction of large game, especially antelopes. (This is still *sub judice*.)

II. Personal measures:
  1. Avoidance of bites by wearing white clothing, high boots, puttees, and the putty pattern of leggings.
  2. Immediate disinfection of a bite by painting it with tincture of iodine or by applying a solution of formalin (1 in 40).

TRYPANOSOME FEVERS.

Definition.—The trypanosome fevers of man are caused by a monomorphic trypanosome allied to *Duttonella vivax* Ziemann, 1905, and to an unspecified germ allied to *Castellanella evansi*, and are characterized by milder symptoms and the absence of meningo-encephalitis as far as is known.

Remarks.—In Macfie's case of infection with a trypanosome allied to *T. vivax*, apart from slight fever there were no symptoms, and after a single injection of atoxyl the trypanosomes disappeared from the blood.

In Lanfranchi's case of accidental laboratory infection there have been irregular attacks of fever lasting seven years, and general debility associated with large patches of cutaneous œdema. But there has been neither mental symptoms nor tremor. He has been treated by atoxyl and tartar emetic.

It will thus be seen that the trypanosome fevers resemble mild infections in animals rather than human sleeping sickness.

Diagnosis.—This can only be made by finding the trypanosomes in the blood.

Prognosis.—This appears to be good *quoad vitam*.

Treatment.—The treatment is atoxyl administered as in sleeping sickness.

Prophylaxis.—Nothing can be said at the present time with regard to this.

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CHAPTER XLVI

SOUTH AMERICAN TRYPANOSOMIASIS

Synonyms—Definition—History—Ætiology—Pathology—Symptomatology—Diagnosis—Treatment—Prophylaxis—References.

Synonyms.—Oppilação; Canguary (both indicate ankylostomiasis); *Schizsotrypanose* or *Douença* de Carlos Chagas, *Coreotrypanosis* (*coris* = bug); *Molestia* de Carlos Chagas, *Tripanozomiase braziliera*, *Tireoidite parasitaria*, *Molestia do barbeiro* (popular name), *Molestia* de Cruz e Chagas.

Definition.—South American trypanosomiasis is an acute or chronic specific disease caused by *Schizotrypanum cruzi* Chagas, 1909, and spread by the bug *Lamus megistus* (*Trialoma megista*) Burmeister, and perhaps other allied bugs.

History.—In February, 1909, Chagas reported that he had frequently found a new trypanosome, which he named *T. cruzi*, in the intestine of a species of Lamus, which occurred in the State of Minas in Brazil. He also reported that he was able to infect marmosets, dogs, cats, guinea-pigs, and rabbits by the bites of the infected insects, and also to grow the parasite on blood agar.

In May, 1909, he announced that he had made an investigation of the mines of the State of Minas, and found the Lamus in large numbers in the houses of the poorer inhabitants. He noticed that the bite was painful, and that the insect was very voracious, and also that it generally attacked people, especially children, at night, biting the face, from which fact the inhabitants called it 'barbeiro' or 'barber.'

He suspected this Lamus of causing a disease marked by extreme anæmia, which occurred especially among the children, and he was able to find in the blood of a two-year-old child during an attack of fever a trypanosome identical with *S. cruzi*, morphologically and biologically. Since then Chagas has not merely worked out the life-history of the trypanosome in man and in the Lamus, but he has also studied carefully the clinical and pathological aspects of the disease, while Vianna has reported upon the histopathology, Dias on the blood, and Guerreiro on the urine.

Chagas has also shown that in all probability the armadillo commonly called 'tatu,' and scientifically *Dasypus novemcinctus*, or less correctly *Tatusia novemcincta*, may be the reservoir for *Trypanosoma cruzi*, and that *Triatoma geniculata* (synonym, *Conor-*

hinus geniculatus) of the family Reduviidæ is one of the carriers of the same trypanosome. He also believes that *Triatoma infestans* and *T. sordida* may be carriers. It may be stated that *T. geniculata* lives in the burrows of the armadillo, the flesh of which is rather a delicacy.

With regard to the history of the discovery of a trypanosome in man in South America, Sambon informs us that in 1904 de Lacerda published a paper entitled 'Etiologia de Beri-Beri' in the *Brazil Medico*, in which he stated that he had found trypanosomes in films taken from the spinal cord of a case of beri-beri. We have been unable to obtain this paper, and therefore cannot verify the statement, nor can we say whether the disease, which de Lacerda was considering, was beri-beri or some other complaint. It would, however, be interesting to have this historical problem elucidated.

Climatology.—The disease is known among the poorer inhabitants of the State of Minas in Brazil, where it appears to attack the whole population, so that the children all become affected and either recover, die, or pass into the chronic stage.

Ætiology.—The disease is caused by *Schizotrypanum cruzi* Chagas, 1909. This trypanosome, which is remarkable because of the large size of its kinetonucleus, is capable of being transmitted by *Lamus megistus*, and perhaps by species belonging to other genera of the Reduviidæ—*e.g.*, *Triatoma*—to domestic animals and to man. The reservoir of the trypanosome appears to be an armadillo—*Dasypus novemcinctus*.

In the blood three forms are seen: the first with a large nucleus and loose chromatin and a terminal kinetonucleus; the second narrower, with an oval nucleus and dense chromatin; the third with a long nucleus. The parasite undergoes schizogony in the lungs, after which the merozoites enter the red blood cells and become trypanosomes again. Sporogony takes place in the bug *Lamus megistus*, the final forms being found in the salivary glands, from which they pass during the act of biting into the vertebrate. (For a description of the parasite and its life-history, see Chapter XIX., p. 427.)

Pathology.—The trypanosomes enter the cells of the various tissues and organs of the body, but especially those of the muscular system, and more particularly those of the muscles of the extremities and back. Inside these cells they assume Leishmania-like forms without flagella, but provided with trophonucleus and kinetonucleus. These forms divide by binary division, and so increasing in numbers, dilate the cell considerably. During this process there is no reaction upon the part of the surrounding tissue, but after a time the cell membrane ruptures, and the parasites which have already become flagellate inside the dilated remains of the cell, which is virtually a cyst, escape. With this escape of the parasites into the tissues the local inflammatory reaction appears, and with the appearance of the trypanosomes in the blood the general symptoms make themselves evident. Whether the parasites produce any toxins or not is unknown, but it is probable that they do so, because of the fatty degeneration described in the liver, as well as because of the other pathological features.

As a result of this activity on the part of the parasites and of the reaction on the part of the body, local pathological changes take place in different organs, and these are in general agreement with the symptoms exhibited by the particular case.

At present there is no evidence of any secondary infection being responsible for any of the essential pathological features of the disease.

Morbid Anatomy.—In an autopsy upon the body of a person dying from the acute phase of the infection, a certain amount of serous effusion is remarked upon opening the abdomen. The liver is seen to be enlarged, and to be in a state of fatty degeneration. The spleen is also enlarged, hyperæmic, and very soft, as are the mesenteric glands. On opening the chest serous effusion is seen in both pleural cavities, as well as in the pericardial sac. The pericardium shows signs of hæmorrhagic pericarditis, while the enlarged heart is in a condition of intense myocarditis. The lymphatic glands of the mediastinum are also swollen and hyperæmic. In the neck the thyroid gland is seen to be enlarged, as are the lymphatic glands. The dura mater is congested, and there is leptomeningitis and encephalomeningitis, and firm adhesions between the leptomeninges and the cerebral cortex. The liquor cerebro-spinalis is increased in amount. There is a generalized myxœdematous condition under the skin.

Histopathology.—As already stated, the most likely place to find the parasites is in the muscular system. In the heart they occupy the central undifferentiated protoplasmatic portion of the muscle cell, and growing therein, destroy the sarcoplasm, and convert the body of the cell into a parasitic cyst without affecting the processes. When this cyst ruptures, the now flagellate parasites escape into the intermuscular tissue, and give rise to patches of interstitial myocarditis. No changes are to be seen in the larger bloodvessels of the heart, nor can parasites be found associated with patches of pericarditis or endocarditis which may be present. In the skeletal muscles the parasites are mostly found in those of the extremities and the back. Here, again, the parasites grow in the centre of the muscle fibre (Fig. 114, p. 428).

In the central nervous system a similar process appears to take place. The parasites invade a neuroglia cell, which becomes converted into a parasitic cyst, on the rupture of which a patch of inflammatory reaction is produced. Parasites have never been seen to invade the nerve cells or the leucocytes of the central nervous system (*vide* Figs. 642 and 643).

A similar invasion of the medulla or cortex of the suprarenal capsule and inflammatory reaction can also be seen in the kidneys, the hypophysis, and the thyroid gland. In animals the parasites have been seen in the testicular tubules, but they have not been noted in the human ovary.

Symptomatology.—There are two principal varieties of the disease—the acute and the chronic.

In the *acute stage* the disease begins with a violent attack of fever in a young child or a new-comer into the district. This fever shows a morning remission and an evening rise, and is associated with a palpable increase in the thyroid gland, œdema of the face, in which characteristic crepitation can be felt by palpation, enlargement of the lymphatic glands in various regions of the body, but especially of the neck; and fugitive œdemas in different parts of the body—as, for example, the forehead and extremities. The spleen enlarges and becomes painful, and the liver also becomes enlarged, and there may be signs of meningitis, and also of albumen in the urine. After a time the attack of fever passes off, only to return after periodical intervals. During an attack the typical trypanosomes can be found in the blood, but during the apyrexial interval they are absent. After these attacks have lasted some time the child either dies, recovers, or passes into the chronic stage.

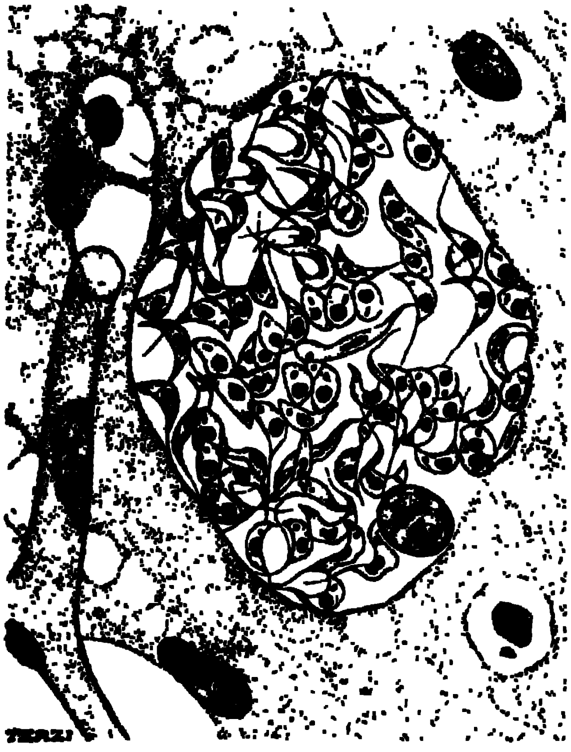

FIG. 642.—NEUROGLIA CELL OF BRAIN DISTENDED TO A CYST AND FILLED WITH *Trypanosoma cruzi*. (× 2,000.) (After Vianna.)

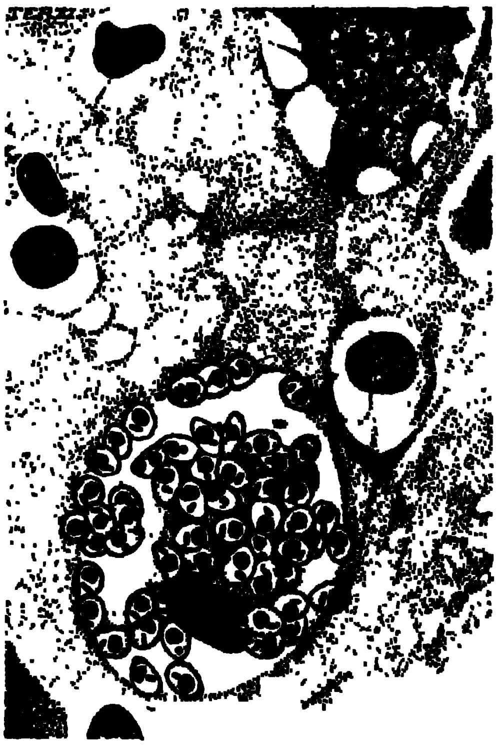

FIG. 643.—*Trypanosoma cruzi* IN A NEUROGLIA CELL OF THE BRAIN. (× 2,000.) (After Vianna.)

In this *chronic stage* the children show signs of marked thyroiditis and loss of hair, with hypertrophy of the lymphatic glands, a dull expression, a peculiar bluish-bronze pallor, tachycardia, and intestinal and nervous disorders, especially convulsions.

Chagas has classified the various symptoms of the chronic stage of the disease into five subvarieties:—

1. The pseudo-myxœdematous form.
2. The myxœdematous form.
3. The cardiac form.
4. The nervous form.
5. The chronic form with acute or subacute exacerbations.

1. *The Pseudo-Myxœdematous Form.*—In this subvariety of the chronic stage there is usually hypertrophy of the lateral lobes of the thyroid gland, more rarely a globular enlargement of the central lobe. This hypertrophy is usually well marked in quite young children, but is by no means evident in older children. In young children the face is thin and the skin of a peculiar light bronze colour, said to be quite different from the pallor of an anæmia. In older children the skin colour is violet-bronze. These colourations are believed to be associated with a parasitic invasion of the suprarenal capsule.

There is enlargement of the lymphatic glands in the neck, axillæ, and groins, while the parotid gland is also often hypertrophied.

In young children the liver and spleen may be found to be enlarged, but in older cases the abdominal signs are not well marked.

With regard to the circulatory system, there may be tachycardia, sinus irregularities, and an extra systole, and the blood-pressure may be lower. Convulsions have been noted, and at times slight fever, while the occurrence of conjunctivitis is also recorded.

2. *The Myxœdematous Form.*—In this form the thyroid gland is atrophied, and associated with the usual symptoms of myxœdema, such as the rough skin, loss of hair, and the presence of a firm œdema not pitting on pressure, together with an arrest of mental development in young children, or a mental degeneration in older persons. The lymphatic glands of various regions are enlarged, and there may be inflammatory eye affections.

3. *The Cardiac Form.*—In the cardiac form there is disturbance of the heart's action associated with arrhythmia, allarrhythmia, extra systole, or sinus irregularities. The greater number of the cases would be classed under Mackenzie's '*Rhythmus nodalis.*'

4. *The Nervous Form.*—Various brain and spinal cord symptoms are seen in this disease—*e.g.*, spastic paralysis in the legs, athetosis in the arms, aphasia, pseudo-bulbar paralysis, or suprabulbar paralysis. They are associated with the other symptoms of the disease.

5. *Acute or Subacute Exacerbations.*—The principal feature of this form is the preponderance of fever, and this may be due to exacerbations of an old infection or to new infections. This form is the cause of much mortality, and is separated from the acute form by the rarity of the parasites in the blood, and by the history of the long duration of the illness. As a rule it occurs in patients who show marked hypertrophy of the thyroid gland, and there may also be signs of suprarenal insufficiency.

Blood.—**The hæmatology has been investigated by Dias, who finds that the hæmoleucocytic formula has a great similarity to that found in African**

trypanosomiasis. As a rule, there is no globular anæmia, but there is a definite diminution in the hæmoglobin and in the specific gravity. The leucocytosis is slight in the acute and exceptional in the chronic cases. In acute cases there is a macrolymphocytosis.

Metabolism.—Guerreiro, from careful experiments associated with urine analysis, concludes that there is a true liver insufficiency in most forms of the disease, but not in the cardiac form unless associated with other symptoms.

Sequelæ.—Chagas considers that *infantilism* may be a sequel of the disease, especially as it is associated with hypothyroidism.

Diagnosis.—The diagnosis must be effected by finding the parasite in the blood during a febrile attack. The disease is most likely to be confounded with ankylostomiasis, from which it can be recognized by the absence of the typical ova in the fæces and the presence of *S. cruzi* in the blood, though, of course, both infections may occur together.

It might also be mistaken for malaria during the febrile attack, especially as there is splenic enlargement, but the absence of the malarial parasite and the presence of *S. cruzi* in the peripheral blood will enable a diagnosis to be made.

In the chronic stage it may be mistaken for goitre, especially when the myxœdematous or pseudo-myxœdematous symptoms are present, and the diagnosis will depend upon the discovery of the parasite or the history.

Prognosis.—The prognosis is most serious in the acute attacks and the acute or subacute exacerbations. The severer cardiac forms are also of grave import.

Treatment.—The indications for treatment are the same as those for African trypanosomiasis, associated with treatment for hypothyroidism.

Prophylaxis.—The prophylaxis must aim at the prevention of the Lamus biting man.

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CHAPTER XLVII

THE KALA-AZARS AND PSEUDO-KALA-AZARS

General—Tropical kala-azar—Mediterranean Kala-azar—The pseudo-kala-azars—Tropical febrile splenomegaly—Toxoplasmosis—Krempf's splenomegaly—Tropical afebrile splenomegaly—References.

GENERAL.

THE present chapter is devoted to those fevers which are known as the kala-azars and those allied conditions, tropical febrile splenomegaly and tropical afebrile splenomegaly, which clinically resemble kala-azar, in one variety of which Castellani has obtained protozoal bodies from spleen which are classified, at present, in the genus *Toxoplasma*.

With regard to the kala-azars, of which Ross has pointed out that the correct name is 'kala-jwar'—*i.e.*, black or mortal sickness—we have already in Chapter XIX., p. 369, pointed out that we consider that tropical kala-azar should be treated, at all events at present, separately from Mediterranean kala-azar, and this we shall do in the present chapter, although the general tendency of modern thought is to consider the two diseases to be identical. We invite the reader's attention especially to the first half of Chapter XIX., in so far as it deals with the *Herpetomoninæ*, and especially to the experimental work of Fantham and Porter (p. 363), as having a direct bearing upon the unknown method of infection of man with the germs of kala-azar.

TROPICAL KALA-AZAR.

Synonyms.—Indian Kala-Azar, Kala-Jwar, Kala-Dukh, Sirkari disease, Sahib's disease, Dum-Dum fever, Non-malarial remittent fever, Cachectic fever, Tropical splenomegaly, Tropical Leishmaniasis, Internal Leishmaniasis,

Definition.—Tropical kala-azar is a subacute or chronic febrile disorder characterized by splenic and often hepatic enlargement, progressive wasting and anæmia, and caused by *Leishmania donovani* R. Ross, 1903. The method of infection is unknown.

History.—In 1869, when the district of the Garo hills was first occupied by the British, a disease believed to be a very severe form of malarial cachexia was found to be endemic. This disease the Garos called 'kala-azar,' which means the black fever, so named from the appearance of the victims. In 1875 it began to spread, and became epidemic, and by its high death-rate attracted attention. In 1882 the first account of the disease was published by Clarke from notes of 120 cases compiled by McNaught, the Civil Medical Officer of the district. In 1889, when it had spread into Assam, following the lines of human intercommunication, Giles investigated the epidemic, and concluded that it was ankylostomiasis. In 1894 Stephens, in his yearly report, stated that the disease, though allied to, was distinct from malaria. In 1897 Rogers reported that it was malarial, and this was further supported by Ross in 1899. In 1902 Bentley ascribed the disease to *Micrococcus melitensis*, on the basis of serum reactions.

Up to this point the history of the disease remarkably resembles the present history of blackwater fever. A change now comes over the ætiology, for, in 1900, Sir William Leishman found the parasites already described under the heading *Leishmania donovani* in films taken post mortem from the spleen of a soldier who died in Netley from fever contracted at Dum-Dum, but he did not publish this discovery till 1903. In July, 1903, Donovan observed the same parasite in blood obtained by splenic puncture performed during life. In 1904 Christophers published a valuable report on the parasite and the disease, and in the same year Rogers observed the development of the parasite into a flagellate organism when splenic blood was incubated at 22° C. in citrate of soda solution. In 1907 Patton showed that the parasite could be found in numbers lying in leucocytes in the peripheral blood, and, further, that it became flagellated in the alimentary canal of bugs.

In 1904 Neave in Omdurman discovered the existence of this disease in a child coming from the Bahr-el-Ghazal province of the Anglo-Egyptian Sudan, and in the same year Philips in Cairo discovered it in two adults coming from the Yemen district of Arabia. In 1907 Pirrie, who had been working in the Sudan, died in England from kala-azar. In 1908 Cummins discovered a case contracted at Singa on the Blue Nile; Carroll recorded a second case from the same district, while Black met with two other cases; Bousfield recorded seven cases from the province of Kassala and one from Mafaza, and Thomson and Marshall found forty-one new cases in children and adults along the Blue Nile towards Abyssinia, which forms an endemic zone, which has been carefully studied by Archibald. It corresponds to the Blue Nile, Sennar, and Kassala districts, while the infection in one case of a woman is regarded as coming from quite a different part of the Sudan—*i.e.*, from Um Ruaba near Talodi. Archibald has studied a small epidemic at Kurmok on the Abyssinian frontier. This Sudan kala-azar is peculiarly interesting because of its limited endemicity (as far as is known) and by the peculiar features shown by Archibald to be associated with its parasite.

In 1913 Gaspar Vianna introduced the intravenous injections of tartar emetic for the treatment of the American mucocutaneous

Leishmaniasis. According to Christopherson the drug was discovered by Basil Valentine in the sixteenth century, and accidentally caused the death of several monks, and thus acquired its name 'antimony'—*i.e.*, *anti-moine*, against the monk. In 1914 Castellani in Ceylon used this method combined with oral therapy for the treatment of tropical kala-azar. In 1915 Rogers treated cases in India in the same manner, and later in the same year Rogers and Hume administered this treatment to six cases of kala-azar in Europeans. Christopherson has successfully employed the same method in the Sudan; and this has now become the recognized method of treatment.

In addition to the above, much work has been done by the Indian investigators, such as Mackie, Cornwall, and others, as well as by Manson, Low, Statham, and others.

Climatology.—The disease is especially spread through the tropics, but is unknown in Tropical America and Oceania. It is found in the Sudan, Arabia, India and Ceylon, Burma, Indo-China, and China.

Ætiology.—Kala-azar is caused by a herpetomonad parasite called *Leishmania donovani* R. Ross, 1903, described on pp. 369-370, which lives especially in the endothelial cells of bloodvessels and lymphatics, and is especially numerous in the spleen, the liver, and the bone-marrow, but is also found in other organs, such as the lungs and the kidney. Especially must be mentioned its presence in the mesenteric lymphatic glands, and in ulcers of the intestinal mucosa.

It can also be found in mononuclear and polymorphonuclear leucocytes in the peripheral blood, but only occasionally, as at other times it is most difficult to find it in this situation. It also at times, but very rarely, lies in the hollow of the biconcave disc of a red blood cell, thus looking as though it was contained therein. The parasites have been cultured from the blood by using the N.N.N. medium.

They are most abundant in the blood towards the fatal end of the illness, and during fever or the presence of intestinal symptoms. They are said to have been found in the motions during an attack of kala-azar dysentery, and also in the scrapings from intestinal ulcers. They have also been found in papules and ulcers in the skin.

As they occur in the peripheral blood and in the skin, it is possible that they may pass into the alimentary canal of some blood-sucking arthropod, but these animals are often naturally infected with flagellate parasites of the leptomonad, crithidial, and trypanosomal types, and therefore the mere finding of a flagellate in the interior of a blood-sucking arthropod which has been fed upon a man or animal infected with *L. donovani* is worthless from an ætiological point of view.

As they occur in the peripheral blood and in the intestinal mucosa, they can equally escape in the fæces in the form of cysts, and thus get into water, from which they can be ingested by some aquatic arthropods, many of which naturally contain flagellates.

The work of Laveran and Franchini, of Fantham and Porter, has demonstrated that these natural arthropodal parasites can by ingestion or by inoculation produce a fatal illness resembling kala-azar in mammals. Archibald, experimenting with human kala-azar parasites in the Sudan, has shown that monkeys can be similarly infected by feeding with kala-azar material, and this, together with the curious endemicity of the disease in the Sudan, and with Laveran, Franchini, Fantham, and Porter's researches, make the possibility of water carriage of cysts from infected arthropods to man worthy of consideration.

From the above it will be clear that, though the parasite is known, the method of infection is still unknown, and the cultivation of the parasite into flagellate form clearly indicates that this is part of the life cycle.

The predisposing causes appear to depend upon, and be capable of explanation by, the habits of man. Thus the disease, when epidemic, always spreads relatively slowly along channels of human intercommunication, and apparently is directly due to the introduction of an infected human being into the district. It runs in families, in which children particularly suffer, while the class of people who are mainly affected are the poorer sections of the European and native communities. Season and sex appear to have no influence, but there is no doubt about the infection of the dwelling or perhaps its water-supply, nor of the capability of the disease spreading from one dwelling to another, or from one water-supply to another.

Pathology.—Introduced into the body, the parasite appears to enter the endothelial cells of a capillary bloodvessel or lymphatic, and to grow therein, and to increase in numbers by simple fission until a very large number—Leishman says upwards of 220—may be counted in one cell. The organs principally affected in this manner are the liver, spleen, bone-marrow, and lymphatic glands, and, to a less extent, the pancreas, kidneys, suprarenals, testicles, and lungs.

The parasites may now escape from the enclosing cell by rupture, and are then taken up by the leucocytes, particularly by the polymorphonuclears, but also by the mononuclears and rarely by the eosinophiles, by means of which they appear in the peripheral blood even in early cases, but are much more common late in the disease, especially if there is diarrhœa due to ulceration of the intestine, in which condition the polymorphonuclear leucocytes are increased in numbers in the peripheral blood, and many of them contain parasites. The further development has still to be worked out, as all that is definitely known is that in cultures the parasite becomes flagellate.

It would appear as though the parasite could produce some sort of toxin which causes the marked changes in the spleen, liver, and bone-marrow, as well as the ulceration of the skin and intestinal mucosa, because sometimes, and in an inconstant manner, it can produce a reaction on the part of the body, as is seen in the formation at times of agglutinins, specific precipitins, inconstant in presence and feeble in action, and useless from a diagnostic point of view, as is complement deviation. At the commencement of the infection there appears to be generally an attempt to produce an immunity, and it is this which produces the rare natural cure in man. It may be the cause of the refractory nature of certain animals to the disease and the limitation of infection in endemic communities. After the infection has obtained its hold on the body as a rule the struggle for immunity becomes less and less, and disappears eventually.

By some means or other the parasite irritates the organ it infects, causing marked changes in the spleen, liver, and bone-marrow, and also causing ulceration of the intestine and skin.

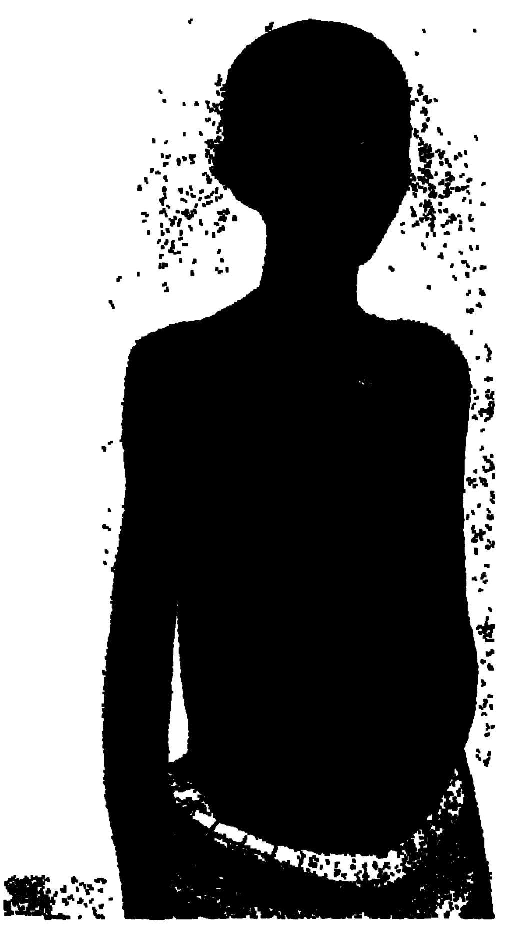

FIG. 644.—INDIAN KALA-AZAR.

The distension of the abdomen by the greatly enlarged spleen should be noted. (Photograph of a case in the Tropical Clinic, Colombo.)

The Blood.—The examination of the blood is most important because, firstly, the parasite may be found in a leucocyte if carefully looked for, even in the early stages of the disease: secondly, the leucocytic changes are of the utmost importance. There is marked anæmia—54·2 per cent. of Rogers' cases giving from 4,000,000 to 2,500,000 corpuscles per cubic millimetre—and the hæmoglobin is reduced in proportion to the erythrocytes, the colour-index being normal. There is a most marked leucopenia, and Rogers reports that in 42·1 per cent. of his cases the leucocytes were 1,000 or less, in 30·3 per cent. 1,000 to 2,000, and in 22·6 per cent. 2,000 to 3,000. The proportion of white to red, according to the same author, is less than 1 : 1,500 in 67·9 per cent., or, if inflammatory cases are excluded, in nearly 90 per cent. of the cases he examined. There is a reduction in the polymorphonuclear leucocytes and in the eosinophiles, and an increase in the mononuclear leucocytes and lymphocytes. The diminution of the polymorphonuclear leucocytes is thought to explain the tendency to bacterial infections. The coagulability of the blood is decreased, which explains the tendency to hæmorrhage, and renders occasionally splenic puncture dangerous. The alkalinity of the blood has been shown by Archibald to be diminished—a fact which may be of some secondary diagnostic importance.

The Urine.—The urine in our cases did not show anything abnormal.

Morbid Anatomy.—The body is much emaciated, and there is marked muscular atrophy, together with œdema, enlargement of the spleen, and often of the liver, ulceration of the skin and intestine, sometimes hæmorrhage in various places, and generally the presence of some complication. The spleen is greatly enlarged, firm, and deep red in colour, though it may at times show malarial pigment. The capsule and septa are thickened, and the whole organ is congested with blood, and contains numerous mononuclear cells and macrophages full of parasites.

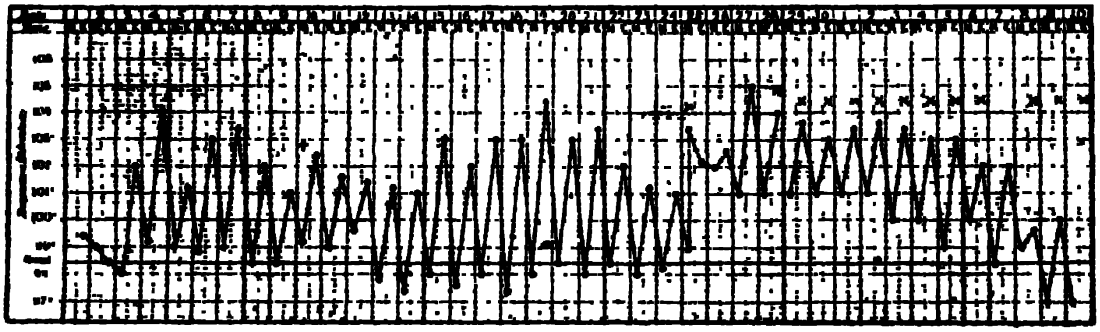

FIG. 645.—TEMPERATURE CHART OF KALA-AZAR FROM A SUDAN CASE. (After Christopherson.)

+, Leishman bodies found; ××××, injection of tartar emetic.

In the liver, which may or may not be enlarged, the most marked changes are in the intralobular capillaries, which are dilated and contain macrophages, derived from their endothelial wall, full of parasites, while the liver cells are atrophied and degenerated. Cirrhosis has been noted in some cases.

The bone-marrow contains numerous parasites in the usual cells, and, as in malaria, the yellow marrow is converted into red, and is soft and diffluent. The skin may show papules and ulcers, in which the parasites can be found, while the colon is often ulcerated, or shows the cicatrices of old ulcers.

Symptomatology—*Incubation.*—The incubation period appears to be very variable, and, indeed, it is difficult, in a chronic disease of this nature, to decide when it first begins. It is said to range from ten days to three weeks or several months.

Onset.—The onset may be heralded by a rigor, which may be repeated daily, and by an attack of irregular, high, remittent fever, which may early show two remissions per diem in a four-hourly temperature chart. This double remission is considered by Rogers to be almost diagnostic of the disease. Towards the end of the third to sixth week of the fever the temperature declines, and the initial stage of the disease may be said to have terminated. During this period, however, the spleen and liver will have enlarged, and may be both painful and tender. Headache is present at times, but is not severe. Nausea and vomiting are unusual, while the bowels are regular, and there is no abdominal distension. The pulse may be slow or quick.

The attack, however, may begin with a continuous fever, which shows two fluctuations in the twenty-four hours, which Rogers considers as almost diagnostic of the disease. In other cases the disease may begin with gastro-intestinal disturbances or with dysenteric symptoms, or quietly, without any marked initial stage, the patient gradually developing an enlarged liver and spleen, anæmia and weakness.

Course.—The course of the disease, after the decline of the temperature, is marked by what is called an apyrexial interval; but it appears that—in some cases, at all events—there is a slight daily rise of temperature, not exceeding 100° F. After some weeks this apyrexial interval ends in an attack of fever resembling the onset. Periods of apyrexia and pyrexia now alternate with one another, while the spleen, and sometimes the liver, enlarge. Anæmia commences and increases, while asthenia not merely appears, but deepens, until the wretched patient presents the typical appearance, which may be described as follows:—He is thin and wasted, with the abdomen much swollen and protuberant, the chest so thin that the ribs show clearly, the arms and legs wasted, the cheeks sunken, the nose sharp, and the ankles puffy, while the skin and tongue are often distinctly darker than they should be, the former being furfuraceous.

On examining the swollen abdomen, the enlarged spleen may be felt reaching almost to the pelvis, while the enlargement of the liver may be marked or may be absent. In this condition intestinal disturbances in the form of diarrhœa or dysenteric attacks are common, and may be due to the actual disease or to complication with true dysentery. Dyspeptic symptoms may also be present.

Hæmorrhages may occur from the nose, the gums, the stomach, the bowels, or under the skin. Papular eruptions are to be seen, especially on the thighs, and ulcers may be present. The weakened, emaciated patient may now die of asthenia, but more usually the long-drawn-out illness is brought to a close by some complication. The total duration varies from about seven months to two years, and generally ends fatally.

Complications.—It appears as though the reduction in the number of the polymorphonuclear leucocytes laid the patient open to invasion by pathogenic bacteria, for septic infections, such as cancrum oris, or lung infections—for example, pneumonia, phthisis, and pleurisy—or abdominal troubles of the nature of diarrhœa, dysentery, and cystitis, are not uncommonly met with, and may cause the death of the patient. Sometimes, after a severe attack of septicæmia or some other complication, the disease is found to be cured, but this is rare.

Diagnosis.—The only certain method of diagnosis is to find the parasite, and as Donovan and Patton have reported its frequent occurrence, even in early stages, in the peripheral blood, this should be possible, especially if aided by dilution with normal saline solution, and centrifugalization and examination of the leucocytes. In our experience, the search for the parasite in the leucocytes of the peripheral blood requires an extremely long time, and is often negative. If the parasites cannot be found in the blood, an attempt may be made to find them by the examination of the exudate obtained by exciting artificial pustulation of the skin by some irritant, as suggested by Cummins. Failing this, there is puncture of the spleen or of the liver, and withdrawal of blood, which can be examined by the microscope. The diagnostic puncture of the spleen in the tropics is, however, not to be undertaken lightly, because splenic enlargement due to leukæmia is by no means unknown, and puncture of the spleen in this disease, or, indeed, in that of chronic malaria, may lead to most unfortunate results. The blood of the peripheral circulation should therefore be examined to exclude leukæmia.

Certainly, the first thing to do is to examine the peripheral blood and exclude leukæmia. Secondly, the coagulability of the blood should be tested by Wright's method, and if found to be decreased, the puncture should not be performed. Thirdly, if the puncture is to be carried out, the liver should be chosen for exploration, not the spleen, particularly in the later stages, in which hæmorrhages are to be feared. In the early stages there may not be so much risk, but it must be done with the greatest care, aseptically, and the patient must be kept at rest for some time afterwards, the site of puncture being covered with an aseptic pad and a firm bandage. The syringe should be sterile, and *perfectly dry*. Rogers recommends that a dose of 30 grains of calcium chloride in a couple of ounces of water be administered directly after a puncture, in order to promote coagulability of the blood. Attempts at cultivation from the blood and inoculations into susceptible animals may also help, rats and monkeys being used by preference.

Differential Diagnosis.—In the early stages the diagnosis has to be principally made from acute malaria and typhoid, when the positive signs in favour of kala-azar are:—(1) Presence of the characteristic daily double remission of the fever; (2) absence of constitutional symptoms, proportional to the severity of the fever; (3) absence of malarial parasites and Widal's reaction, though, of course, the latter reaction is negative in true typhoid during the first week; (4) marked enlargement of the spleen; (5) great leucopenia, especially in relation to the erythrocytes, which, however, may also be found in typhoid and malaria; (6) increase in mononuclear leucocytes; (7) presence of *Leishmania donovani* in the leucocytes.

In advanced cases the diagnosis has to be made from malarial cachexia and ankylostomiasis by (1) the presence of *Leishmania donovani* in the leucocytes of the peripheral blood, or in the juice from the liver and spleen; (2) by the absence of the typical febrile attacks of subtertian or tertian fever: (3) by the absence during the febrile attack of malarial parasites; (4) by the absence of ancylostomes, or, if they are present, by the continuation of the symptoms after their expulsion. Mixed infections of kala-azar and malaria may occur.

Prognosis.—The prognosis is much less serious than before the introduction of the tartar emetic treatment. Formerly the mortality was about 98 per cent. It is true that some people recover after having nearly died from a complication, or, more rarely, without this episode, but why they recover is not known.

Leucocytosis and increase of the polymorphonuclears are considered to be good signs, while leucopenia and polymorphonuclear decrease are bad signs. Complications, of course, increase as a rule the gravity of the prognosis.

Treatment—*Essential Treatment.*—As soon as a diagnosis is made give *tartar emetic* either—

(*a*) Intravenously (this is the method to be preferred);
(*b*) Intramuscularly;
(*c*) Orally combined with (*a*) or (*b*).

Intravenously.—Give 2-10 cubic centimetres of a sterile 1 per cent. solution in warm normal saline solution daily for five to ten days, and then every other day, and finally twice a week. This is the best method of treatment.

Dose for Children.—This is as follows:—

INTRAVENOUS DOSAGE OF 1 PER CENT. TARTAR EMETIC.

Age.	*Dose.*	*Number.*
Under one year ..	¼-1 c.c.	One daily for seven days
One to five years	1-3 c.c	Ditto.
Five to ten years	1-5 c.c.	Ditto.
Ten to sixteen years	1½-8 c.c.	Ditto.

Important.—The sterilization of the tartar emetic solution must be made in flowing steam on two or three consecutive days, and must not be performed in an autoclave, in which the drug is liable to decomposition and may then cause serious symptoms. Some authorities advise using a solution merely filtered through a Chamberland filter. One of us has used a solution containing ½ per cent. carbolic, which in practice renders unnecessary a sterilization by heating.

Intramuscularly.—Intramuscular injections are painful and often become inflamed. The following solution may be used:—

Tartrate of antimony	8 grains.
Carbolic acid	10 minims.
Glycerine	3 drachms.
Bicarbonate of sodium	¼ grain.
Distilled water	1 ounce.

The dose is ½-1 cubic centimetre every other day injected intramuscularly into the gluteal region.

Martindale's formula may also be used:—

Antimonii oxidi	gr. $\frac{1}{60}$.
Glycerin. Aq. dest.	āā ♏xv.

One ampoule.

Combined.—Oral administration may be combined with intravenous or intramuscular injections. The following mixture may be given:—

Tartrate of antimony	5 grains.
Bicarbonate of sodium	30 grains.
Glycerine	1 ounce.
Chloroform water	1 ounce.
Water	to 3 ounces.

The dose is one to two teaspoonfuls in water three times a day.

Rogers regards sodium antimonyl tartrate, given intravenously, as being more efficacious than tartar emetic. Colloidal antimonial preparations have been recommended.

Symptomatic Treatment.—*Hæmorrhagic symptoms* may be treated by calcium lactate in 10-grain doses twice or three times a day. *Diarrhœa* may be combated by bismuth subnitrate in 10-12 grain doses, with or without 5-10 grains of salol, every four to six hours, as may be required. *Intestinal parasites* should be looked for and treated as prescribed in the chapters pertaining to the different forms. *The heart* must be watched and cardiac tonics or saline injections given if required (*vide* Treatment of Malaria, p. 1188).

General Treatment.—The patient should be kept in bed and well nursed during this treatment.

Diet.—The diet should be good and nourishing, but if there is much diarrhœa it is necessary to restrict it to milk, Benger's food and the like, soups, etc.

Prophylaxis.—As the method of infection is unknown, all that can be done is firstly to segregate the sick and carefully disinfect his motions, as well as protect him against blood-sucking arthropods. Secondly, to remove the healthy from the infected area, and to disinfect or destroy the clothing, furniture, and houses, while a complete change of the drinking-water supply is essential. If this latter cannot be done and the water-supply is a well, it may be sterilized by blowing in steam, as in the case of prophylaxis against the guinea-worm (p. 1971); or if this cannot be done, the simple boiling of all drinking-water should be carried out. It does not appear probable that infection comes about via unbroken skin.

MEDITERRANEAN KALA-AZAR.

Synonyms.—Infantile kala-azar, Infantile leishmaniasis, Mediterranean leishmaniasis, Febrile splenic anæmia (Fede), *Anæmia infantum a Leishmania* (Pianese), *Leishmania anæmia* (Jemma and di Cristina), *Marda tal biccia* (Malta), *Ponos* (Greece), *Malattia da mensa* (Sicily).

Definition.—Mediterranean kala-azar is a subacute or chronic specific disease due to *Leishmania infantum* Nicolle, and clinically closely resembling tropical kala-azar, but occurring in temperate or subtropical climates.

Historical.—Fede several years ago described in Italy a form of splenic anæmia among young children characterized by irregular fever, progressive anæmia, and a fatal ending. He considered it a disease by itself, separating it from the non-febrile type of splenic anæmia. In 1904 Laveran and Cathoire found a Leishmania in films from the spleen of a child who had died of an ill-defined disease in Tunisia. Pianese in 1905 called attention to the similarity of the symptoms of Fede's splenic anæmia with kala-azar, and described parasitic bodies in the spleen of the affected children morphologically identical with *Leishmania donovani.* Later Nicolle suggested for the disease the name of 'infantile kala-azar,' and completed the study of the parasite, which he called *Leishmania infantum.* Gabbi considers the disease to be identical with tropical kala-azar, having found it also among adults. A fuller account of the history will be found on p. 373.

Cristina and Caronia in 1915 applied to this complaint Vianna's tartar emetic treatment for American muco-cutaneous leishmaniasis.

Climatology.—The malady is met with in Southern Europe, in the northern regions of Africa, and perhaps Egypt. Future investigations will probably show that it is endemic in many countries.

Ætiology.- The malady is due to *Leishmania infantum* Nicolle. The description of this parasite will be found on p. 373. Nicolle has succeeded in reproducing the disease in monkeys, and less typically in dogs. He has also found that dogs may be spontaneously affected with a leishmania; in fact, in his opinion, the dog acts as a reservoir of *L. infantum,* and its ectoparasites, such as fleas, may possibly serve as the transmitting agents to human beings. These views have been tested experimentally by Basile, but to-day doubt is cast upon canine leishmaniasis being the same disease as that in man, and the flea infection of man is also considered to be doubtful.

The majority of the cases occur in young children of two to three years of age, among whom there is a slight preponderance of males. The disease sometimes occurs in more than one member of a family, and more often begins in the spring or early summer.

Pathology.--The pathology has been carefully studied by Pianese, who finds that the post-mortem lesions are similar to those observed in Indian kala-azar, the spleen and liver being greatly enlarged. Microscopically, there is great increase of the lymphoid tissue in the spleen and hypertrophy of the islands of Langerhans in the pancreas. In the bone-marrow there is hyperproduction of the myeloid and lymphoid tissues.

Symptomatology—*Onset.*—The disease begins in a very insidious manner, and is usually first noticed when the child has some disturbance of the alimentary canal, such as an attack of vomiting and diarrhœa, when the spleen may or may not be found to be enlarged; and as the child is anæmic and has a very irregular fever, the complaint is wont to be diagnosed as malaria, especially as some seizures are apt to come on suddenly, and to be associated with rigors.

The child becomes pale, ceases to be interested in its games, and suffers from attacks of diarrhœa, alternating with periods of constipation, from attacks of irregular fever separated by apyrexial intervals, and from epistaxis.

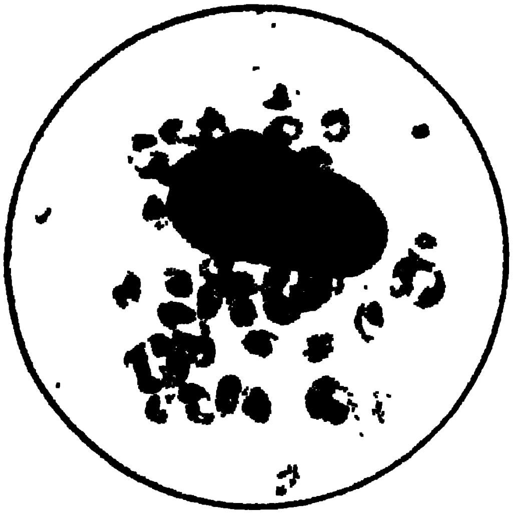

FIG. 646.—*Leishmania infantum* NICOLLE.

(After Marzinowsky.)

FIG. 647.—CHILD SUFFERING FROM INFANTILE KALA-AZAR.

(After Marzinowsky.)

Course.—After the above symptoms have lasted some time, the spleen begins to enlarge, and presently protrudes from under cover of the ribs; the attacks of fever become more marked; hæmorrhages from the nose and gums and into the skin are seen, and the diarrhœic or dysenteric attacks become pronounced. The child now wastes and becomes progressively anæmic: the face, conjunctiva, and whole body taking a peculiar white tinge, and the disease may be said to be fully established.

With regard to the special symptoms, the fever is very irregular, with exacerbations sometimes twice a day—in the morning and in the evening—and sometimes several times a day. High temperatures at times appear in cycles, or there may be sudden falls to subnormal temperatures.

The alimentary canal is always disturbed, but the appetite is preserved, and may even be increased, although the little patient is suffering from alternate attacks of diarrhœa and constipation; but this is not always so, and some observers have recorded anorexia. The motions may be very foul, containing undigested food, and at times blood and mucus. Ulcerative stomatitis, and even noma, may occur, and the last may appear on the face or on the genitalia. Noma appears to be not uncommon in Greece.

The spleen, as stated above, is always enlarged from the time of the full establishment of the symptoms, but this enlargement is not stationary. On the contrary, it steadily increases until an enormous size is sometimes reached, so that it fills the left side of the abdomen and projects across the median line into the right half, causing the abdomen to bulge and become prominent. On palpation it is found to move, and notches may be felt through the attenuated abdominal wall. It moves with the respiratory movements, and may be altered in position from side to side, and up and down by manipulation. There is not, however, any constant relationship between the progress of the disease and the size of the spleen. Jemma, Di Cristina, and Critien state that it diminishes with a persistent and profuse diarrhœa, especially during the last few days of life.

There is not always a concord between the temperature and the pulse-rate; on the contrary, the latter is almost constantly rapid, even during the apyrexial intervals, but may rise to 150 to 160 beats per minute during attacks of fever. Hæmic murmurs may occur over the heart, but are rare. The blood is pale, and shows a decrease in the number of erythrocytes (1,500,000 to 3,000,000), and in the hæmoglobin (below 50 per cent.), which, however, is reduced in proportion to the red corpuscles; and also in the leucocytes (1,500 to 3,000), though the leucocytic formula is mononuclear (70 to 80 per cent.), being especially composed of medium-sized cells. The mononuclears are increased at the expense of the polymorphonuclear cells, which make up the remaining 20 to 30 per cent. There is usually some poikilocytosis and anisocytosis, but nucleated cells are rare or absent. The opsonic index is diminished below that which is normal for a healthy child, and is especially low for *Bacillus coli communis*, which is held to be responsible for the frequency of the intestinal symptoms. Œdemas of the face, hands, genitalia, and feet, coming on suddenly and disappearing suddenly, are not unusual; they have a tendency to bilateral symmetry, but are influenced by the position of the patient, and may occur at any stage of the disease. At times they are painful and may show signs of inflammation.

The liver is very generally enlarged, but to a much less extent than the spleen. On palpation, its edge is felt to be smooth and hard, and is not tender.

As the spleen and liver enlarge, the abdomen also enlarges and becomes prominent, while the superficial veins may stand out distinctly, and there may be a slight degree of ascites at times.

The urine is usually normal, but there may be slight signs of albuminuria, or a decrease in the output of urea. The lymphatic glands are as a rule not enlarged.

The mental and physical activity of the child decreases as the disease progresses; it emaciates, and becomes extremely pallid, thereby assuming a prematurely aged appearance. The bones become evident, especially the ribs and shoulder-blades, and the child dies from exhaustion, often due to an attack of dysentery or diarrhœa. Spontaneous recovery may take place, but this is rare.

Complications.--Respiratory complications are not unusual. Bronchitis is common, while broncho-pneumonia and pleurisy may occur, as may a rapidly developing fatal dyspnœa, which is probably due to œdema of the glottis. Perhaps noma, as already mentioned, is a fairly common complication in Italy and Greece, and should come in this place as a complication rather than a symptom of the disease. Otitis media has been recorded not merely as a complication, but also as a cause of death. Ankylostomiasis associated with lipuria has been recorded as a complication.

Diagnosis.—The symptoms more or less closely resemble those of kala-azar, but differ in that this disease occurs in children and is inoculable into dogs, while kala-azar occurs mostly in young adults and is with difficulty inoculable into dogs. The temperature chart may resemble that of kala-azar, but is generally more irregular. The characteristic clinical symptoms of the disease are the enlarged spleen, the irregular fever, and the pallor occurring in a child. The essential feature in the diagnosis is the parasite, which may be obtained by splenic puncture, by liver puncture, by examination of the bone-marrow obtained by a modified trocar and cannula, as designed by Caccioppoli, to which a Potain's aspirator with a strong pump is attached: rarely by blood examination. Other methods are by vesication and examination of the fluid; and by lumbar puncture, if there are cerebral symptoms.

Having obtained the splenic or hepatic pulp, etc., the diagnosis may be made by microscopical examinations and by cultivation on the medium devised by Novy and McNeil, and modified by Nicolle, usually known as the N.N.N. medium (p. 377).

It has been suggested by Cochrane that removal of one of the post-cervical lymphatic glands might be adopted as a diagnostic method. The removed gland is cut, and a smear made, when numerous parasites may be seen. This method is said to be the most certain means of diagnosis. It is recommended that the glands be removed under the influence of a local anæsthetic.

Differential Diagnosis.—The differential diagnosis has to be made from kala-azar, undulant fever, enteric fever, malaria, other forms of splenic anæmia, and syphilis.

Kala-Azar.—This fever occurs in adults, and is characterized by the double daily rise of the temperature, and by the difficulty of successful inoculation into dogs. In this disease the spleen is not so markedly enlarged.

Undulant Fever.—In contrast to undulant fever, in infantile kala-azar the temperature is much less regular, never showing a typical undulating type; the enlargement of the spleen is much greater; the articular symptoms are lacking, and Wright's agglutination test is negative.

Enteric Fever.—From enteric, infantile kala-azar differs by the splenomegaly, by the irregular fever, by the absence of Widal's reaction.

Malaria. -The absence of the typical blood parasites, and the fact that quinine has no influence on the irregular fever, are points of diagnostic value.

Other Forms of Splenic Anæmia.- From the splenomedullary leukæmia, infantile kala-azar is distinguished by the leucopenia; from syphilitic splenomegaly, by the history and inutility of mercury and salvarsan; from the various types of infantile afebrile splenomegaly, by the fever and the presence of the parasite; from the splenomegaly found in rickety children, by the absence of deformity of the bones and by microscopical examination.

Prognosis.—The prognosis is much more favourable since the introduction of the tartar emetic treatment, the mortality having been reduced from 90 per cent. to less than 20 per cent.

Treatment.—This is the same as for tropical kala-azar (p. 1297).

Prophylaxis.—As canine leishmaniasis (p. 377) is now considered to be a separate disease, and as the flea is doubtful as an infective agent, prophylaxis cannot be advised until more is known as to the method of infection, but the suggestions made under the heading of Tropical Kala-Azar may perhaps be applicable, and in any case it is unnecessary to keep dogs and fleas in a house.

Basile has sufficiently indicated the possibilities of this method of infection being correct to make the simple methods of prophylaxis of such a fatal disease imperative even before the full proof of the researches has been obtained.

THE PSEUDO-KALA-AZARS.

These are febrile and afebrile diseases which resemble kala-azar in that they are associated with splenomegaly, anæmia, and often emaciation. They can be divided into:—

Tropical febrile splenomegaly.
Toxoplasmosis.
Krempf's splenomegaly.
Tropical afebrile splenomegaly.

TROPICAL FEBRILE SPLENOMEGALY.

Synonyms.—Tropical splenomegaly, Pseudo-kala-azar, Esplenomegalia tropical (Columbia), Wenku (Karonga), Gobora or Tebi (New Guinea).

Definition.—A chronic irregular febrile disorder of unknown causation, characterized by splenic hypertrophy and gastro-intestinal disturbance, followed by emaciation.

History.—A form of febrile splenomegaly resembling kala azar has been long known in the tropics; but the typical parasites of that infection cannot be found either during life or after death. Though well known, there is but little literature upon the subject. Woolley first gave an excellent account of the disease as seen in the Philippine Islands, and Day and Ferguson as seen in Egypt. We have repeatedly in local publications called attention to the disease in Ceylon. Gabbi has ably described the disease in Italy, and so has Leys, in 1917, from Karongo, and it is probably the same disease as that described by Breinl, in 1915, in New Guinea. In 1916 Spagnolio recorded cases from Calabria and Sicily.

In one form of this complaint (p. 1305) Castellani has found protozoal bodies, *Toxoplasma pyrogenes*, which may be causal (*vide* p. 490), but there may be many varieties of the disease.

Climatology.—The disease has been reported from India, Ceylon, China, the Philippines, Egypt, Arabia, Tunis, Algiers, the Belgian Congo, Italy, and South America.

Ætiology.—The causation of the disease is quite unknown. Gabbi suggests that it may be a filterable virus.

Pathology.—It is thought probable that the disease may be a primary infection of the alimentary canal, and that the fibrosis is secondary, but we would rather distinguish this from the ordinary forms of polyfibrosis, and would consider that the seat of the disorder was in the spleen and liver, and that the alimentary canal signs were secondary.

Morbid Anatomy.—On post-mortem examination, the body is seen to be emaciated as a rule, but there may be œdema of the feet and legs, and there may be ascites if the liver is seriously affected. Upon opening the abdomen, the principal object of interest is the extremely enlarged firm spleen. The liver may be enlarged and smooth, and does not show the hobnailed appearance of alcoholic cirrhosis, while the lymphatic glands in various regions of the body may be slightly enlarged. The intestines show signs of catarrhal or ulcerative enteritis. The bone-marrow is diffluent and pale in colour. Hæmorrhages may at times be found in different parts of the body. Microscopical examination reveals hyperplasia of the lymphoid elements of the spleen, associated with hyperplasia of the fibrous tissue, dilatation of the vascular sinuses, and sometimes hæmorrhages. The microscopic examination of the liver shows the usual appearances of monolobular and polylobular cirrhosis. The bone-marrow is seen to be congested and hæmorrhagic, and the hyaline cells are increased, while the granular cells are reduced.

Symptomatology.—The onset of the disease is quite gradual and unnoticed by the patient, although at times a history of diarrhœa, dysentery, or of attacks of fever may be obtained. Usually the patient comes to the hospital complaining of weakness and vague rheumatic pains, although he may come in the later stages because of the ascites. On examination, the patient is found to be more or less emaciated, and to have a large firm spleen projecting from under the ribs, and sometimes making a considerable protuberance of the thin abdominal wall. The amount of anæmia is usually not extreme, the average number of red corpuscles being between 2,500,000 and 3,500,000, while microcytes, megalocytes, and polychromatophilia are not unusual. The leucocytes are more or less normal. Frequently there is some fever of an irregular type, and there may be exacerbations, and at times there may be a double remission similar to that found in kala-azar; but there may be long periods of apyrexia. In addition, in a few cases there may be all the signs and symptoms of cirrhosis of the liver, with the abdomen distended from ascites.

By some authorities the disease has been subdivided into two stages—the first or splenic stage before, and the second or hepatic stage after, the hepatic cirrhosis. The first may last for many years, but the latter is much shorter, lasting a variable number of months, and ending fatally by the patient passing into a condition of coma, sometimes accompanied by jaundice. Death in the first stage is, in our experience, not rare, and may be due to hæmorrhages or exhaustion.

Complications.—Pregnancy is a serious complication, and may hasten the end, even after the child has been born. Ankylostomiasis and other parasitic diseases may occur along with tropical febrile splenomegaly.

Diagnosis.—The leading features of the disease are the great enlargement of the spleen, associated with wasting and irregular fever, in people in whom examination fails to reveal any obvious parasitic cause. Tropical febrile splenomegaly must be differentiated from kala-azar by the absence of *Leishmania donovani* in the spleen pulp as obtained by puncture. It can also be distinguished from chronic malaria by the absence of the typical parasites or pigment from the splenic juice, and from cirrhosis of the liver by the presence of the enlarged spleen. From leukæmia it is easily distinguished by the absence of a leucocytosis. From infantile kala-azar it may be distinguished by the absence of *Leishmania infantum*, as seen in the splenic juice. The disease can be distinguished from Banti's disease by the febrile attacks, and apparently splenic removal does not effect a cure.

Prognosis.—The illness is very chronic, but the prognosis is bad, as no cure is at present possible, and the patient tends to go from bad to worse.

Treatment.—Arsenical injections are the most valuable, and salvarsan may be tried. Removal from the endemic area is advisable.

Prophylaxis.—As the ætiology is unknown, nothing can be said under this heading.

TOXOPLASMOSIS.

In 1913 Castellani recorded a case of splenomegaly associated with fever of long standing and terminating fatally, in which he had found protozoal bodies which eventually received the name *Toxoplasma pyrogenes* Castellani, 1913 (*vide* p. 490).

Morbid Anatomy.—The body was much emaciated, and the principal feature was the greatly enlarged, smooth, not very hard spleen, which was reddish in colour. No malarial parasites could be found, but there were some light yellowish pigment granules, quite different from malarial pigment.

Toxoplasma Pyrogenes.—This was rarely found in the blood, but was abundant in the spleen. (For a description, see p. 490.)

Symptomatology.—The fever starts in youth and lasts many years, defying all treatment. In character it is intermittent, reaching 103° to 105° F. at times. The attacks of fever do not start with shivering, and the fall is not associated with sweating. The spleen is much enlarged and hard, while the liver is also enlarged, but neither organ is tender on pressure. All the other organs are normal, and there is no enlargement of the lymphatic glands.

Blood Counts.—The red blood-corpuscles in an advanced case number 2,000,000, the leucocytes 5,200 per c.mm. A few nucleated red cells are present, and basophilia and chromatophilia are marked. The leucocytic count is as follows:—Polymorphonuclear leucocytes, 50 per cent.; lymphocytes, 40 per cent.; large mononucleurs, 7 per cent.; eosinophiles, 3 per cent.; hæmoglobin, 30 per cent.

No malarial parasites could be found, and the serum reactions for typhoid, the paratyphoids, and Malta fever, were absent.

The urine sometimes contained a trace of albumen.

Course.—The case grew gradually worse, emaciation set in, and the patient died.

Treatment.— Quinine was given by the mouth and intramuscularly in doses of 30-60 grains a day without effect.

KREMPF'S SPLENOMEGALY.

In 1917 Krempf described a case of splenomegaly in a young Chinaman. He suffered from a malarial infection, and stated that in his village near Tientsin splenomegaly was frequently observed in both sexes and at all ages.

On making a splenic puncture, Krempf found bodies either enclosed in red cells or free in the plasma. They were only found in the spleen.

The red cells were deformed and contained a capsule 10 × 5 microns in size, inside which lay a vermicular sporont often curved like the letter U. Extracted from a red corpuscle, these bodies measured 20 × 1·5 microns.

These bodies were believed to be the sporonts of a hæmogregarine, and were named *Hæmogregarina hominis* Krempf, 1917. No further history of the case is given.

Recently Raubaud, examining the blood of a lady who had resided for two years in the Congo, observed that some red cells contained a hæmogregarina 9-11 μ by 2·8-3·5 μ, which differed from Krempf's parasite by having a crescenting, not vermicular shape. Raubaud has named it *Hæmogregarina inexpectata*. There was no fever, and no enlargement of the liver or spleen. The blood, however, showed a marked mononucleosis.

AFEBRILE SPLENOMEGALY.

Synonym.— Pseudo-Banti's disease.

Definition.—A chronic afebrile disorder characterized by splenomegaly and severe anæmia.

History.—There is no literature on the subject as far as we know.

Climatology.—We have observed it in tropical Africa, Ceylon, and India, and probably it will be found in many other places.

Symptomatology.—The disease begins insidiously in either children or adults, but usually the case is not observed until either the anæmia becomes well marked or the splenomegaly attracts attention. The symptoms are more or less severe anæmia and a painless firm enlargement of the spleen, without increase in size of the liver or other important signs. The blood shows the ordinary signs of a severe anæmia, but no parasites can be observed. There is no diarrhœa, and the mucosa of the mouth is not inflamed or ulcerated.

Diagnosis.—The disease can be differentiated from malaria by the absence of fever and of the absence of the parasites in the blood and spleen; from kala-azar by the absence of the parasites in the spleen; from forms of febrile splenomegaly by the absence of fever; from leucocythemia by the absence of the great increase of the white blood cells. From other forms of splenic anæmia it may be differentiated by the absence of any history or signs of rickets, syphilis, etc.

Prognosis.—Patients appear to live for years.

Treatment.—This is purely symptomatic, but arsenic may be administered.

Léger's Disease.

Léger has recorded a case, from Guiana, of prolonged fever with great enlargement of the liver, in which he found organisms of two types. Some were 3-5 μ in length by 1 μ in breadth, with a flagellum 3-5 μ long. Others were of oval shape, without any flagellum. Léger considers his parasite to differ from *Hæmocystozoon brasiliense* Franchini (p. 1468), as it never contained any pigment, and encysted forms were absent.

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CHAPTER XLVIII

THE RELAPSING FEVERS

General—*Louse group:* European—North African—Indian—Manchurian—*Tick group:* Tropical African—Persian—American—References.

GENERAL.

The relapsing fevers are caused by various species of spirochætes, and may for purposes of description be arranged partly by their carrier and partly by their geography as follows:—

A. *Louse group:*—
  1. European relapsing fever.
  2. North African relapsing fever.
  3. Indian relapsing fever.
  4. Manchurian relapsing fever.

B. *Tick group:*—
  1. Tropical African relapsing fever.
  2. The tick fever of Miana, Persia.
  3. American relapsing fevers.

THE RELAPSING FEVER OF EUROPE.

Synonyms.—*English:* Recurrent fever, Five Days' fever, Spirillum fever, Five Days' fever with relapses, Typhus Recurrens, Seven Days' fever (not Rogers'), Icteric typhus, Remittent fever, Bilious typhoid, Epidemic remittent fever, Miliary fever, Relapsing fever. *French:* Fièvre à Rechute. *Italian:* Febbre Ricorrente. *German:* Rückfallfieber, Die Hungerpeste.

Definition.—An acute specific relapsing fever, caused by *Spiroschaudinnia recurrentis* Lebert, 1874, and spread from man to man by lice, *Pediculus corporis* de Geer, 1778, and by *P. humanus* Linnæus, 1758.

History.—Hippocrates was the first writer to describe an epidemic of relapsing fever in Thasos, but this knowledge was entirely lost, and the reference was not understood until after relapsing fever was properly defined. Strother and other observers refer to fevers with relapses in London and in Ireland in the eighteenth century. In 1826-27 there was an epidemic of fever in the United Kingdom, during which it was recognized that there were two distinct types of typhus—viz., a mild and a severe. In 1842 this mild type again appeared in Scotland, and, to a lesser extent, in England, and continued in the years 1843, 1846, and 1847. In 1843 Henderson of Edinburgh defined this mild type as a fever distinct from typhus, and about the same time it was recognized in Germany, and somewhat later in Russia.

In 1868 there was an epidemic in Berlin, when Obermeyer, one of Virchow's assistants, first saw a spirochæte in the blood of a patient; but he does not appear to have been very certain about this at the time, for he waited till the next epidemic in 1872, and even then did not publish his account till 1873. This spirochæte was named *S. recurrentis* by Lebert in 1874, and *S. obermeyeri* by Cohn in 1875, and was proved by Münch, of Moscow, to be the cause of the disease by the successful inoculation of blood containing the spirochætes into healthy human beings—an experiment which has since often been repeated accidentally at post-mortems. It has been inoculated with success by Metchnikoff and others into monkeys and mice. In 1888 Sakharoff suggested that this organism was a protozoon—a view which later met with great support.

In Russia, where the disease has been well known since 1863, there is a popular belief that it is spread by the bed-bug *Clinocoris lectularius* L., which belief was supported by Flügge in 1891. In 1897 Tictin found that he could infect monkeys by inoculation of the blood obtained by crushing bugs which had very recently been fed on a patient—*i.e.*, within forty-eight hours.

Spirochætes have been found in bugs during relapsing fever epidemics by Karlinski in 1902, and later by Schaudinn. Nuttall has successfully transmitted *S. recurrentis* from mouse to mouse by the bites of bugs. Dönitz's hypothesis, that *S. recurrentis* is conveyed by ticks, has not been supported by experiments.

The rôle of the louse in this disease has been studied by Koch and by Werner and Wiese in 1917, but requires the accurate study given to the North African type by Nicolle, Blaizot, and Conseil. It has also been studied by Toyoda, who has shown it to be closely related to the North African type by means of immunity experiments.

Climatology.—The disease is endemic in Russia, Ireland, Turkey, the Balkans, Denmark, Norway, Bohemia, and in some parts of Poland and Germany, while the same or a similar type is found in Lower Egypt, in Southern China, and perhaps in the Philippines. There, however, appears to be some doubt about the presence of the disease in these islands; the authority for the statement is McCrae, in Osler's 'System of Medicine.'

Ætiology.—This type of relapsing fever is caused by *S. recurrentis* Lebert, 1874, which is generally to be found in the peripheral blood during the attacks, but is usually absent in the apyrexial interval, though individuals may occasionally be found after prolonged search. (For description of the organism, see p. 443.)

This spirochæte is carried from the sick to the healthy by the agency of lice, *P. humanus* and *P. corporis* (see p. 917). The subject, however, requires further study on the lines of the North African type (*vide infra*). It is known that the human blood is infective during the pyrexial and apyrexial stages, and that the spirochætes reach the cœlom of the louse between the second and eighth day after the transmissive feed. It can also be spread by direct inoculations such as may take place accidentally in laboratories or at post-mortems.

The blood is not merely transmissive to the louse during the time when the spirochæte can be found therein, but also during the apyrexial interval. The louse may be infective for a few hours after a transmissive feed, and perhaps a few cases of human infection may be accounted for in this way, but this is not the usual method.

After a transmissive feed the spirochætes quickly disappear from the alimentary canal of the louse, and do not reappear in the cœlomic fluid until the eighth to ninth day after the feed; but before this the louse becomes infective from the third to fifteenth day, and usually on the sixth day the louse is most infective.

Infection is not conveyed by the louse bite, but by the parasite escaping from the body of the crushed louse and entering man through excoriations in the skin, generally made by scratching. One crushed louse is sufficient to produce the disease.

The incubation period under experimental conditions appears to be six to eight days.

The louse is not pathologically affected by the germ, of which it is the natural reservoir, the spirochæte being passed from one generation to the next succeeding generation, as has been shown by the discovery that the young of infected lice are themselves infective.

Pathology. -The presence of the spirochætes in the blood is associated with fever, which must be due to toxins produced by these organisms, though the severity of the symptoms bears no relationship to the number of the organisms found in the peripheral blood. The spirochætes disappear from the circulation when the temperature falls to normal. The disappearance of the parasites from the blood is brought about by the presence of antibodies (agglutinins and parasiticidal substances). In those cases, however, in which relapses occur, the blood remains infectious during the intervals. This is due to some parasites resisting the action of the antibodies. These resistant spirochætes after a time multiply again in large numbers, giving rise to the relapse. Levaditi and Roche have demonstrated that serum collected after a first attack destroyed the spirochætes which caused the attack, but had no effect whatever on the spirochætes which caused the second attack. The relapses, therefore, are caused by the survival of resistant types of spirochætes, and recovery depends upon the existence of protective substances in the blood. The immunity acquired after one or several attacks may last for some weeks or months. Animals can be hyperimmunized by repeated inoculations after recovery from the first attack. The serum of such hyperimmunized animals shows definite protective and curative properties.

Morbid Anatomy.—The principal pathological feature of the post-mortem is the enlargement of the liver and spleen, the latter organ reaching a weight of 1 to 2 kilogrammes at times. On section, the spleen is dark-coloured and soft, with enlarged follicles, and on microscopical examination shows congestion and a cellular increase. The liver is enlarged, and its lobules are poorly defined, while microscopically cloudy swelling and fatty infiltration may be seen, as well as leucocytic infiltration into the portal system. The kidneys are enlarged and congested, and microscopically show cloudy swelling and fatty degeneration of the cells, while the stomach shows signs of inflammation, and the heart is soft and flabby. The bronchi are generally congested, and contain frothy mucus, and the lungs show hypostasis. The brain may be congested, and all the organs may be stained yellow with bile.

Symptomatology.—*The incubation period* is said to vary between two and twelve days, but in accidental inoculations it is *about seven days*. During this period prodromal symptoms, in the form of slight malaise, may be felt.

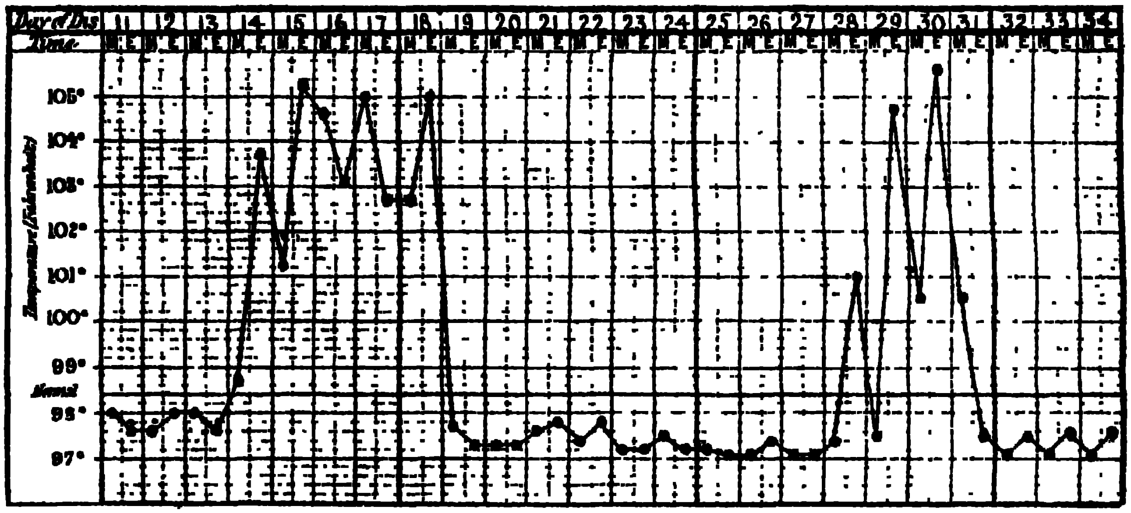

FIG. 648.—TEMPERATURE CHART OF THE RELAPSING FEVER OF EUROPE.

The onset is usually sudden, but it may be gradual, the patient suffering from rheumatic-like pains, headache, and constipation. When it begins suddenly, there are rigors, with severe frontal headache, pains in the back and limbs, epigastric pain and tenderness, associated with a sense of weakness. The face becomes flushed, the conjunctivæ injected, and the temperature rises to 103° to 104° F., with a pulse-rate of 110 to 120, quickened respirations, and sometimes nausea and vomiting.

The Course.—The temperature continues high until the sixth or seventh day, during which period the skin may be yellowish in colour, hot and damp from perspiration, with at times a rose-coloured macular eruption, disappearing on pressure, on the thorax, abdomen, and legs, which lasts for a day or so. The tongue is moist, red at the tip, and covered with a white fur. Vomiting of greenish-yellow matter may occur, but nausea is always present, and thirst is common; the bowels are usually constipated, and diarrhœa is more a complication than a feature of the disease. The liver is enlarged and tender, and so is the spleen, which may reach a considerable size. The heart sounds are normal, but the pulse-rate is quick, reaching 120 to 140, or even more, per minute; but it is not dicrotic. The erythrocytes and the hæmoglobin are reduced in amount, while a polymorphonuclear leucocytosis may be present. Spirochætes can be found in the blood, and occasionally can be seen engulfed by leucocytes. There is generally a troublesome cough, with scanty bronchitic expectoration, and râles, which can be heard over the chest and trachea. The respirations follow the pulse-rate, being increased to 48 to 50 per minute if the temperature is high. The pains in the muscles and joints continue, and sleeplessness may result, while a noisy delirium is not rare, but stupor is uncommon. The urine is febrile, and may contain a little albumen. About the sixth or seventh day the crisis, sometimes ushered in by a rigor, intervenes, with violent perspiration, or diarrhœa, with or without epistaxis, and with a sudden rapid fall of temperature, while the pulse and respirations also return to normal, and the patient falls into a deep sleep, and awakens much better.

The Intermission.—The intermission now begins, during which the temperature returns to normal. The spleen often remains enlarged, the temperature chart may show small rises, and the patient's strength slowly improves.

The Relapse.—The disease may now end; but this is exceptional, and more usually, about the fourteenth day from the first commencement of the illness, the *relapse* occurs, beginning with a rigor and symptoms resembling the attack, but often more severe, and, after lasting three or four days, terminating in a crisis, which generally ends the illness. Very rarely is there a *second relapse*, in which case the same symptoms occur, but much less severely, and a *third relapse* is most uncommon. *Convalescence* is sometimes slow.

Complications.—The complications are numerous, affecting the lungs in the form of bronchitis and pneumonia, or the alimentary canal as dysentery, diarrhœa, and hæmatemesis; while cerebral hæmorrhage, conjunctival hæmorrhage, iritis, and corneal ulcers, have all been recorded.

Abortion often complicates the first relapse in pregnant women.

Diagnosis.—In the first instance, before the relapsing character has appeared, the disease requires to be diagnosed from malaria, typhus, typhoid fever, yellow fever, and seven days' fever. The principal positive signs indicating relapsing fever are:—(1) Presence of the spirochætes in the blood; (2) agglutination or Löwenthal's reaction, which consists of taking a drop of blood from the suspected case and adding it to another drop of blood containing spirochætes taken from a patient, mixing the two drops together, and covering with a cover-glass, which is then sealed and placed in an incubator at 37° C. for half an hour. A positive reaction is indicated by the clumping of the spirochætes into non-motile masses.

Differential Diagnosis.—*Malaria* can be diagnosed by the discovery of the malarial parasite in the blood.

Typhoid is indicated by the positive results of hæmo-cultures and by the fever having started gradually. Widal's reaction is not of much help during the first week. *Typhus* can be separated by the absence of spirochætes, by a negative Löwenthal's reaction, and by the presence of its characteristic rash. *Yellow fever* can be diagnosed by its black vomit, though at first the differentiation may be impossible without a microscopical examination of the blood. *Dengue fever* is characterized by its slow pulse and, of course, by the absence of spirochætes. *Weil's disease* may be distinguished by the more marked jaundice and by the different nature of the spirochætes, which are seldom found by the simple microscopical examination of the blood.

Prognosis.—The prognosis is usually favourable. Marked jaundice is a bad sign, while pregnant women generally abort. The mortality appears to vary considerably, being, according to Murchison, only 4 per cent. in the United Kingdom: while, according to Sandwith, it is 14·4 per cent. in Egypt, which is nearly the same percentage as that reached in Russia. The causes of death are toxæmia in the first attack, and collapse in the first intermission, but it may be caused by one of the above-mentioned complications.

Treatment.—This may be discussed under the following headings:—

1. Specific Treatment.
2. Symptomatic Treatment.

Specific Treatment.—Salvarsan or neosalvarsan or their substitutes may be administered either by intramuscular injection or, better, intravenously. This is a specific treatment, most efficacious, but care should be taken not to inject a large dose, as certain patients, especially, it seems, those suffering from Asiatic relapsing fever, stand the drug badly, cases of death having been recorded, even after a medium dose, such as 7½ grains (0·5 gramme). According to Mouzels, an intravenous injection of 4 or 5 grains (0·3 gramme) does not give rise to any unpleasant symptom, and is generally sufficient to make the spirochætes disappear from the blood and cure the attack. If, however, another attack of fever develops, a second injection of the same dose may be given.

Symptomatic Treatment.—Pains in the head and muscles may be relieved by small doses (2 to 3 grains) of salicylates, aspirin, antipyrin, or by quinine. If these pains are very severe, opium or a hypodermic injection of morphia may be necessary. *Epigastric pain* may be relieved by fomentations sprinkled with tincture of opium, while *vomiting* should be treated with ice, champagne, and bismuth mixtures, though occasionally morphia or codeine may be required. Effervescing ammonium carbonate mixtures are often grateful.

A dry, troublesome *cough* may be relieved by codeine or small doses of heroin; in other cases an expectorant mixture will be found useful. *Constipation* must be treated by laxatives or enemata, and high temperatures by cool sponging, which, however, will but seldom be required. The complications must be met by the treatment laid down in textbooks on general medicine.

Prophylaxis.—Prophylaxis consists in the destruction of lice by steaming clothes, as can be done in railway trucks by leading in steam from the engine or by boiling clothes, while the patient is thoroughly bathed. For further particulars see the prophylaxis of typhus (p. 1338).

THE RELAPSING FEVER OF NORTH AFRICA.

Synonyms.—Algerian relapsing fever; Egyptian relapsing fever; Arabic: Homa el Hugga, Homa en Naxy, Naushah.

Definition.—An acute specific fever caused by *Spiroschaudinnia berbera* Sergent and Foley, 1910, and spread by the agency of *Pediculus corporis* de Geer, 1778.

History.—It was noticed by the surgeons of Napoleon's army in Egypt, and later by Griesinger in 1851, when it was called 'bilious typhoid'; while more recently Sandwith, Cummins, Bousfield, Balfour, and Graham-Smith, have published excellent accounts of the disease. In 1910 Sergent and Foley differentiated *S. berbera* Sergent and Foley, in a case in South Oran. The transmission of the disease by lice has been worked out by Nicolle, Blaizot, and Conseil. Toyoda's immunological experiments show that this fever is closely related to the European type.

Climatology.—It is known to exist in Algeria, Tunis, Tripoli, Egypt, and the Anglo-Egyptian Sudan.

Ætiology.—It is caused by S. *berbera* Sergent and Foley, 1910, spread by the agency of lice, as shown by Nicolle, Blaizot, and Conseil (see p. 447).

Symptomatology. The length of the incubation period is not known, but is believed to be more than twelve days. The fever, which may be associated with rigors, reaches its height during the first twenty-four hours, and afterwards shows morning remissions. The spleen enlarges, and the liver becomes tender and painful in some cases; but jaundice is generally absent. Vomiting is present, but diarrhœa is absent. The attack is apparently not very severe. Apyrexia lasts from two to nine days, and is followed by one, two, or, more rarely, three relapses.

Diagnosis.—The spirochætes must be found in the blood, as the cases may occasionally resemble cerebro-spinal meningitis and acute rheumatism.

Prognosis.—This is usually good, the mortality being nil in fifty cases.

Treatment.—This is the same as for the other relapsing fevers.

THE RELAPSING FEVERS OF ASIA.

There are probably a number of relapsing fevers in Asia, but we only know two which have lice as carriers, and these are:—

1. The Indian relapsing fever.
2. The Manchurian relapsing fever.

The Relapsing Fever of India.

Definition.—An acute specific relapsing fever caused by *Spiroschaudinnia carteri* Manson, 1907, and spread by the louse in all probability.

History.—Relapsing fever is one of the endemic diseases of India, being traceable back into the eighteenth century. The credit of first clearly defining the disease, however, rests with Lyall in the epidemic fever in the Punjaub in 1852-53; but Vandyke Carter, in 1876-77, in the Bombay Presidency found spirochætes in the blood of patients suffering from fever, and his work on the subject, published in 1882, is to be regarded as the Indian classic on this fever. Schellack, in 1907, separated this spirochaete from *S. recurrentis* and *S. novyi* by finding that it is not agglutinated by the serum of animals infected with these parasites. Rogers points out that the disease has often been confounded with typhus fever in India. In 1911 Stott suggested that two varieties of fever may be included under this term, and recent research shows that several varieties of relapsing fever probably exist in India. Types of relapsing fever, which may possibly be different from the Indian ones, occur in China and French Indo China, while the Arabian type may be identical with the West African relapsing fever.

Climatology.—The real home of the disease appears to be the Bombay Presidency, but it is also known in the Punjaub and in the Kumaon Hills of the North-Western Provinces.

Ætiology.—The cause of the disease is the spirochæte found by Vandyke Carter in 1877. It is inoculable into man, as was proved by Carter inoculating himself twice, with an interval of two and a quarter years. It can also be inoculated into monkeys, but not into rats and mice. Bugs are capable of retaining it alive in their alimentary canals for from four to seven days when obtained from monkeys, but do not appear to be so effective in obtaining it from man, as only one in fifty-three were found infected after feeding on human beings. Infected bugs are capable of transmitting the disease to monkeys. Rogers, however, thinks that mosquitoes may be found to be more effective than bugs. Mackie has brought forward evidence in favour of *Pediculus corporis* being a carrier. (For description of the spirochæte, see p. 446.)

S. carteri is separated from *S. duttoni* by the latter being far more easily inoculable into animals and producing numerous relapses when injected into monkeys, while, according to Lamb, the former only causes one relapse. Moreover, the two spirochætes may be differentiated by immunization and agglutination tests. *S. macaci*, observed by us in monkeys in Ceylon, appears to be closely related to *S. carteri*, and may be identical with it.

Strong, experimenting with white mice, has come to the conclusion that the Indian *Spiroschaudinnia* is closely allied to the European and North-American types.

Pathology.—The morbid anatomy resembles that of the European type.

Symptomatology.- In accidental inoculations in the post-mortem room the incubation period varies from three and a half to seven days, during which prodromata resembling those of the European type may occur.

The onset is generally sudden, but in most cases without the rigors defined in Europe, though chilliness occurs, and the disease progresses as in the Obermeyer fever. On the fall of temperature to subnormal, however, on the sixth or seventh day, which is associated with profuse perspiration and polyuria, instead of the patient feeling better, he often becomes collapsed, with a small weak pulse and a cold clammy skin, in which condition he may resemble at first sight a cholera patient. In the first intermission, which lasts from three to twelve days -generally about eight days—the patient improves slowly, there being much debility, and in one case in six there is a sudden temporary rise of temperature after the crisis. Spirochætes are not to be seen in the [illegible] but Carter and Pisani have described peculiar structures. [illegible] first relapse occurs about the fourteenth day of the disease and the seventh of the intermission, and resembles the first attack, but the temperature may reach a higher level, and the illness is shorter, ending in a crisis.

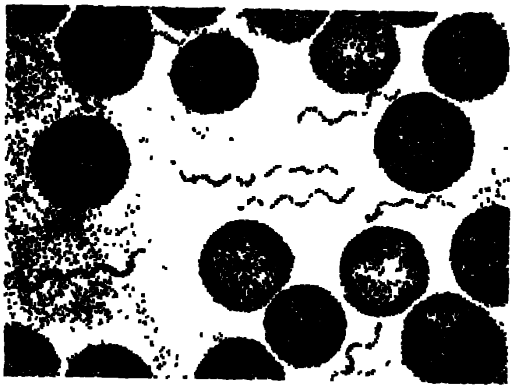

FIG. 649.—SPIROSCHAUDINNIA FROM A CASE OF ASIATIC RELAPSING FEVER.

(From a microphotograph by J. J. Bell)

The second intermission may last about ten days, being longer than the first, and a second relapse takes place, often commencing with chills. The liver does not markedly enlarge, but the spleen increases in size. The fever is remittent or intermittent, and the crisis is not marked. It is now rare for the disease not to end, but after an interval of fourteen to seventeen days a third relapse may take place, with a sudden rise of temperature, which lasts one to four days. Very rarely a fourth intermission of about eleven days ends in a fourth relapse, lasting only two days.

With regard to the frequency of the relapses, Rogers gives the following percentages:—

Without relapse	23·8 per cent.
With one relapse	49·2 „
With two relapses	20·0 „
With three relapses	5·0 „
With four relapses	2·0 „

Varieties.—The typical course may be varied in about 25 per cent. of cases, and present (*a*) *a short, irregular, remittent fever*; (*b*) *a so-called bilious remittent fever*, called by Carter 'icteric fever.'

(*a*) *Short, Irregular, Remittent Fever.*—This is very like malaria, from which it is only to be diagnosed by blood examination.

(*b*) *So-called Bilious Remittent Fever* (*Icteric Fever*).—So-called bilious remittent fever very closely resembles typhus fever, and to some extent yellow fever, showing deep jaundice, with an eruption of red spots. The temperature is irregular, and the pyrexia prolonged; prostration comes on early, and may develop into a 'status typhosus.' The death-rate of these cases is high, being 70 per cent. They are to be diagnosed from typhus by the blood examination, and from yellow fever by the absence of black vomit.

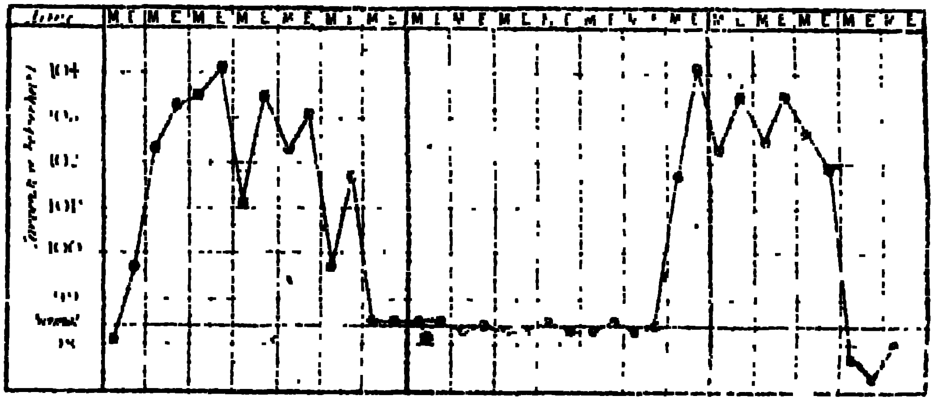

Fig. 650.—Temperature Chart of the Relapsing Fever of India. (Chart made by Major Archibald.)

Complications.—These are the same as in the European type.

Diagnosis.—This is based on the microscopical examination of the blood.

Prognosis.—A prolonged, irregular first attack, ending by lysis, and attacks showing marked jaundice are bad omens.

The mortality is higher than in Obermeyer's type, being 18·02 per cent., of which about one-half take place in the attack, and one-quarter in the first interval, and one-fifteenth in the first relapse, and the remainder from complications.

Treatment.—The treatment and diet differ in no respect from that already laid down, except that these patients often stand large doses of salvarsan badly, and therefore one should not give more than 5 grains of the drug by intravenous injection; moreover, the disease being of a severer type than the European form, and sudden heart failure being common, cardiac stimulants should be given during the attack, and preparation made for preventing the collapse by means of hypodermics of strychnine and ether, or camphor in ether, as well as by hot bottles, blankets, etc.

Prophylaxis.—See remarks with reference to the European type.

Manchurian Relapsing Fever.

This type of relapsing fever is due to a spirochæte which Toyoda in 1916 demonstrated by immunity experiments to be distinct from the African and the European types. The organism is short, 7-20 microns by 0·4 micron, and its spirals number 4-8; it is spread by lice.

Liver enlargement and albuminuria are physical signs of importance. The first paroxysm lasts five to thirteen days, the first interval two to fourteen days; the second attack one to nine days, interval two to thirteen days; the third paroxysm lasts one to six days, the third interval two to ten days; the fourth paroxysm lasts two to six days.

The mortality rate is 5·3 per cent. Two paroxysms are common.

THE TICK GROUP.

THE RELAPSING FEVERS OF AFRICA.

The tick relapsing fevers of Africa may be classified as follows:—

1. West African relapsing fever.
2. East African relapsing fever.

1. The Relapsing Fever of West Africa.

Synonyms.—Tick fever (Livingstone), African tick fever.

Definition.—An acute specific relapsing fever caused by *Spiroschaudinnia duttoni* Novy and Knapp, 1906, and spread by *Ornithodoros moubata* Murray.

History.—The peoples of Africa from time immemorial have had a dread of tick-bites, which they thought caused fever, and this appears to have been noted by Livingstone, Kirk, Hinde, and many other people, with the result that a tick fever of an unknown nature was spoken of as occurring in Africa. Nabarro, in August, 1903, was the first to observe a spirochæte in human beings in Uganda, but as his publication, through no fault of his own, did not appear till much later, his discovery was forestalled by those of Ross and Milne in 1904, and Dutton and Todd, also in 1904, who found the cause of the tick fever to be a spirochæte, the latter observers also proving that it was introduced into the blood by the bite of a tick—*Ornithodoros moubata*. Since that date Koch, Todd, Novy and Knapp, Breinl and Kinghorn, and others, have studied the disease carefully. Fränkel has proved by biological tests that the spirochæte of East African relapsing fever differs from *S. duttoni*, as observed in West Africa, and Nuttall proposed the name *S. rossi* Nuttall, 1908, for this new species; but recent researches seem to have proved the identity of the two conditions.

Climatology.—The disease is found in Angola, the Congo Free State, Uganda, late German East Africa and Portuguese East Africa, and in the Valley of the Zambesi. Franco, Robledo, and others have described a spirochætiasis in Colombia, which is caused by a spirochæte morphologically resembling *S. duttoni*, and said to be spread by *Ornithodoros turicatus*, with reference to which it may be noted that Büldow observed relapsing fever in the Andes in 1865. Robledo asserts that it is spread by the bite of *Ornithodoros megnini*.

The climatic conditions required appear to be heat and moisture, but according to Franco's observations, the disease can occur at an altitude of 7,000 feet. No observations appear to be recorded as to variations due to season. Carter's investigations would tend to show that Arabian relapsing fever is either a separate form of fever, or is allied to this West African form, as it may be spread by an *Ornithodoros*.

Ætiology.—The cause of the fever is *S. duttoni* Novy and Knapp, 1906, which is proved to be distinct from the other spirochætes, because an animal immunized against one of these is capable of being successfully inoculated by it. *S. duttoni* can be inoculated into a number of animals—namely, dogs, goats, sheep, rabbits, guinea-pigs, rats, and mice—but not into cats, chickens, pigeons, or goldfish. The spirochætes can pass through the placenta into the circulation of the fœtus, which they infect. These organisms are easily seen in the blood during an attack, but disappear during an apyrexial interval. The spirochæte is described on p. 444.

The life-history in the vertebrate has been worked out by Breinl, who, as already described, showed that just before the crisis the spirochætes become encysted and undergo schizogony into small bodies, from which the new generation develop. Leishman has demonstrated that when the spirochætes pass into the intestinal sac of the tick they lose their motility and their characteristic appearance, while the central core of chromatin segments into small masses, which are set free into the lumen of the gut. These small bodies, which resemble small rods, or are rounded, like micrococci, appear to multiply in the body of the tick, and to pass into the cells of the Malpighian tubules and into the tissue of the ovary. In the latter position they enter the immature eggs, and can be traced through all stages of development into the adult ticks. In the embryo, and in all the later stages of development up to and including the adults, they are found as small chromatin bodies lying in the cells of the Malpighian tubules. Inoculation of crushed tissue containing these bodies produces a typical infection. From his experiments, Leishman concludes that it is by these chromatin bodies that the disease is carried from the egg to the new generation of ticks, and that infection of man does not take place via the salivary glands, but by the small bodies gaining access to the wound produced by the tick's bite, by being voided in the Malpighian secretion passed by the tick during feeding, or perhaps by regurgitation of the intestinal contents. More recently Leishman and Hindle have shown that the tick produces infection only as the result of its infected fæces contaminating the tick-bite. This is a typical example of the contaminative mode of infection.

The principal predisposing causes are anything which facilitates the life of the tick, such as bad hygienic conditions, which are well exemplified by the native huts of Africa. These huts contain many cracks in the walls and floor, which afford shelter to the tick, and hence predispose to the disease.

Pathology.—Very little can at present be said as to the pathology. The post-mortem reveals only an enlarged firm spleen, while smears taken from the liver and lungs show large numbers of spirochætes.

Symptomatology.—The symptomatology still requires careful investigation on the lines carried out by Carter in India, but much good work has been done on the subject by Dutton, Todd, R and others.

Incubation.—The period of incubation is usually about seven days, but it may extend to eleven or twelve days.

The tick-bite may be accompanied by local inflammatory symptoms, but in some cases the bite is not even noticed. According to Wellman, natives believe that when the tick-bite is accompanied by a severe local reaction, the individual probably escapes fever, and Nuttall calls attention to the possible protective effect of a local reaction.

Usually mental heaviness, lack of activity, profuse sweating, and constipation, are mentioned as prodromal symptoms.

Onset.—The attack may come on gradually, with a feeling of malaise, faintness, and a disinclination for food, or even vomiting, and a slight rise of temperature. In a few hours the temperature will have risen to 103° to 105° F., associated with headache, pains in the back and limbs, and intense pain in the region of the spleen, and chilliness. There is vomiting, first of food, and then of bile, with often diarrhœa, and even at times streaks of blood in the motions. The spleen is generally found to be enlarged, and spirochætes in scanty numbers occur in the peripheral blood, but may be hard to find.

Course.—The next day the symptoms are worse, and the patient is hot and restless, complaining of thirst and splenic pain, and often troubled by a cough. The temperature shows a morning fall, without improvement in the symptoms, and an evening rise, during which the pains increase, and the patient may become delirious. The liver does not enlarge, but the spleen projects below the costal margin. Spirochætes are now found in greater numbers, but diminish remarkably before the crisis. There is a slight decrease in the red cells and hæmoglobin, and a marked leucocytosis before the crisis, while polychromatophile degeneration is noted in the red cells, and a very marked increase in blood platelets. The symptoms last three to four days, and end by a crisis marked by profuse sweats and a fall of temperature below normal. On the day before the crisis there is a pseudo-crisis, with a fall of temperature, but no improvement in the symptoms.

Intermission.—The patient feels weak and tired, but slowly regains his appetite and strength, and no parasites are found in the blood. The disease may now terminate, or the intermission may last from one to twenty-one days, according to Ross; but five to eight days is more usual.

Relapse.—The first relapse begins with a rise of temperature and a return of the original symptoms, and also of the parasites into the peripheral blood. After lasting three to four days, it ends in a crisis marked by sweating, and showing a pseudo-crisis on the preceding day.

Intermissions and relapses follow one another regularly or irregularly, the intervals being from one day to two months, and the relapses usually lasting three days, and showing a pseudo-crisis on the second day and a crisis on the third day. As many as five to eleven relapses may take place, and end by reducing the patient both in weight and strength. Œdema of the eyelids has been noted in the relapses.

Complications and Sequelæ.—Iritis is frequently observed.

Clinical Varieties.—According to Ross, there appears to be a marked difference in the severity of the attack in new-comers, such as Europeans, and natives. Though the attack shows much the same symptoms in natives as in Europeans, it is often far less severe, and the spleen may not enlarge. The attack frequently lasts twenty-four to forty-eight hours, and ends by crisis, after which the patient rapidly recovers, as a rule without a relapse. Should this, however, take place, it is found to be less severe than the attack. Koch believes that these mild attacks and the native immunity are due to infection in early childhood. Dutton and Todd, on the other hand, describe cases very much resembling that in the European, with enlargement of the spleen, and with more than one relapse, leaving the patient anæmic, thin, and weak. Hence it may be concluded that the disease shows two types in natives—a mild type and a severe type—and that the latter may end in death.

Diagnosis.—This can only be made by finding the spirochætes. Löwenthal's method of agglutination can be applied in doubtful cases.

Prognosis.—This is usually good for both the natives and Europeans, but death may occur in both races, and is signalled by a rapid fall of temperature without improvement of the symptoms.

No figures have so far been recorded with regard to the mortality, but it may be taken that it, as a rule, is low, though under adverse circumstances it may be high. Dutton and Todd record that of twenty men who contracted the disease in one caravan, ten died.

Treatment.—This is the same as for the European form (see p. 1313).

Prophylaxis.—The prophylaxis is based on the avoidance of localities where ticks abound and the destruction of these parasites. Koch rightly advised that Europeans should camp at least 20 to 30 yards away from infected native huts and rest-houses.

2. The Relapsing Fever of East Africa.

The relapsing fever found in Uganda and East Africa is clinically indistinguishable from the West African type, and is carried by the same tick, but the *Spiroschaudinnia*, according to Fränkel, is a different species (*S. rossi* Nuttall, 1908). Recent researches seem, however, to identify it with the West African type.

THE TICK FEVER OF MIANA, PERSIA.

Definition.—A specific fever of unknown cause, brought about by the bite of a tick (*Argas persicus* Oken, 1818).

Historical.—Dupré, in 1809, first described this disease, stating that the bite of *A. persicus*, locally known as 'Guerib-guez' 'Garib-guez' 'Miané-bug,' or 'punaise de Miana' (Mallet de Mianeh), was at times dangerous, producing prolonged illness. Kotzebue, in 1819, stated that the natives were immune, and only foreigners suffered. Fischer de Waldheim, in 1823, said that the bite was fatal, and Heller, in 1858, described the effects as being caused by the mechanical injury of the bite of the tick. Taschenburg, in 1873, considered the symptoms to point to a disease, and not merely to the effects of the bite of the tick; and Schlimmer, in 1874, considered the immunity of the natives to be due to the fact that they had been bitten, and so become vaccinated. Megnin, in 1882, showed that the bite *per se* was not dangerous, and later was supported by Fumouze and Loundsbury.

Ætiology.—The causation of the disease is quite unknown, but some virus must be inoculated when the tick bites, for the disease is apparently confined to Persia; and the experiments of Méguin, Loundsbury, and others show that in certain regions the effects of the bite are insignificant.

Manson thinks that this virus will some day be found to be a spirochæte, which, indeed, is not unlikely, as *A. persicus* is well known to be the carrier of *Spiroschaudinnia marchouxi* Nuttall, 1904, which causes a very fatal disease in fowls. Native Persians probably develop a relative immunity due to previous slight infections, but new-comers suffer severely.

Symptomatology.—The knowledge of the symptoms of the disease is very meagre. Severe pain is felt at the site of the bite of the tick, and this is followed by remittent fever lasting from a few days to several weeks, delirium, convulsions, and even at times by death.

Treatment.—The treatment is entirely symptomatic, but salvarsan might be tried.

Prophylaxis.—According to Nuttall, the Persians burn their villages when they suffer severely from the attentions of the tick. In order, however, to devise a rational method of prophylaxis, it must be remembered that *A. persicus* is essentially a parasite of the domestic fowl and other birds, and that its eggs are laid in batches of 20 to 100 in cracks in the walls, and take three weeks to develop into the larva, which, after sucking blood, in eight days becomes the nymph. This may require several weeks before it becomes the adult, which is said to feed only once a month. After considering this life-history, it will be obvious that fowls should be disinfected with a kerosene emulsion, creozozone, or oil of sassafras in the case of old birds, while young birds may be isolated in cages until the ticks drop off. Houses and fowl-houses should be cleansed and treated by lime and corrosive sublimate, and old nests and roosts should be burnt, and after that the new fowl-houses may be sprayed with kerosene emulsion.

THE RELAPSING FEVERS OF AMERICA.

The relapsing fevers of America comprise:—

1. North American relapsing fever.
2. Central American relapsing fever.
3. South American relapsing fever.

1. Relapsing Fever of North America.

Definition.—An acute specific fever caused by *Spiroschaudinnia novyi* Schellach, 1907. Mode of infection not known.

History.—Relapsing fever has been known in America for many years, being recognized as far back as 1844; but it was considered to be identical with the European type until, in 1906, an Englishman who repeatedly travelled between New York and the West Indies was treated by Carlisle in New York for fever which relapsed, and in which spirochætes were found. Novy and Knapp studied these spirochætes, and showed that they were distinct from *S. duttoni*. Later, Mackie also studied them by the agglutination method, and agreed with Novy, who had concluded, from morphological reasons, that they were distinct from *S. carteri*. Finally, in 1907, Manteufel compared them with true *S. recurrentis*, and found that the serum of a person suffering from their type of fever did not agglutinate true *S. recurrentis*. Subsequently Schellach, after studying and comparing the different spirochætes, named this particular species *S. novyi* Schellach, 1907.

Climatology.—The disease is known in North America and in Europe. In America the disease is acquired naturally. In Europe the cases recorded are due to laboratory infection.

Ætiology.—The cause of the disease is *S. novyi* Schellach, 1907.

Symptomatology.—The symptoms appear to be much the same as in the European type of fever. The incubation period seems to be at least five to seven days in duration, though cases have been recorded in which symptoms developed almost immediately after exposure to infection. In experimental cases it varied between six and eight days. The duration of the first attack is about five to six days, and it often begins with rigors; the tongue is moist, except in grave cases, and the jaundice is mild, except in severe cases; but the vomiting of bile is not uncommon, while diarrhœa is only moderate in amount. Tympanites, hiccough, and hæmorrhages from the nose, stomach, and bowels, as well as the kidney, may be present in severe cases. The apyrexial interval is usually seven to ten days, and is followed by the relapse, which is not uncommonly absent. Usually there is only one relapse, and more rarely two to five relapses.

Mortality.—The mortality is not high, varying between 2 and 6 per cent.

Treatment.—The treatment is the same as in the European type.

2. Relapsing Fever of Central America.

Darling has described cases of relapsing fever in Panama, clinically similar to the North American type, but the organism has not been definitely classified.

3. Relapsing Fever of South America.

In South America (Colombia) a relapsing fever occurs in which the spiroschaudinnia resembles more closely *S. duttoni* than *S. novyi*. According to Robledo, this parasite is carried by *Ornithodoros turicatus*.

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CHAPTER XLIX

TYPHUS

Synonyms.—Typhus exanthematicus, Synochus putrida, Spotted fever, Gaol fever, Prison fever, Brill's disease; *French*, Typhus exanthematique; *Italian*, Tifo esantematico, Tifo petecchiale; *Spanish*, El Tarbardillo; *German*, Exanthematischer typhus, Fleckfieber; *Dutch*, Vlekkoorts; *Arabic*, Homma typhuisa, Tkout fever; *South Africa*, M'betalala = black fever.

Definition.—Typhus is an acute specific fever of unknown but probably protozoal cause, spread by the agency of *Pediculus corporis* de Geer, 1778, and characterized by a sudden onset, a maculo-petechial eruption, and severe toxemia, lasting some twelve to fifteen days, and ending in a more or less abrupt lysis.

History.—The early history of typhus is wrapped in obscurity by reason of its confusion with plague: for though Hippocrates mentions the word 'typhus,' he applied it to stuporous and delirious conditions, and does not appear to have been acquainted with the fever in question. This confusion with plague continued until Fracastorius, in the sixteenth century, called it 'petechie,' and gave such an account as enabled them to be separated from one another, though the nomenclature at first indicated that they were related, and it was not until 1760 that the term 'typhus' was first applied to the disease by Boissier de Sauvages. In an interesting historical paper Crawford has shown that the only possible explanation of some of the old outbreaks is by means of the louse.

During the eighteenth and nineteenth centuries typhus was well known in Europe, but included typhoid and relapsing fevers, from the former of which it was distinguished by a long series of researches, beginning with those of Strother, Gilchrist, and Huxham, in the early eighteenth century, and ending with Still's classical work in 1837, while the history of the differentiation from the latter has already been described in the chapter on the Relapsing Fevers.

For a long time the disease passed unrecognized in the tropics, and, indeed, in the *Lancet* of 1871 it is even debated as to whether it could exist in those regions; but though it is impossible to deny that Lyell, in his observations in 1852, mistook relapsing fever for it, and that Fairweather in 1869 was confusing it with typhoid, it would appear as though Lyons, in 1869, clearly recognized the disease as occurring in North-West India, where it is now well known to be endemic, and it has since been reported from many parts of the tropics.

Brill's disease appears to be a mild form of typhus fever, attenuated, perhaps, by environment and improved sanitation. He has failed to produce the disease in monkeys.

It is curious the way in which different epidemics have been reported as being characterized by special features; thus the Serbian epidemic of 1914–15 showed a great tendency to gangrene of the feet, while those in Silesia and Ireland have been associated with bronchial and pneumonic complications.

Causal Agent.—The next point in the history is the search for the causal agent. In 1908 Yersin and Vassal succeeded in communicating the disease from man to man by the inoculation of blood, but failed to infect rats, guinea-pigs, or rabbits.

In 1909 Nicolle first produced typhus in a monkey by injecting the blood from a patient, thus showing that the virus was present in the peripheral blood. Later it was discovered that guinea-pigs also could be infected.

In 1910 Ricketts and Wilder, in Mexico, showed that the virus was contained in the blood serum, from which it could be removed by filtration through a Berkefeld candle.

In 1911 Wilder repeated the filtration experiments with confirmatory results, but subsequent experiments showed that the control monkey may have been immune, a point subsequently confirmed by Nicolle, Conor, and Conseil.

In 1911 Nicolle, Conor, and Conseil considered that the virus was mainly associated with the leucocytes, and that the plasma was merely virulent from the débris of these cells. Red blood-corpuscles and cerebro spinal fluid were proved not to contain the virus.

In 1912 Anderson and Goldberger showed that the evidence was in favour of a parasite living freely in blood plasma, and not of an intraleucocytic localization; and, further, they confirmed the work of Ricketts and Wilder.

In 1917 Miss Robertson summarized these investigations by stating that there is *no recorded experiment* which demonstrates that an injection of the filtered serum from a typhus patient can produce an infection. The conclusion is that the virus is too large to pass through the pores of a Berkefeld candle in good condition. Further, this virus is capable of producing a reaction on the part of the patient, because after an attack there is a solid immunity against subsequent attacks, both in men and animals.

The causation of typhus remains undiscovered, though many researches have been made, first by Hallier, who in 1868 described a fungus as the causal agent; and then by Klebs, who found bacilli in 1881; and by Mott and Blore, who in the same year described minute, screw-like, motile organisms as present in the blood during life, and micrococcal-like bodies found in cells between the muscular fibres of the heart after death.

In 1891 Hlava described ovoid bodies which he believed to be part of a streptobacillus; in 1892 Thoinot and Calmette saw flagellate bodies; and in 1892 Lewaschew found a motile organism, sometimes like a thread, sometimes oval and flagellate; in 1893 Dubieff and

Brühl described a diplococcus; in 1899 Balfour and Porter found another diplococcus. In 1903 Gottschlich described a *Piroplasma* existing in non-motile endocorpuscular and flagellate free forms in cases in Egypt, but these parasites may have only been cellular degenerations; and Horiachi described a bacillus which he isolated from the fæces and urine of Japanese troops which in the war in Manchuria suffered from a disease which was probably typhus. Krompecher, Goldzieher, and Augyan have described intracorpuscular bodies somewhat resembling a *Piroplasma*. In 1909 Rabinowitsch grew an aerobic coccobacillus; in 1914 Hort and Ingram described a pleomorphic bacillus, and in 1915 Plotz a pleomorphic bacillus, the so-called *B. typhi-exanthematici*. In 1916 Penfold, and later Miss Robertson, found a blood diphlococcus. In 1919 Borrel, Cantacuzene, Jonesco and Nasha have isolated a capsulated cocco-bacillus somewhat similar to one previously found by Pretjetschsky.

In 1910 Ricketts and Wilder saw some curious double bodies in the blood of a number of cases. In 1913 Hegler and Prowazek saw numerous long, round, and diplococcal bodies in the leucocytes some time after infection began, but not at the commencement thereof. These bodies are believed to be the same as those described in 1905 by Rabinowitsch as 'Turkischen Reizformen.' In addition, they observed the forms described by Ricketts and Wilder, not merely in the blood, but also in polymorphonuclear leucocytes in the exudate of a blister. During convalescence the bodies agglomerate in the cells, and finally tend to disappear. Post-mortem trachoma-like bodies were found in the endothelial cells of the heart, the lung, the liver, and the kidney. They are found in infected monkeys, but not in guinea-pigs. Infected lice were seen to contain small coccoid and diplococcal bodies. These bodies are believed to be Chlamydozoa, and to be allied to Lipschutz's genus *Strongyloplasma*.

Prowazek distinguishes them from Doehle's bodies. To summarize, these bodies appear in the leucocytes on the third day of the illness, and persist until convalescence, in one case as late as the nineteenth day of the illness. These bodies are called *Rickettsia prowazeki* Da Rocha-Lima, 1916, and according to this author are never found in typhus-free lice, but can be found in lice infected by sucking infected blood: then they penetrate into the cells of the alimentary canal of the louse on the fourth to fifth day after an infective feed, and multiply therein, and do not reach full development until the eighth to ninth day. In this situation they are very small, shortly elliptical, or oval, and often lie in pairs. Noller in 1916 considers that the ætiological rôle of this organism is no longer doubtful, and in 1917 Foulerton considered that it was probably a phase in the evolution of the ætiological agent. In 1919 Arkwright, Bacot and Duncan confirm Da Rocha-Lima observations. Bradford, Bashford, and Wilson state that they have succeeded in cultivating the virus, using Noguchi's method, from the blood of two cases. The virus, according to these authors, consists of minute coccus-like bodies, Gram-positive, grouped in pairs, varying in size from 0·3 μ to 0·5 μ, capable of passing through Berkefeld N and V filters.

The Carrier.—With regard to the spread of the disease, there was a great conflict of opinion as to whether it was infectious; most certainly it does not cross air-spaces, though it seems to be associated with bedding, fomites, furniture, and dirt, which causes the suspicion that the agent may be an animal parasite. Moreover, the fact that it only appears in the cool season of the tropics, and its rapid disappearance in the warm season, is also in favour of its transmission by some animal. Its non-infectious nature has been proved by Jürgens keeping twenty healthy men confined with twenty typhus patients freed from lice, with negative results; therefore suspicion is aroused that it may be spread by a blood-sucking parasite, perhaps an insect.

Patton has shown that *Clinocoris lectularius* Linnæus, 1758, is found along the north-west frontier of India; and Husband and MacWalters draw attention to the fact that the distribution of this bug curiously coincides with the distribution of typhus in India.

These latter observers point out that in an epidemic occurring in a gaol, the hospital was found infected with bugs, which occurred nowhere else. On the destruction of these pests the epidemic ceased. Moreover, they draw attention to the fact that predisposing causes of typhus, such as dirt, overcrowding, and the way in which the infection hangs about bedding, buildings, and furniture, are easily explicable on the bug hypothesis. Sambon, in his article on Rocky Mountain fever in Allbutt and Rolleston's 'System,' advances arguments in favour of the identity of Rocky Mountain and typhus fevers; but Husband and MacWalters' researches are not in favour of a tick being the carrier of the disease. It may be that typhus and Rocky Mountain fevers are caused by allied protozoan parasites spread by different blood-suckers. In Glasgow the flea was suspected to be the cause of the dissemination of the disease. Nicolle suspected *Pediculus corporis*, and this was soon confirmed on epidemiological grounds, which Crawford supported by a study of the history of the epidemics.

In 1909 Nicolle, Comte, and Conseil transmitted the virus from infected monkeys to non-infected monkeys by means of the bites of lice, *Pediculus corporis* de Geer, 1778. In 1910 Ricketts and Wilder found that they could immunize monkeys against infection with virulent blood by the bites of infected lice. In 1911 Wilder showed that lice became infective between the second and fifth day after feeding, thus proving that the causal agent had undergone some sort of development in the louse. In 1912 Anderson and Goldberger supported Wilder, and concluded that *P. humanus* Linnæus, 1775, and *P. corporis* de Geer, 1778, could both become infected, and that this infection could be transmitted by the crushed insects or by their bites. In 1914 Sergent, Foley, and Vialatte found cocco-bacilli in lice, and in the same year Prowazek and Rocha-Lima found short elliptical coccal bodies and rods. In handling the infected lice both these observers contracted the disease, and Prowazek died. The further investigations of Rocha-Lima have already been noted, and it only remains to say that he found that lice kept at 23° C. did not become infective, and the organism did not develop, but at 32° C. the organism did develop, and the lice became infective. These results are in direct contradiction, as regards temperature, to those of Nicolle, Comte, and Conseil, of Ricketts and Wilder, and of Anderson and Goldberger, and directly opposed to the distribution of the disease. Da Rocha-Lima believes the virus is passed on to a second generation of lice, of which larvæ produced from eggs laid by a louse six days after an infective feed are themselves infected. The organism will develop in the human and not in the pig louse.

In 1917 Da Rocha-Lima pointed out that Ricketts and Wilder, Gavino and Girard, and McCampbell, have found the parasite in human blood; Von Prowazek in leucocytes; and himself in blood, in smears, and in sections.

Also in 1917 Otto and Dietrich obtained infections best by allowing lice to feed on the fifth to seventh day of the illness, as only 4-5 per cent. became infected on the twelfth day, and all are negative after the fall of the temperature. They infected lice from a patient *sine exanthem*, and they confirm Rickettsia. On the other hand, Brumpt is of opinion that this organism in the louse has nothing to do with typhus. Arkwright, Bacon, and Duncan's recent observations are in favour of *Rickettsia prowazeki* playing an etiological rôle. Futaki's *Spirochæta exanthematotyphi*, found in April, 1917, has been proved to have nothing to do with the disease.

Serological Investigations.—In 1916 Nicolle and Blaizot prepared an immune serum in horses and asses by the inoculation of emulsions of spleen and suprarenal capsules of infected guinea-pigs, and tested its curative power on non-immune guinea-pigs, in which it prevents the disease if inoculated in the stage of incubation, and stops the fever at the onset and during the first and second day, but later its action is doubtful. They then tested it upon nineteen human patients, when all cases treated in the early stage recovered quickly, the temperature fell, the pulse and urine quickly improved, but the nervous symptoms required repeated inoculation. It was used in maximum doses of 10 c.c. per diem. In cases in which the disease had been progressive for some time the serum acted slowly. In 1918 Netley and Blaizot showed that the so-called Brill's disease in Paris is typhus, and that guinea-pigs rendered immune to the Parisian typhus are immune to the Tunisian strain.

Prophylaxis.—Many observers (Maitland, Strong, Hunter, Jackson, Castellani, etc.) have demonstrated in practice the vital importance of louse destruction in the prophylaxis of the disease.

Relapsing Fever.—Since 1739 it has been noticed that typhus and relapsing fever go side by side in an epidemic. We now know that the reason is because they are both spread by lice.

Climatology.—Typhus is essentially a disease of temperate and cold climates, and therefore is well known to occur in Europe and America.

In the tropics it principally appears in places situated at high altitudes, or where there are cool seasons, in which case it disappears in a most remarkable manner as soon as the warm season sets in.

In Africa it is said by Hirsch to be endemic in Nubia, and has been carefully studied in Egypt by Sandwith, where he says that it has been definitely recognized since 1836, and where a few cases are reported every year in the spring months. It is also reported from Tripoli, Tunis, Algeria, and Morocco. In Asia it appears to occur only in epidemic form in Asia Minor and Syria, but is believed to be endemic in Persia, and possibly also in Afghanistan, because it is said to be regularly imported into India by caravans from this country. In India an endemic area exists on the west of the Indus, stretching from Beloochistan in the south to Yusufzai, Hazara, and Kashmir in the north, and then passing eastwards along the ranges of the Himalayas, where it is especially prevalent at Kulu, and also passing southwards into the district of Rawal Pindi. In Ceylon we have met with a few cases in European sailors, who have, however, acquired the disease elsewhere. It occurs in Indo-China; in Northern China, where it is endemic, becoming epidemic every spring; and in Japan, where it occurs yearly in the province of Hiogo. It does not occur in Australasia or Oceania. In tropical America it is endemic in Mexico, rare in Central America, absent in the West Indies, the Guianas, Colombia, and Venezuela, and is rare in Brazil, though it is common in Peru and Northern Chili.

This climatology depends upon the louse and the air temperature which is best for the parasite to develop therein.

The Louse.—As *Pediculus corporis* belongs to man, it can go wherever man goes, but typhus fever does not, being absent in the tropics during the hot seasons.

The Parasite.—The fact that most observers believe that a low temperature is necessary for the development of the virus in the louse is borne out by the climatology, being limited to the cold and temperate climates, and only appearing in tropical or subtropical climates during the cold weather or in the hills.

In Mexico it is found on the lofty plateau, in India in the hills, in Egypt and Northern Africa in the cool season, and it will be remembered that the clothes louse is exposed to the effects of air temperatures.

Epidemiology.—Epidemics are caused by anything which favours the propagation of and dissemination of lice. The principal factors which do so are (1) massing together of people of all classes; (2) retaining these masses under conditions which render personal cleanliness and clean clothing difficult or impossible. Such conditions are typically produced in times of war and famine, and exist endemically among the poor. To these we must add a third condition, (3) an atmospheric temperature not too high—*i.e.*, a Temperate Zone temperature. All this has been well exemplified in the Serbian epidemic of 1914-15, when nearly one-tenth of the population died from the disease.

Ætiology.—The causal agent, which is unknown, is spread by means of the louse, *Pediculus corporis* de Geer, 1778. This insect obtains the virus from the blood of a case in which it is present from the fifth to twelfth day, but in greatest abundance from the fifth to seventh day, and from which it is absent after the fall of the temperature. The louse requires some eight to nine days' interval before it becomes infective. It probably remains infective for the rest of its life, but it is not certain whether it passes the virus on to the next generation or not. When an infected louse bites a non-immune human being, some six to ten to twelve days elapse before symptoms appear. An attack of typhus confers an immunity upon man and susceptible animals. Natural immunity exists in many animals.

With regard to *Rickettsia prowazeki* Da Rocha-Lima, 1916, Brumpt, in 1918, found that it was present in seventy-two *P. corporis* removed from healthy persons who never had had or subsequently did have typhus fever. The bites of these lice did not cause the disease in susceptible animals, nor did they infect the persons who handled them. *Pediculus humanus* has no *Rickettsia prowazeki.* Brumpt's researches tend to show that *R. prowazeki* is not the causal agent of typhus fever, while the observations of Arkwright, Bacot, and Duncan are favourable to Da Rocha-Lima's theory.

Futaki in April, 1917, reported the presence of a spirochæte which he named *S. exanthematotyphi* Futaki, 1917, in sections of typhus kidneys and in the urine of patients, but in 1918 Mijashima, Kusama, Takano, Yabe, and Kanai proved that it was non-pathogenic to guinea-pigs and monkeys which are susceptible to the typhus virus. It therefore has nothing to do with typhus. *Doehle's scarlet fever bodies* have been found by Lopez Vallejo in typhus, but have nothing to do with either disease. Hort has described peculiar coccoid bodies in filtered blood. Bradford, Bashford, and Wilson state that they have grown minute bodies, similar to those they have found in trench fever.

Pathology.—According to Zuelzer, the liver and spleen begin to increase in size during the incubation period, and reach their maximum size at the commencement of the illness, while von Chiari looks upon the congestion of the conjunctiva as due to the action of the virus on the walls of the small vessels, causing perivascular infiltration, which he looks upon as a sign of the roseolar rash in this situation.

The virus can produce immune bodies in infected animals. In man a second attack is rare, but has been recorded, and relapses have been known to occur.

The virus lives in the blood from the fifth to the twelfth day, but is scarce after the seventh day and absent after the fall of the temperature, when it is evidently killed by the immune substances produced by the reaction of the body.

Morbid Anatomy.—Death is most common about the tenth day, being due either to the action of the virus of the disease or to complications such as pneumonia and septic infections. The spleen is enlarged and engorged if the post-mortem takes place up to the middle of the second week, but not later. There is œdema of the lungs and hypostatic pneumonia, cloudy swelling and fatty degeneration of the heart, cloudy swelling of the liver and kidneys, and hyperæmia of all the organs. The cerebro-spinal fluid may show a slight lymphocytosis.

The muscles are dry and the rectus abdominalis may show Zenker's degeneration. The spleen is enlarged, dark red in colour, with juicy dark red pulp, while the kidneys may show punctate hæmorrhages.

Symptomatology—*Incubation.*—This varies from four to five to twenty-one days, according to the older views, but the more correct opinion is some four to ten to twelve days.

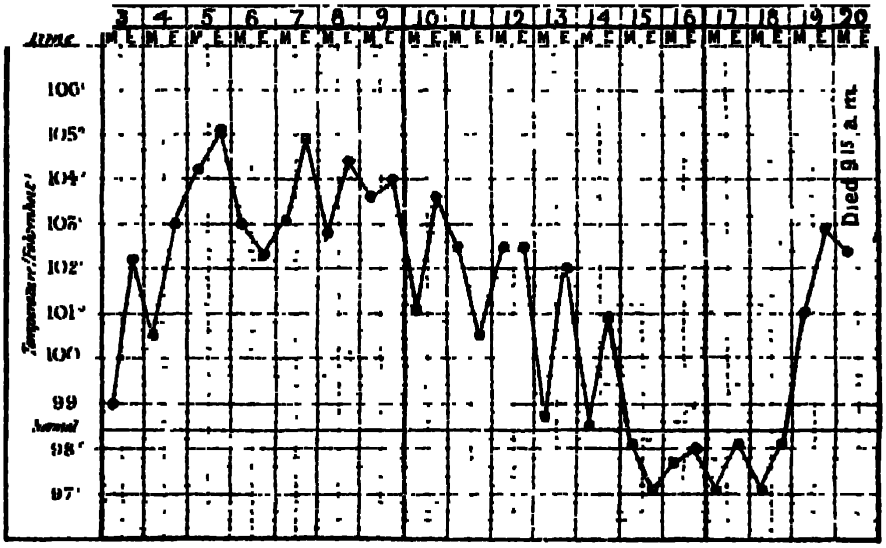

Fig. 651.—Temperature Chart of Typhus Fever.

Prodromal symptoms are often entirely absent, or consist of vague feelings of fatigue, giddiness, and headache.

Attack.—The onset is usually sudden, being characterized by frontal headache; pains in various parts of the body, of which pain in the chest, giving rise to the suspicion of pneumonia, is important; rigors; marked rise of temperature from 101° to 104° F.; quick pulse (100 to 120); flushed face and suffused eyes; quickened respirations; and a sensation of great weakness. Rarely, however, the onset is slow and typhoid-like.

Course.—The duration of the symptoms is from fourteen to eighteen days. During the first two or three days the temperature continues to rise at night, with remissions in the morning, to a maximum of about 104° to 105° F. on the second to fourth days, during which time the tongue becomes dry, swollen, and cracked, with a thick brown deposit on the dorsum, while the tip and sides are red; nausea may be experienced, but vomiting is rare, and the bowels are either constipated or normal.

The nervous system is early affected, the patient being apathetic, drowsy, with a dull expression. The changes in the blood are of the utmost importance, and should be carefully studied. There is sometimes an increase in the red cells, with a corresponding increase in the hæmoglobin, and a leucocytosis, which is usually well marked, being on an average about 24,000 per cubic millimetre, but varying between the extremes of 8,000 and 54,000. The differential leucocyte count is also of importance, for in cases uncomplicated with malaria or other protozoal infections the polymorphonuclear increase is a characteristic feature, and may exceed 90 per cent., while the mononuclears and lymphocytes may be reduced, especially if the case is to end fatally, while eosinophiles are often entirely absent—a most characteristic feature in a case in the tropics, where worm infection is common. The mononuclear decrease is, however, not so evident in cases about to recover, nor is it present in natives in the tropics, who, of course, are liable to previous protozoal infections, and this may lower the relative polynuclear count in these regions to 60 per cent. or less.

Though there is sometimes an increase in the red and almost always in the white corpuscles, the specific gravity is said to be lower than normal, which is rather extraordinary, and must indicate, if true, considerable alterations in the plasma. As the disease progresses the rapidity of the pulse increases, and may reach 140 per minute, and is usually small and of low tension. The blood pressure, according to Rizzuti and Scordo, shows nothing characteristic. The respirations are always quickened, and there are generally signs of pharyngitis, bronchitis, or broncho-pneumonia, while delirium is not uncommon, especially at night.

The Rash.—Definite preliminary rashes are rare, but there is often very marked flushing of the face, neck, and upper part of the chest, with a *cutis marmorata* or subcuticular mottling of the skin of the lower part of the chest and abdomen. The true rash appears on fourth to fifth day, in the form of roseolar macules, like those seen in typhoid fever, but often more abundant. They are first, seen upon the abdomen, and later spread to the chest, arms, and legs on the two latter of which, at all events in recent epidemics, they are rare, although, according to the older authors, they first appear and are most abundant in this position. The roseolar spots at first disappear on pressure, and later some of them may slowly fade away, while others, ceasing to disappear on pressure, become petechiæ, though it is rare for them to develop the dark blue appearance of the petechiæ of such eruptions as those of purpura. This petechial eruption must not be confused with flea-bites, which are characterized at first by a central hæmorrhagic spot, which is surrounded by a circular hyperæmic zone, disappearing on pressure and fading in a day or so and leaving a perfectly circular, dark red, not raised petechial spot which does not disappear on pressure.

A petechial eruption may also appear somewhat later, but is often wanting, and when widespread is an indication of a bad prognosis. A miliary eruption may appear later in the attack, and be followed by a desquamation. After the appearance of the eruption the leucocytosis becomes more marked, as do the nervous symptoms, the patient suffering from severe delirium, which may become quite violent; or he may show a stuporous condition, which becomes a semi-coma, and in fatal cases deepens into a profound comatose condition.

Termination.—As a rule the duration of the fever is from fourteen to eighteen days. On or about the fifteenth day the temperature generally falls by crisis or by rapid lysis, which may extend through three to five days, the rash fades, the spleen becomes normal, the leucocytosis increases, and convalescence begins.

In more serious cases the toxæmia may become severe during the first week, and the patient may die from the seventh to tenth day or even earlier.

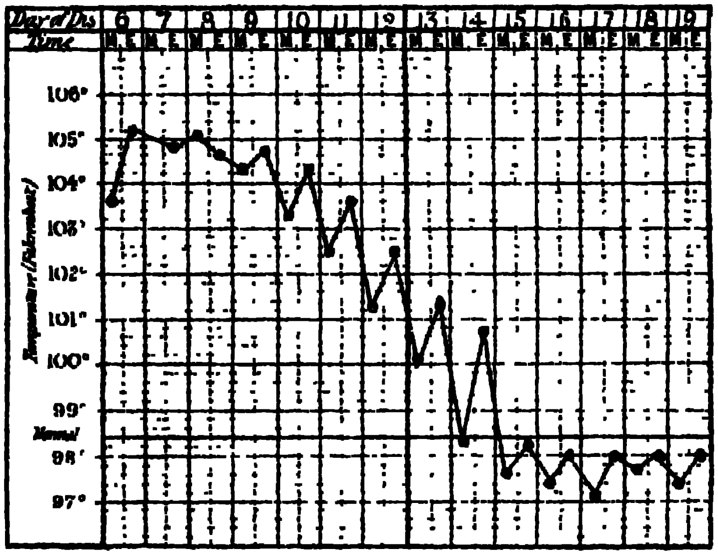

FIG. 652.—TEMPERATURE CHART OF TYPHUS FEVER.
(Chart made by Dr. G. C. Shattock.)

Convalescence.—This may be slow, and not rarely there is danger during this stage, as the general condition may not improve with the cessation of the fever, and death may ensue some two to three weeks after defervescence. In such cases the pulse does not improve, and the patient becomes weaker and weaker until he dies. These are very trying cases for the medical practitioner. Myocarditis may develop during this stage, and shows a weak irregular pulse.

Varieties.—The varieties which may be mentioned are: (1) Mild or ambulatory cases. (2) Abortive attacks. (3) Malignant attacks, causing death on the second or third day. (4) Typhus *sine exanthem*—*i.e.*, typhus without the rash. (5) Typhus in children. This is usually mild, and it is said that death in uncomplicated cases properly looked after is rare. Moreover, these cases are important because they are apt to be missed. Rigors are rare, and often the temperature rises by steps, while the fever lasts only some nine to thirteen days. Bronchitis is frequent. The spleen is constantly enlarged, but the rash is generally scanty. Insomnia is not frequent, but high temperatures often occur. Children remain throughout the illness in a condition of semi-stupor, and waste in a remarkable manner. (6) Typhus with an extensive exanthem all over the body and into the mouth, with or without patches of gangrene.

Complications and Sequelæ.—*Mixed infections* with relapsing fever, malaria, pneumonia, typhoid, and acute miliary tuberculosis occur. *Complications* are:—Parotitis, ending often in suppuration, gangrene of the feet, and polyarthritis, neuritis, hemiplegia, severe mental depression, amounting almost to melancholia (seen during convalescence) may be mentioned. Also bubonic swellings, venous thrombosis, diarrhœa, otitis media, abscesses, and boils occur, while jaundice, endocarditis, and meningitis are rare, but myocarditis is fairly common.

Diagnosis.—This may be most difficult, especially in children. The cardinal points in the diagnosis are:—

(*a*) *Incipient Typhus.*—(1) The sudden onset, with sometimes headache, rigors, and vomiting. (2) The congested eyes and face, and the subcuticular mottling of the skin over the chest. (3) The mental confusion and stupor, associated with the log-like attitude of the whole body. (4) The leucocytosis.

(*b*) *Fully Developed Typhus.*—(1) The typical rash. (2) The leucocytosis. (3) The history of the sudden onset, etc.

Remarks on the Diagnosis.—*Leucocytosis* averages 24,000 per c.mm., and is present in proportion to the gravity of the illness; it is therefore of double value, diagnostic and prognostic. It persists through the fever, and declines after the return of the temperature to normal, and reaches the usual count on or about the twelfth day after defervescence.

The differential count shows polymorphonuclear leucocytes 65-78 per cent., lymphocytes 23-34 per cent., mononuclear leucocytes 7-14 per cent. Eosinophile leucocytes are rarely met with, but in rare cases may reach to 2-6 per cent.

Weil-Felix Reaction.—From the blood of patients suffering from typhus Weil and Felix isolated a bacillus, which they grew on agar and called X_{19}, O. This was completely agglutinated by the serum of typhus patients.

For the reaction the organisms must be grown on neutral agar slants, and must be alive. Cultures of two to three days' growth are best. The reaction is said to be positive on the sixth day of the illness, and to be useful in retrospective diagnosis. Some observers believe that the reaction is due to a mixture of the true virus with *B. proteus*, but others consider it to be of the nature of a par agglutination. The organism X_{19} belongs to the *Bacillus proteus* group of organisms. It is not suggested that the organism has any causal effect in the production of typhus fever. It may give complement deviation when used as an antigen with typhus serum, which is negative to Wassermann's reaction. A modification of the Weil-Felix reaction with killed X_{19} is called 'Neuber's diagnosticum.' It is praised by some and condemned by others.

The *differential diagnosis* has to be made from pappataci fever, dengue fever, relapsing fever, malaria, 'enteroidea' fevers, rat-bite fever, cerebro-spinal meningitis, pneumonia, septicæmias or pyæmias, and uræmia.

From *pappataci fever* it can only be recognized at its commencement by the presence of leucocytosis and the absence of leucopenia, and the same holds good for *dengue fever*.

From *relapsing fever* it may be diagnosed by a blood examination showing the absence of spirochætes and the presence of leucocytosis, as well as by the clinical symptoms, but especially the mental disturbance.

From *malaria* it can only be separated by the absence of the malarial parasites, which may be present in double infections, and by the leucocytosis.

From '*enteroidea*' *fevers* it may be distinguished by the often abrupt onset, by the leucocytosis, and by the absence of the specific 'enteroidea' organisms in the blood and fæces.

From *rat-bite fever* it may be known by the absence of the mark of a rat-bite, absence of the enlarged lymphatic glands, and of the spirochætes in the blood.

From *cerebro-spinal meningitis* it may be told by the clear cerebrospinal fluid containing no meningococci, and by the absence of stiffness of the neck, Kernig's sign, and the presence of the typical rash.

From *pneumonia* it may be parted by the absence of definite apical or basal dulness, of the bronchial respiration, as well as by the character of the sputum, with absence of blood.

From *septicæmias and pyæmias* by blood cultures showing an absence of pyogenic organisms, by the absence of blood destruction, and by the presence of cerebral symptoms. From *septicæmic plague* it can be distinguished by the course and blood cultures.

From *uræmia* it is known by the presence of fever and by the analysis of urine.

From '*flea-bites*' the diagnosis, of course, has only to be made in cases of fever, and can be done by the history, the patient often stating that the rash was in existence a long time before the fever. The distribution is on the limbs equally to the body. The rash is composed of a number of petechial spots of a dark red colour and *perfectly circular* in outline (see p. 1334).

From *smallpox*, by absence of the fall in the temperature on the fourth day, absence of shotty papules appearing on the face on the fourth day; but the diagnosis in times of contemporaneous epidemics may be almost impossible. When in doubt and before the specific rash appears the presence of well-marked vaccination marks are in favour of typhus.

From *influenza*, by the absence of the catarrhal symptoms.

From *plague*, by the absence of the buboes and the plague bacilli therein

To facilitate the diagnosis in cases of typhus with a faint rash Dietsch recommends applying a rubber band round the arm. This procedure makes the rash below the point of application more visible, and may cause formation of petechiæ.

Prognosis.—The case-mortality is variously stated as being from 10 to 50 per cent. The signs indicative of serious trouble and grave prognosis are the absence of eosinophiles in the blood, decrease in the number of the mononuclears, slow pulse, severe petechial eruption or nervous symptoms, alcoholism, pulmonary complaints, meteorism, gangrene, and cyanosis of the face.

The signs indicative of a hopeful prognosis are an increase in the eosinophiles and mononuclears, the absence of the petechial eruption and slight nerve symptoms.

Mortality is low in the young and extremely fatal in the old; it is slightly more fatal in males than in females, while alcoholism, kidney disease, are bad prognostic elements, as is a fat or very muscular subject. Pregnant women generally abort, and this complicates the chance of recovery. Complications are generally serious in regard to prognosis.

Treatment.—The patient should be placed in an airy, well-lighted room, sparsely furnished, and placed upon a diet of milk, broths, jellies, etc., while plenty of water is allowed to be drunk. Careful attention and nursing are required, especially when delirious The temperature should be controlled by cool sponging, and the nervous symptoms by ice to the head, hyoscin, bromides, or morphine, while the heart is supported by hypodermic injections of strychnine, digitalin, etc. Nicolle finds that the serum of convalescent cases for ten to twelve days after the temperature has fallen to normal has prophylactic and curative properties when given in doses of 20 c.c., repeated if necessary, and has manufactured a special horse serum for this purpose. He suggests that in grave cases it should be given intravenously. Salvarsan and neosalvarsan have been tried without any great success.

Prophylaxis.—This is summarized in one word, ' lousing,' in which we include the destruction of lice on the person and on the clothes.

The procedure is sufficiently simple: the person goes into a room, takes off the clothes, which are steamed or boiled, passes into another room, and is sprayed with kerosene oil or petrol, passes into a third room, and receives clean or sterilized clothes.

The sterilization of the clothes may be conducted by boiling, but better still by making them into lightly packed bundles and placing them into a truck or room into which steam is blown. This is easiest done in a truck, the steam being brought from the engine.

A campaign against lice may be conducted on the following lines:—

A. *Methods applied to Man:—*

I. Give illustrated lectures, so that people may understand about the louse, its habits, its association with disease, and its prevention.

II. Advocate the use of soap and water and of the frequent bath, as well as of clean linen frequently changed.

B. ***Methods applied to the louse*** :—

I. ***Pediculicides*** :—

(*a*) ***Dry Heat.***—Lice and nits can be killed by exposing them for fifteen minutes at 60° to 65° C.

(*b*) ***Moist Heat.***—Lice and nits are killed instantaneously by moist heat at or over 80° C.

This is the method most used for clothing, which may be boiled or exposed to steam, but must not be in tightly rolled bundles.

C. ***Chemicals*** :—

For Use on the Person.—Kerosene oil or petrol spray or vaseline, or cresol soap.

For Use on Stored Clothing.—Naphthalene.

II. ***Lice Repellents:***—

Better-class patients:—Dusting powder of menthol 3-5 grains, zinc oxide 1 ounce.

Poorer-class patients:—Naphthalene as a dusting powder.

III. ***Special Points*** :—

Head Lice.—Shave the head or cut the hair very short, or wash the hair thoroughly with 1 in 40 carbolic acid lotion, which is left to act for an hour, the head being wrapped up in a towel in the form of a turban. Then wash the head with soap and water and apply a dressing to any raw areas, carbolic vaseline (2 per cent.) or white precipitate ointment may also be used to destroy head lice.

Body Lice.—The following drugs arranged in order of efficiency (according to Castellani and Jackson) may be used:—

1. Petrol and kerosene oil.
2. Plain vaseline.
3. Guaiacol.
4. Anise preparations.
5. Iodoform.
6. Lysol, cyllin, etc.
7. Carbolic acid, 5 per cent.
8. Naphthalene.
9. Camphor.

IV. ***General Insecticides*** :—

The experiments of Castellani and Jackson in Serbia have demonstrated that ***pyrethrum*** is a very feeble pediculicide, while sulphur, boric acid, perchloride of mercury, when used in powder, have no action whatever.

Substances which may be efficient pediculicides may, however, have little or no action upon other insect parasites of man, such as bugs and fleas. For example, iodoform will kill lice in ten to fifteen minutes, but has no action on bugs and little on fleas. Pyrethrum acts more powerfully upon bugs than upon lice. In order to formulate a general insecticide several chemical substances must be combined. As an example of a general insecticide for use against lice, bed bugs, and fleas, the following is given:—

Equal proportions of naphthalene, previously soaked in guaiacol or creosote, pyrethrum, zinc oxide.

The wearing of undergarments made liceproof by soaking in various disinfectants (crude carbolic acid and soft soap emulsion), as recommended especially by Bacot, is useful. Legroux's 'sachets' or small bags containing naphthalene treated with citronella oil may be used.

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CHAPTER L

THE SPOTTED FEVER OF THE ROCKY MOUNTAINS

Synonyms—Definition—History—Climatology—Ætiology—Morbid anatomy —Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—The intermittent tick fever of Wyoming—References.

SPOTTED FEVER OF THE ROCKY MOUNTAINS.

Synonyms.—Black fever, Blue disease, Rocky Mountain spotted fever, Spotted fever of Montana, Rocky Mountain fever, Piroplasmosis hominis, Spotted fever of Idaho, Tick fever of the Rocky Mountains.

Definition.—An acute endemic febrile disorder, associated with a petechial or purpuric eruption of the skin, which occurs after the bites of infected ticks, *Dermacentor andersoni* Stiles, 1905 (which is the same as *D. venustus* Banks, 1908), and probably other ticks—*e.g.*, *D. molestus* and *D. maturatus*—in certain regions of the Rocky Mountains.

History.—The first case of the disease is believed to have occurred in Bitter Root Valley, in 1873, and from that date until 1902 it is said that about 200 cases were observed, with a mortality of 70 to 80 per cent. During this period it was generally known as the 'black fever,' the 'blue disease,' or the 'spotted fever.'

In 1898, according to Anderson, Major M. W. Wood made an unpublished report on the disease to the Surgeon-General of the United States Army. In 1899 Maxy wrote a paper on 'The So-called Spotted Fever of Idaho,' which he described as an acute, endemic, non-contagious, but probably infectious febrile disorder, characterized clinically by a continuous, moderately high fever, severe arthritic and muscular pains, and a profuse petechial or purpuric eruption of the skin, appearing first on the ankles, wrists, and forehead, but rapidly spreading to all parts of the body. In 1902 Gwim and McCullough read separate papers on the disease at a meeting of the Montana State Medical Association, and in the same year Wilson and Chowning were deputed to investigate it in the Bitter Root Valley. As a result of their investigation, they concluded that it was caused by a *Piroplasma*. They believed this *Piroplasma* to be parasitic in a squirrel (*Spermophilis columbianus*), and to be spread to human beings by a tick, *Dermacentor reticulatus*

(= *D. andersoni* = *D. venustus* Banks *nec* Marx). In 1903 Anderson was instructed to investigate the disease, and as a result of his inquiries he supported Wilson and Chowning as regards both the parasite and the tick. In 1905 Stiles published his zoological investigation into the cause, transmission, and source of Rocky Mountain spotted fever, in which he failed to find evidence of the existence of the parasite in man or squirrel, and of the transmission by the tick. His researches were supported in the same year by Ashburn. In 1906 King found distinct experimental evidence of the transmission of the disease by the tick. From 1906 until his recent death Ricketts has been working at the ætiology of the malady, and has proved that the tick *D. andersoni* spreads the disease—a conclusion which he has supported by experiments on guinea-pigs and monkeys: but he says that the credit for proving the transmission of the disease from man to man by the tick must be given to McCalla and Brereton. In 1908 Ashburn and Craig published an excellent paper on this and the tsutsugamushi disease, which they indicate to be distinct from one another, and in this paper Ashburn accepts the transmission by the tick. Ricketts in 1909 found that there were really two different ticks implicated in the spread of the disease, and these were recognized as *D. venustus* Banks, 1908 = *D. andersoni* Stiles = *D. venustus* Marx, 1897, *pro parte*, and *D. modestus* Banks, of which we have been unable to find a description. It is obvious that there is great confusion as to the correct nomenclature of the ticks causing this fever. We follow Stiles, and call the best-known tick *D. andersoni*.

Climatology.—The disease is only known in the United States, in Washington State, Oregon, Montana, Idaho, Nevada, Wyoming, Utah, and Colorado. It has not been reported from New Mexico, as far as we know, but the causal tick is found there and the fever probably exists therein. In Montana it is found in the Bitter Root Valley, on the eastern slopes of the Bitter Root Mountains, and from there to the western bank of the Bitter Root River, by which it is apparently bounded, the worst area being from Lo-lo to Como, a distance of about fifty miles in length, but only about four to five miles in breadth. This country has a considerable snowfall, which, though it begins to melt in March, lies on the mountains until mid-June. The melted snow drains into the river, which does not reach low-water until July. It is only during this period that the ticks (*D. andersoni*) appear in large numbers, and infest men and animals who pass through the forests, thickets, and uncultivated regions. The disease is also known at Rock Creek, 20 miles, and at Bridger, 200 miles, east of the Bitter Root River. In Idaho it occurs throughout the entire valley of the Snake River, including its tributaries, and the foot-hills in the neighbourhood. In Wyoming it is found at Cody and Meetceste. In Nevada it is only known in the north, in the valley of the Quinn River, where it was recognized as far back as 1887. In Oregon it is said to be mild, and to be found only in the eastern portion, towards Idaho.

In 1915 it was noticed at Ismay and Fallow in Montana, which was an extension of its distribution. Possibly it occurs in Alaska.

It will be noted that these districts extend from 40° to 47° N. latitude, and that the elevation is about 3,000 to 4,000 feet above sea-level, and are sharply defined regions in valleys or at the foot of hills.

Wilson and Chowning noted that the cases occur from March to July, as is shown by the following list, taken from their report:—

March	6	cases
April	24	,,
May	46	,,
June	35	,,
July	5	,,
Spring (exact month not known)	10	,,
Total	126	cases.

This seasonal occurrence is associated, as stated above, with the prevalence of *D. andersoni* during the same months. There is a growing suspicion that there is a difference between the Montana and the Idaho strains of infection.

Ætiology.—According to Wilson, Chowning, and Anderson, the cause of the disease is a *Piroplasma*, but Stiles, Ashburn, and Ricketts have failed to find this parasite. Stiles, Ashburn, and Craig seem to have thought that the disease was due to a trypanosome. If so, this has not been confirmed. The bacterial growths so far obtained from cultures of internal organs or of the blood can be considered as merely accidental contaminations.

Ricketts has shown that blood taken from a human being suffering from the disease can be inoculated successfully into guinea-pigs and monkeys (*Macacus rhesus*), and that the transmission from animal to animal can go on apparently indefinitely (100 generations). These inoculations produce a disease characterized by an incubation, a fever, an eruption, and post-mortem appearances similar to those found in human cases. No bacteria can be cultivated from the internal organs or blood of the infected animals, but the virus exists not merely in the serum, but so closely attached to the corpuscles (white and red) that it cannot be separated from them by washing; moreover, it will not pass through the pores of a Berkefeld filter. Immunity follows an attack, and hyperimmunity can be induced in guinea-pigs.

Fricks by centrifuging infected serum for four to six hours at 2,000 revolutions per minute separated a virulent deposit, in which he found in the serum bright red granular and light blue bodies when stained by Giemsa and in the corpuscles elongated chromatinic bodies. He hesitates to draw any conclusion concerning these bodies, but thinks that the virus multiplies in his cultures. Wolbach finds diplo-bacillary-like bodies, resembling those found by Ricketts, in large numbers in endothelial cells in and around vessels and lymphatics, and in the muscle cells of vessels. He thinks that these organisms may possibly be allied to spirochætes. He has been unable to cultivate them.

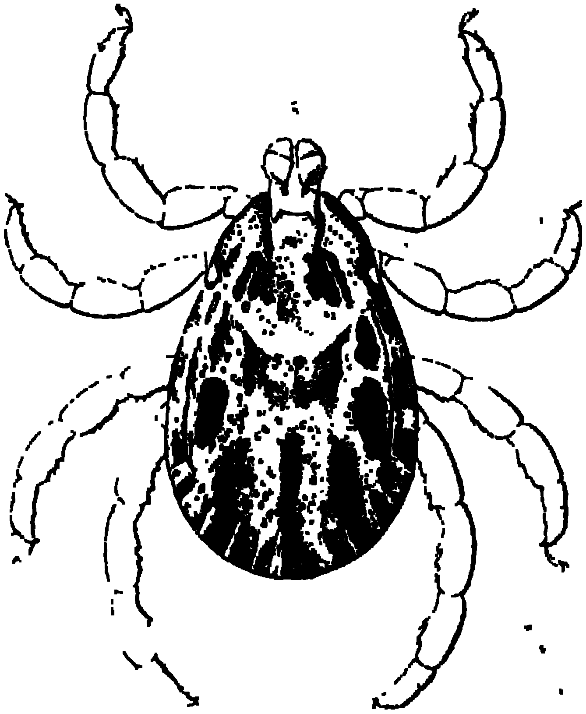

Fig. 653: Male.

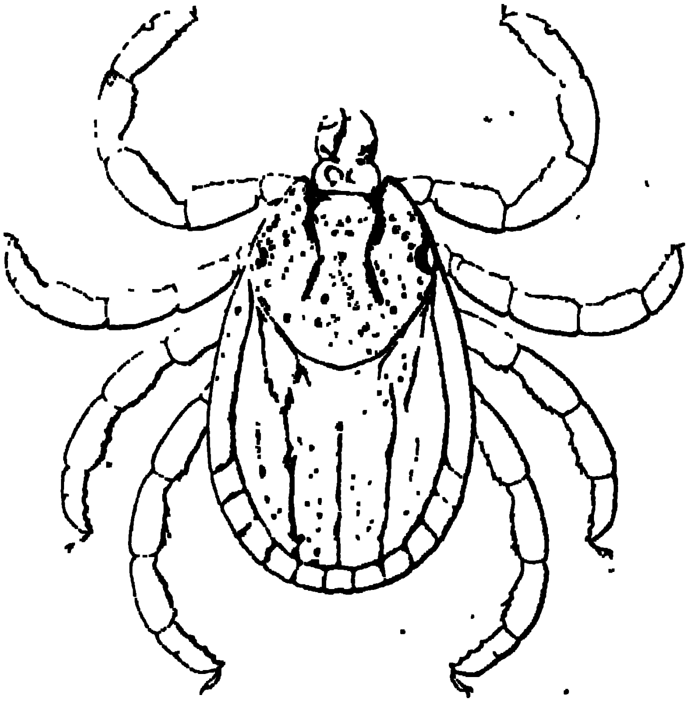

Fig. 654: Female.

Figs 653 and 654.—*Dermacentor andersoni* Stiles, 1905.

The virus can be acquired and transmitted by the larva, the nymph, and the male or female adults of *Dermatocentor andersoni*;

and in a few instances can pass through the eggs into a second generation of ticks. According to Ricketts, the Idaho disease is spread by *Dermatocentor modestus*, and the Montana by *D. venustus* Banks, 1908, *nec* Marx, 1897 (= *D. andersoni* Stiles, 1905). He is inclined to think that there is a difference between the two forms of fever, especially as the former has a death-rate of some 5 per cent. and the latter of about 90 per cent.

Infected ticks are found but sparingly in Nature. Thus, of 513 ticks found on animals, 296 or more were allowed to attack guinea-pigs, with the result that only one of the animals took the disease after an incubation of seven days. The infected guinea-pig was found to have thirty-six male ticks upon it, all of which had come from a horse.

A tick fed on a human being suffering from the disease communicated it first to a man and afterwards to a woman by its bites. Ricketts, examining the blood of patients and the eggs of infected ticks, has observed peculiar bacillary-like structures, which show bi-polar staining. He has not succeeded in cultivating the germ. Wolbach in 1916 and 1918 has confirmed Ricketts' observations. Arkwright, Bacot and Duncan consider the Rickettsia bodies found in Rocky Mountain Fever to be slightly larger and usually longer and more lancet-shaped than those observed in typhus and trench fever. Michie and Parsons have no doubt that the infective agent is in the salivary glands of the tick. Transmission to a tick requires twenty four hours, and infection of a guinea-pig one hour and forty-five minutes at least. The tick is the natural reservoir of the parasite of the disease and lives upon domestic animals, horses, and cattle, as well as upon six varieties of wild rodents, including *Citellus columbianus* and *Marmota flaviventes*, and the jack-rabbit; but according to Fricks sheep are unsuitable as hosts, but this has failed to be confirmed. There is no doubt that the parasite of the fever multiplies in the tick, and there seems to be an opinion that *Dermatocentor andersoni* (= *D. venustus*) in Montana produces a fever with a 90 per cent. mortality, while *D. maturatus* in Idaho one with a 5 per cent. mortality. See also Chapter XXXV.

With regard to *predisposing causes*, there are sex and age influences to be noted. Men are more frequently attacked than women, and the most common age is from fifteen to fifty years, both of which merely signify that persons performing outdoor work run a greater risk of infection than those otherwise employed.

Pathology.—During the fever the virus can be found in the red and white cells as well as in the serum. It also exists in the liver and spleen.

Morbid Anatomy.— Rigor mortis is well marked, and the skin shows lividity in dependent and petechiæ in non-dependent parts, and at times the marks of the tick-bites may still be visible.

The pleura, lungs, and pericardium, and most of the organs, are normal, but petechiæ may be seen on the epicardium; while the liver and spleen are enlarged, congested, and soft, and the kidneys are congested, and may show subcapsular hæmorrhages.

Histo-pathology.—The microscope shows capillary congestion of the organs, with an excess of leucocytes, and an extravasation into and pigmentation of the skin. Acute parenchymatous degenerations of the heart muscle, the spleen, liver, and kidneys, are also to be noted.

Symptomatology.—*Incubation.*—The incubation period varies from two to seven days, during which prodromata, in the form of irritation in the tick-bites, from which pains may radiate, and chilliness with malaise and nausea, may be experienced.

Onset.—The illness often begins with a distinct chill, accompanied by severe headache, pains in the back and other parts of the body, and a rapid rise of temperature to 103° to 104° F., associated with a furred tongue, a dry skin, yellow and congested conjunctivæ, an irritating cough, at times epistaxis, and the passage of febrile urine.

The fever continues to rise, with slight morning remissions, until a maximum of 105° to 107° F. is reached about the fifth to the twelfth day. About the third day (second to seventh) a macular eruption appears on the wrists and ankles which quickly spreads up the arms and legs on to the back, forehead, chest, and abdomen, so that the whole body is included in about one to two days. The macules vary in size from 1 to 5 millimetres in diameter. They are not elevated, and at first disappear on pressure, but later become permanent, and finally turn petechial about the sixth to the tenth day. Associated with the eruption is a dusky-red mottling of the skin, and often a subicteric tinge of both the skin and the conjunctivæ. The eruption is, however, by no means always well marked, and, in fact, mild cases have been reported in which it was absent.

The pulse is from the first very rapid, reaching from 110 to 150 per minute, and not as a rule in proportion to the temperature. At first full and strong, it becomes gradually feebler and smaller, and is often dicrotic, and in severe cases may be intermittent and irregular. The blood shows a diminution of the erythrocytes and hæmoglobin, with a slight increase in the total number of leucocytes and a relative increase of the mononuclear leucocytes; but in considering these blood-counts, allowance must be made for the altitude at which the disease occurs. Œdema of the face and limbs may be present in severe cases

Course.—At first the tongue is covered by a thick white fur, but later it becomes dry, cracked, and brownish, and sordes collect on the teeth. Nausea may be present during the first week, but is more common in the second, and generally lasts till the end of the illness. Constipation is usually present throughout the attack, and the liver is often slightly enlarged, while the spleen extends beyond the costal margin, and is tender. There is usually a slight sore throat, and there may be signs of a mild bronchitis, associated with an increase in the number of respirations, which may reach from twenty-six to sixty per minute.

The urine presents the usual febrile character, and often contains a trace of albumen, which occasionally may reach considerable proportions, and be accompanied by a few granular casts. More rarely the urine may be scanty or even suppressed. The mind is usually clear, but in severe cases a low muttering delirium may occur.

Terminations.—After the fever has reached its height on the fifth to the twelfth day, the temperature either declines by lysis, and recovery takes place, or it remains high, and, a typhoid state developing, death ensues. If the former event is to take place, the temperature, falling by lysis, reaches normal about the fourteenth to the eighteenth day, the eruption commences to fade, and desquamation begins, which extends all over the body, while the other symptoms gradually abate and the patient becomes convalescent. If, however, death is to ensue, the temperature remains about 104° to 106° F., but sometimes shows a sudden final fall just before the fatal event.

Convalescence.—Convalescence may take some time, and it is said that the sites of the eruption are clearly visible even twenty-four days after recovery if a warm bath is taken.

Complications.—Pneumonia is a comparatively frequent complication, but gangrene of the fingers, toes, and skin of the scrotum and penis may occur. Nephritis, cardiac weakness, and meningitis are possible complications.

Diagnosis.—The malady may be difficult to differentiate from typhoid fever, typhus, and the Japanese river fever. From *typhoid fever* it can be distinguished by the more acute onset, the petechial eruption, commencing on the hands and wrists, the absence of marked intestinal symptoms, and the presence of leucocytosis. In doubtful cases all the modern bacteriological methods—serum reaction, search for the *Bacillus typhosus* in the blood, stools, and urine—will have to be used to exclude typhoid.

The distinction between spotted fever and *typhus* on clinical grounds seems to us impossible. Though in typhus the disease may end more often by crisis than by lysis, all the other clinical symptoms, and the appearance of the eruption, are practically identical; in fact, Sambon and others believe that the Rocky Mountain spotted fever and typhus are the same entity. Possibly typhus and Rocky Mountain spotted fever are due to two varieties of the same organism, or two very closely allied species, in the same way as African, European, American, and Asian relapsing fevers are due to very closely allied organisms. It has been noted that guinea-pigs are susceptible to inoculation of Rocky Mountain fever virus. Inoculation of blood, especially if taken at the end of the febrile stage, produces pronounced swelling of the scrotum in guinea-pigs, and this has been suggested as a test to differentiate Rocky Mountain fever from typhus. Recent immunological studies have thoroughly established the difference between Rocky Mountain fever and typhus.

The *tsutsugamushi fever* may present a course very similar to the Rocky Mountain spotted fever, but the presence of one or more eschars near the genitals or the axilla, and the eruption beginning on the face, and not becoming petechial, are characteristic.

Prognosis.—It appears that the prognosis is much more serious in some localities than in others. In Montana the mortality has been as high as 90 per cent., while in Idaho it has always been very low (5 per cent.). The reason for this difference may be that there are two distinct varieties, one spread by *D. andersoni* (*D. venustus*) and the other by *D. maturatus*. When the eruption is not much marked and not generalized, the prognosis is favourable.

Treatment.—Quinine has been advised and given in large doses, but it does not show any specific effect. Atoxyl and salvarsan have no effect. Adrenalin has also been advised. The treatment can be only symptomatic. To relieve the severe headache cold applications may be used, or, with prudence, small doses of antipyrin, or pyramidon, or Dover's powders. Large quantities of water should be drunk, so as to flush out the kidneys. The water may be slightly acidulated. Tepid sponging is useful and refreshing. When the temperature rises above 103° F., cold sponging should be used, and, if necessary, the cold bath or cold pack. Should the pulse become small and irregular, cardiac stimulants must be administered. The room should be darkened, and the patient kept undisturbed.

The diet should be liquid, chiefly milk and broths. Alcoholic stimulants may be indicated in some cases.

Prophylaxis. This may be considered under two headings:—

(*a*) Man.

(*a*) *Man.* This consists in avoiding as much as possible localities where the ticks are abundant, and destroying these arachnids. A tick should be removed by applying ammonia, turpentine, kerosene, or carbolized vaseline, and then the bite may be cauterized with pure carbolic acid. Some authorities advise the internal administration of quinine, but this does not prevent the development of the fever.

(*b*) *The Tick.* The prophylaxis campaign against the tick is divided into:—

1. Destruction of ticks.
2. Removal of natural tick hosts.
3. Protection of domestic animals against the tick.

These ends are accomplished by periodic dipping of cattle and horses in the usual arsenic solution to destroy the ticks, by poisoning and shooting rodents, by restricting the movements of domestic animals from infected areas, and prohibiting the entrance of animals into these areas during the period from February to July.

The arsenical solution used as a dip is composed of the following ingredients:—

Sodium carbonate	24 pounds.
Trioxide of arsenic	8 ,,
Pine tar	2 gallons.
Water	to 500 ,,

A galvanized tank is used containing 30 to 40 gallons of water, which is brought to the boil. The sodium carbonate is now added and dissolved by stirring, and then the arsenic is dissolved in the same way. The fire is now stopped and the pine tar added in a thin stream and thoroughly mixed by stirring. The solution so formed is the stock and can be diluted to 500 gallons as required.

THE INTERMITTENT TICK FEVER OF WYOMING.

Definition.—An intermittent fever due to the bite of *Dermacentor andersoni*.

History and Geography.—This fever was described by Kieffer in 1907 as being found at Fort D. A. Russell, in Wyoming, United States of America, but his account so far has not been confirmed.

Ætiology.—The fever comes on after the bite of *D. andersoni*—*i.e.*, the same tick which causes the spotted fever of the Rocky Mountains—but no specific organism has so far been described.

Symptomatology. The incubation period varies from three to seven days, after which the disease begins suddenly with a rigor, nausea, vomiting, and pains in the joints and muscles. The temperature rises between 103° and 104° F., and continues high for twenty-four to forty-eight hours, after which a remission of forty-eight hours occurs, and then another attack, and so on for three to seven attacks. Less frequently the attack resembles typhoid, with a ladder-like rising temperature and abdominal symptoms, but Widal's reaction is absent. There is marked decrease of the erythrocytes and hæmoglobin, and a slight lymphocytosis, due to increase in the number of the large mononuclear leucocytes.

Treatment.—Hypodermic injections of arsenic in some form are recommended as the best treatment for the disease. Salvarsan should be tried.

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CHAPTER LI

TSUTSUGAMUSHI FEVER AND ALLIED FEVERS

Synonyms—Definition—History—Climatology—Etiology—Pathology—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—Allied fevers—References.

TSUTSUGAMUSHI FEVER.

Synonyms.—Japanese River fever, Flood fever, Island disease (Shima disease) Kedani disease ('kedani' is the hair louse), Akamushi disease ('mushi' is the Japanese for a bug or insect; 'akamushi' means 'red insect'), Shima mushi disease (Island bug disease), Tochu bio, Shashitsu, Pseudotyphus

Definition. Tsutsugamushi disease is an acute endemic febrile disorder caused by the bite of a mite, *Microtrombidium akamushi* Brumpt, 1910, producing a small local necrotic area, painful enlargement of the proximal lymphatic glands, and an exanthematous eruption.

History.—Tsutsugamushi disease is said by Ashburn and Craig to have been mentioned under the term 'shashitsu' in Chinese writings more than one thousand years ago, when it was described as a fever due to the bite of a mite, which produced a pustule in summer-time in people who entered those parts of the country which had been flooded by the spring rains. The Japanese literature on the subject is considerable, but the descriptions written in European languages are not extensive, the earliest contributions being by Palm in 1878 and Baelz in 1879, while Ashburn and Craig, in 1908, give an excellent account of the disease and its causation, together with a comparison with the spotted fever of the Rocky Mountains.

Climatology.—The geographical distribution is limited to the island Nippon, of Japan, where it is confined to the districts Akita-ken and Nugata-ken ('ken' means a 'district'), in which certain lands are flooded in June, in the former district by the Rivers Omonogawa and Minasegawa, and in the latter by the Rivers Shinanogawa, Akagawa, Uwonumagawa, and Hajadegawa. Further, it is limited to certain parts of the regions flooded by these rivers. The floods only last a few days, and the regions do not become dangerous till after a few weeks, when a red mite appears, which may attack any person entering these places. In fact, so great is this danger that the lands have been abandoned, except by the very poor, who enter them in order to cultivate hemp or corn, or to gather mulberry-leaves to feed silkworms. The disease is to a limited extent transportable with corn, hemp, and other articles. It occurs most frequently from the middle of July to October.

According to Weir, a similar disease exists in Korea; to Dowden, in the Malay States; to Schöffner, in Deli; and to Noc and others, at Saigon.

Ætiology (*vide* also pp. 726 and 920).—The causation of the disease is not known, but there are three theories which have been supported by various investigators.

These theories are:—

1. *The Bacterial Theory*. Many bacteria have been described as the cause of the disease, the first being a *Proteus*, found by Balz and Takana, associated with staphylococci and streptococci in the lungs, sputum, and urinary sediment.

2. *The Protozoan Theory*.—Ogata considers that the cause of the disease is a *Plasmodium*, which he states he has found in the blood of numerous patients. Ogata's observations have not been confirmed. In 1917 Hayashi claimed that the parasite was a *Piroplasma* which existed in monkeys, guinea-pigs, and calves, inoculated with blood from a patient, in the form of granules and rod shaped, globular, and annular masses in giant cells found in the lymphoid tissue, especially of the guinea-pigs.

Myashima has found rodlets in the akamushi and in inoculated animals.

Nagayo, Miyagawa, Mitamura and Imamura state that they have cultivated an oval non-capsulated non-motile organism from patients suffering from the disease.

3. *The Chemical Theory*. Tanaka believes that the true cause is a toxin contained in the body of the mite, and introduced by its bite.

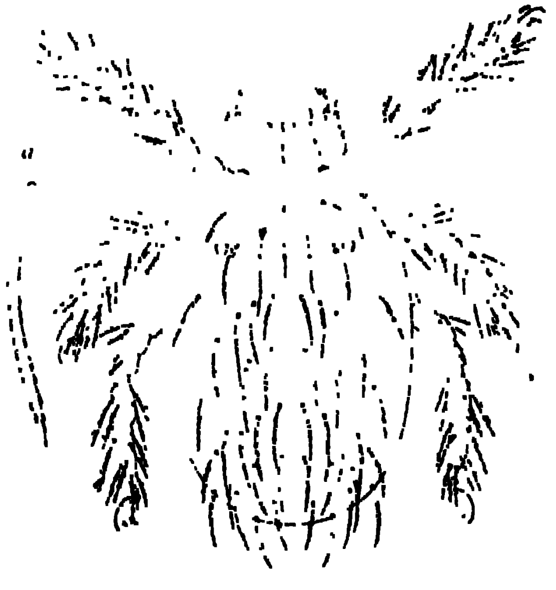

FIG. 655.—*Microtrombidium akamushi* BRUMPT.
(After Hirst, from the *Journal of Economic Biology*.)

The only certain facts which we know concerning the ætiology of this disease is that the symptoms follow the bite of the larva of *Microtrombidium akamushi* Brumpt, and that immunity is not conferred by an attack. This larva (akamushi), which, though bright red or orange in colour, is so small that it is almost invisible to the naked eye, is found in large numbers on the inner surfaces of the ears of field-mice (*Arvicola natanedzumi* Sasaki) caught in July and August in the infected regions. The akamushi of other regions do not cause the disease, which, of course, is against the chemical theory as to the ætiology. Miyajima claims to have infected monkeys by inoculating blood derived from a person suffering from the disease, and also by the bites of the mites. Mice and guinea-pigs are said to be immune—a statement which, however, is opposed by Ogata. The larva has been reared and adult mites obtained by Nagayo, Miyagawa, Mitamuar, and Imamura, as well as by Miyajima and Okumura. The last-named suggest that the correct name for the mite is *Leptus akamushi* (Brumpt).

Only poor people enter the infected lands during the months of July to October, and as any person who does so is liable to infection, the disease is mostly found among the poor.

Pathology.– The post-mortem reveals a small ulcer, sometimes still covered by an eschar at the site of the bite, and enlargement of the proximal lymphatic glands. The spleen is enlarged and softened, the lungs are œdematous and congested, and the bronchial mucosa is often slightly swollen and reddened, and the kidneys are inflamed. We are not acquainted with any description of the histology of the organs.

Symptomatology.—The incubation period varies from four to ten days (4-7 Scheube), during which there may be a feeling of prostration, giddiness, and general malaise, but definite prodromata are wanting.

The disease begins with a chill and rigors, accompanied by severe pain in the forehead and temples, and a sensation of weakness, while the temperature quickly rises to 101° to 103° F. The patient usually complains of pain in certain enlarged lymphatic glands, which, on inspection, are found to be tender, quite distinct from one another, and freely movable under the skin. A search in the region drained by these glands may reveal a circular vesicle measuring 2 to 4 millimetres in diameter, but more usually one or more black or brownish necrotic areas of skin, surrounded by a dullish red areola, are found. These areas indicate the sites of the bites of the mite.

The temperature continues to rise during the next few days, reaching a maximum in the second week, when it may be as high at 105° F. During this time the eschar has been thrown off the necrotic area, and reveals a circular punched-out ulcer, the periphery of which is red and infiltrated, but not painful nor tender. About the fifth to the seventh day an eruption appears on the face in the form of large red papules, which may become confluent on the cheeks, giving the face a swollen appearance. From this situation the eruption spreads all over the body, but more in the form of macules than papules. These maculæ, which are 2 to 5 millimetres in diameter, fade on pressure, but quickly return.

when the pressure is removed, and do not itch. Between the spots on the trunk and forearms follicular papules may be noted, but the eruption is not so well marked on the arms and thighs.

At first the pulse is full, and not very rapid, varying from 80 to 100 per minute; later it may become small and quick, and at times dicrotic. The first cardiac sound is often impure, and the transverse diameter of the cardiac dulness may be increased.

In the blood the red cells are found to be diminished, and the hæmoglobin proportionately reduced. In mild cases there is often an increase in the large mononuclear leucocytes and lymphocytes, but in severe cases the total number of leucocytes is often diminished, though there may be a relative polymorphonuclear increase.

The tongue is at first moist and slightly coated, but later it becomes dry, brown in the centre, and glazed at the tip and edges. The gums in some cases are spongy, and bleed, while sordes may collect on the teeth, and a few punctiform spots be noted on the palate. The epigastrium and left hypochondrium are tender; the liver, however, is not as a rule palpable, though the spleen is usually slightly enlarged.

The nose and throat are normal, but the rate of the respirations is increased, and the breath-sounds are harsh and accompanied by rhonchi, which can be heard all over the chest. Usually there is a certain amount of coughing, but the expectoration is scanty.

The urine is diminished in quantity, high-coloured, and may contain albumen, and often gives the diazo-reaction. Strangury may occur.

The conjunctivæ are early injected, a feature which becomes more marked as the disease progresses, and is associated with lachrymation.

From the very first there is a great hyperæsthesia all over the body, and there may be delirium at night, and difficulty in hearing.

About the fourteenth day of the illness the eruption begins to fade and the fever to remit, and in the next five or six days the temperature falls by lysis to normal, and, the general condition rapidly improving, convalescence begins. Recovery is usually quick, and by the twenty-first day from the commencement of the attack the patient is well.

In bad cases, however, coma and hyperpyrexia may develop in the second week, and cause the death of the patient. In other cases death may be caused by complications, which may arise either in the second week or during convalescence.

Varieties.—Severe types of the disease end in death about the ninth to the fifteenth day from hyperpyrexia, cardiac failure, pulmonary œdema, or from complications. Mild types, showing only the bite and the enlargement of the lymphatic glands, and associated with but little fever or eruption, quickly end in recovery.

Complications.—The commonest complications are parotitis, melæna, mania, and cardiac failure with pulmonary œdema.

Diagnosis.—The differential diagnosis from Rocky Mountain spotted fever and typhus has already been discussed (p. 1347). At the onset—when the inguinal or other lymphatic glands are enlarged and painful—plague might be suspected. The presence of the necrotic area, and, in any doubtful case, the microscopical examination of the gland juice, which in plague contains numerous bi-polar staining bacilli, will enable a diagnosis to be made.

Prognosis.—The prognosis is good in the young, and in second and third attacks, which are always milder than the first. It, however, gets worse as age progresses, and especially in first attacks. The mortality is about 30 per cent., but increases markedly with age, being only 12·5 per cent. in the first, and 57 per cent. in the seventh decade of life.

Treatment.—Quinine is generally administered, but it does not influence the fever to any marked extent. Salvarsan might be tried. Narcotics may be required to combat the sleeplessness, and constipation must be relieved by purgatives and enemata. Phenacetin, antipyrin, and salicylates are generally badly borne by the patient.

Prophylaxis.—The prophylaxis consists in the avoidance of the infective regions during the months of July to October inclusive, while the cultivation of the infected regions, and especially the planting of *Eucalyptus globulus* and *Paulownia imperialis*, are advised, as well as the smearing of the exposed parts of the body with eucalyptus oil and balsam of Peru, which are said to keep away the mites.

The natives believe that the manuring of the infected lands with human fæces for three consecutive years will make them free from the mites, provided there is no flooding during that period.

ALLIED FEVERS.

PSEUDO-TYPHUS OF DELI, SUMATRA.

In 1902 Schüffner observed a peculiar fever in Deli, Sumatra, which he described in 1913, and which he thinks may possibly be due to a tick.

In occurs from June to August and from November to January.

The site of the inoculation is marked by a small red spot, followed by necrosis of skin and inflammation of the local lymphatic glands. The necrotic ulcer may measure 2-7 mm. in diameter, and shows little tendency to heal, while other lymph glands enlarge.

On or about the second to third day a roseolar eruption appears all over the body, being most marked upon the trunk and flanks, and less so on the face and limbs. This eruption slowly fades during eight to ten days. Sometimes it is but slightly marked; sometimes it is hæmorrhagic and followed by desquamation.

The fever is like that in enteric fever, and is associated with severe nervous symptoms.

Diarrhœa is rare, but pulmonary complications are not unusual, and albuminuria is generally present. The blood shows an increase in the white cells, particularly the lymphocytes, while the eosinophiles are diminished.

No organisms could be found in the blood, and there were no reactions to serum tests for the enteric fevers, nor could monkeys be infected by inoculation.

KOREAN CONTINUED FEVER.

A somewhat similar fever to the Sumatra fever is described by Weir. It occurs in spring and early summer. No bite is mentioned, but there is the rash; no diarrhœa, but frequent pulmonary complications and the nervous symptoms. The course of the fever is often short and terminates by lysis.

MALAY STATES FEVER.

Dowden in 1915 described a somewhat similar fever in the Federated Malay States, but gave no ætiological information.

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CHAPTER LII

RAT-BITE AND CAT-BITE FEVERS

Rat-bite fever—Cat-bite fever—Squirrel-bite disease—Addendum References.

RAT-BITE FEVER.

Synonyms.—Sodoku (So = rat, doku = bite); Fièvre par Morsure de rat Morso-di-Topo; Rattenbisskrankheit.; Rattenbeetziekte.

Definition.—A relapsing fever of long duration characterized by redness and swelling at the site of a rat-bite, often by a generalized papular eruption, and caused by *Spiroschaudinnia morsusmuris* Futaki, Takaki, Taniguchi, and Osumi, 1916, living in the mouth of *Epimys norvegicus* Erxleben, 1777, in many parts of the world, and inoculated by means of their bite.

History.—Rat-bite fever is mentioned in Japanese medical books from the most ancient times, and Scotch, French, and Spanish literature have references to the disease, but it was not until Katsura in 1899 and Miyake in 1899 reported cases that any interest was taken in the malady. In 1908 some twenty-one Japanese investigators, according to Hora, had reported some thirty cases, which have recently been increased very considerably. It has also been recorded by Horder in England; by Proescher in the United States, in which the literature of the nineteenth century shows occasional cases among settlers; by Frugoni in Italy, who has given a very good general account of the malady, and by Lou and Cockin from East Africa. As we stated under this heading in the first edition of this book, there is a curious belief in Ceylon that a rat's bite is a serious injury, and is apt to be followed by a chronic disorder which is popularly called leprosy, but which we have never been able to see. In Ceylon the belief is that the rat's bite is only pernicious in the breeding season. And in Japan Hora's case is stated to have been due to a bite of a female rat which was suckling its young. It is said that the same disease may follow the bite of a weasel, and it is known that weasels kill rats, and therefore it is possible that infection may come in this manner to the weasel.

In 1898 Millot and Carpentier, and in 1907 Roger, drew attention to the existence of the disease in France.

In 1908 Ogata considered that the causal organism was a sporozoön (Rattengift sporozoön). In 1914 Schottmüller obtained a nocardia, which he called *Streptothrix murisratti*, from the blood of cases of the disease. This organism has been supported by the observations and experiments of Blake and others, but is now merely of historical interest. Douglas, Colebrook, and Fleming, in 1918, found a streptococcus, while Coles has suggested that more than one germ may be the causal agent.

In 1916 Futaki, Takaki, Taniguchi, and Osumi discovered a spirochæte in the lymph glands and pathological products of patients suffering from the disease. In the same year Costa and Troisier reported cases in France.

Climatology.—As the rat is widespread, so the disease is found in many parts of the world, being recorded in Japan, China, Ceylon, India, Dutch Indies, East Africa, England, France, Italy, Balkans, Holland, Germany, and North and South America.

Ætiology.—Futaki and his collaborators, in 1916, reported the presence of a spirochæte 9-10 microns in length in the lymph glands and in the tissue fluid from the bitten area. Later they found in man and inoculated animals shorter and thicker spirochætes 2-6 microns long, with regular close steep waves and a filament at each end. Ishiwara, Ohtawara, and Tamura, in 1916 and 1917, in investigations with regard to experimental rat bite, found spirochætes morphologically identical with the short forms described above, and Kitagawa and Mukoyama, in 1917, found forms measuring 6-10 microns in length, with a smaller one measuring some 4 microns and a larger measuring 12 microns, in their inoculated guinea pigs.

In 1917 Kaneko and Okuda, in performing a post-mortem on a case, found:—

1. *Long spirochætes*, 6-10 microns in length, with numerous small, steep, irregular waves, identical with Futaki's long spirochæte.

2. *Short spirochætes*, 1·7 5 microns in length, with two to six steep, close, regular waves, identical with the short spirochæte of Ishiwara and Futaki, and also to the spirochætes found by Ido and his collaborators in guinea-pigs bitten by rats and so infected.

These short parasites have been found by Ido and others in human blood films taken at the height of the disease. Kaneko and Okuda found the spirochætes in the kidney in casts in the straight tubules, the canals of Henle, and the intercalary portion of the boundary layer. They have also been found in the cortical cells of the suprarenal capsules and in an interstitial space in the testicles, but not in other organs.

The long and the short spirochætes belong to the same species, as is proved by pure cultures. The long spirochætes are considered to be old forms, and are exclusively found in human tissues. The short spirochætes are the typical young forms, and can be found in the blood of patients suffering from rat-bite fever, as well as in experimental animals. In no instances have they been found in healthy guinea-pigs, white rats, or mice. They are absent from the blood and tissues of infected animals receiving salvarsan treatment.

Ido, Ito, Wani, and Okuda have demonstrated that the serum of persons who have recovered from the disease contains an immune body which destroys *S. morsusmuris*, as demonstrated by Pfeiffer's test and by the fact that the guinea-pigs employed for this test remain well.

Human serum shows definite spirochætolytic and spirochæticidal properties eleven months after the onset of the disease.

These researches make it probable that *S. morsusmuris* is the ætiological agent of the disease.

Naturally infected guinea-pigs have been seen by Niowaka, Yoshizawa, and Mumento, who have shown that the disease can be spread from guinea-pig to guinea-pig by subcutaneous injections of the saliva or by bites of infected guinea-pigs. The organisms may possibly live in the salivary glands of rats. The men mostly infected are agriculturists and sailors, but it has been seen in soldiers in the trenches and persons living in ordinary houses.

Row regards the strain found by him in Bombay as being different from the Japanese strain

Pathology.—At first the reaction against the organism is weak, but later immune bodies specific against the spirochætes are found.

Morbid Anatomy.—Only four post-mortem examinations are on record—viz., those by Miura and Toriyama in 1897, by Blake in 1916, and two by Kaneko and Okuda in 1917.

In the first the conditions were increase of the cerebro-spinal fluid, hyperæmia of the meninges, inflammatory œdema of the lungs, and cloudy swelling of the liver.

In the second there were acute ulcerative endocarditis, subacute myocarditis, interstitial hepatitis, glomerular and interstitial nephritis, infarcts in the spleen and kidney, hæmorrhages and œdema of the lungs. Microscopically, degeneration and necrosis of the cardiac muscles; polymorphonuclear infiltration into the liver and into the shrunken kidney, but many of the changes may have been due to the nocardia found by Blake.

In the third case there were no marked pathological changes, except parenchymatous changes in the organs, such as hyperæmia, swelling, and degeneration of the tubular epithelium of the kidney. There is degeneration, necrosis, and destruction of the liver cells, particularly in the centre of the lobule, with hyperæmia and fatty degeneration of the periphery of the lobule, with also hæmorrhages. No abnormalities in the spleen, lymphatic glands, or bone-marrow, except that the local lymph glands show a hyperplasia of the parenchymatous cells. Catarrhal changes are seen in the mucosa of the stomach, as well as catarrhal cystitis, congestion of the lungs and meninges, and degeneration of the muscles of the leg and nerve cells of the brain cortex and spinal cord.

The skin near the bite shows hyperæmia, œdema, and polymorphonuclear infiltration into the corium and subcutaneous tissue, but no changes in the epidermis.

The changes found in experimental animals agree with those seen in man.

Symptomatology—*Incubation.*—The incubation period varies from seven to twenty-two days, but the average is twelve days. During this period the wound caused by the bite heals.

The Attack.—The onset is sudden. The site of the bite, which, in the large proportion of cases, is on the head or upper extremity, becomes red and swollen, and an ulcer forms, while the regional lymph glands become enlarged. The temperature now rises (103° to 105° F.), the pulse becomes small and rapid, and there may be sensations of chilliness, while an eruption of purple spots, which often resembles erythema polymorphum, appears on the body, and the patient feels very ill, with pains in the muscles and joints, and perhaps delirium. In a few days the temperature declines and the patient feels well.

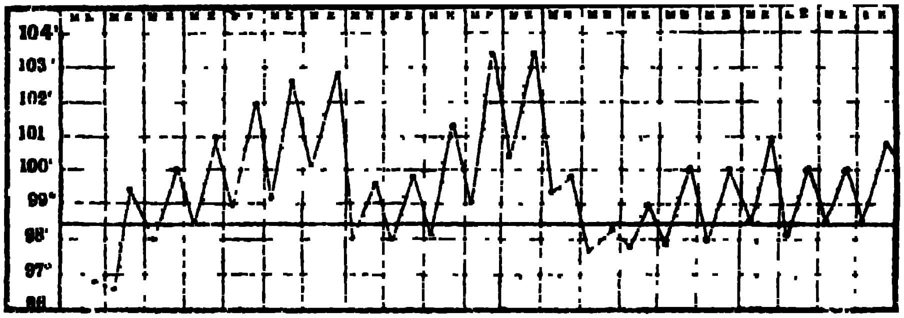

FIG. 656.—RAT-BITE FEVER.

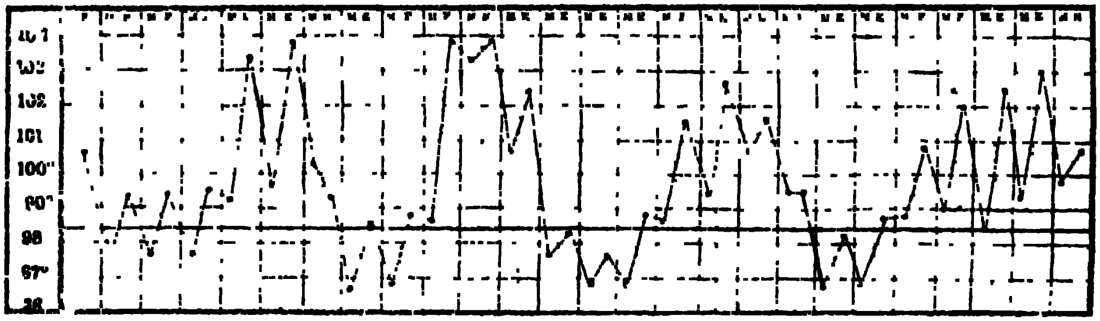

FIG. 657.—RAT-BITE FEVER.

Relapse.—After a few days or a couple of weeks of apyrexia, however, the attack is repeated, and these intervals of apyrexia and attacks of fever may be repeated for months or years. The relapses may be fairly regular, at five days' intervals, for months, and may be preceded by premonitory symptoms. Thus Hora's case had about ten relapses a year for a period of seventeen years. The blood may show eosinophilia. During the fever red cells are about four millions and the leucocytes about six to twelve thousand. In the interval there may be only four thousand leucocytes. Death may occur in old people from exhaustion, or in others from complications.

Varieties.—Three different types of the disease are described: a febrile type with a marked eruption, a febrile type with nervous symptoms, and an abortive type; but the first is most common.

Complications.—Sloughing and gangrene at the site of the bite and nephritis may occur.

Diagnosis.—The presence of a relapsing fever associated with a purple-coloured eruption and a non-suppurative adenitis following a rat-bite should make the diagnosis easy. The discovery of the spirochæte in the blood confirms the diagnosis.

Prognosis.—This is good, as the mortality is only about 10·5 per cent., and death is most usually due to collapse or septicæmic symptoms during the first attack, or to nephritis or to complications.

Treatment.—Treatment by salvarsan is quite successful. For details of the treatment see pp. 1313 and 1560. Mercury has been recommended by Borelli.

Prophylaxis.—The rat-bite should be thoroughly disinfected.

CAT-BITE DISEASE.

Definition. A relapsing fever caused by a spirochæte, probably identical with *Spiroschaudinnia morsusmuris*, introduced by a cat's bite or scratch.

History. Cat-bite disease was first described in Japan by Fujida and Sato in 1902, while Izumi and Kato, in 1917, brought forward evidence to show that the causal organism was a *spirochæte*, probably identical with *S. morsusmuris*. In 1917 Sano described a case due to scratches caused by a cat.

Ætiology.--Futaki and Ishihara, Ido, Ite, Wani and Okuda, Izumi and Kato, have all found spirochætes in the blood of patients. They were discovered by the first named and confirmed by the others. The last named believe this spirochæte to be the same as that causing rat-bite, because--

I. The serum of a patient suffering from cat-bite, when mixed with an equal quantity of guinea-pig blood containing rat-bite spirochætes, immobilizes them. When repeated with normal and syphilitic serum the spirochætes are not affected.

II. When 1 cubic centimetre of guinea-pig blood containing rat-bite spirochætes is mixed with 2 cubic centimetres of the blood of a patient suffering from cat-bite, and then the mixture injected into the peritoneal cavity of a guinea-pig and removed in an hour, no spirochætes are found. In a control guinea-pig the spirochætes were abundant and active.

III. In II. the first guinea-pig remained healthy and the control died.

Symptomatology--*Incubation.*--This varies from ten to twenty-one days.

Attack.--The onset begins with some premonitory symptoms, followed by fever, pains in the muscles and joints, enlargement of the spleen and the lymphatic glands. Infiltration of the skin takes place near the site of the bite, and macular or urticarial eruptions which spread all over the body.

The bite may heal readily or may ulcerate deeply.

Course.--The fever is of the relapsing type, the intervals being some three to nine days, and without treatment the disease will last for months.

Diagnosis.--This is the same as for rat-bite fever.

Prognosis.—This is good *quoad vitam*, except in old age or debilitated persons.

Treatment.—One injection of salvarsan will cure some cases, while others require several injections.

SQUIRREL-BITE DISEASE.

Synonym.—Eichhörnchen-Bisskrankheit.

Schottmüller described a case of this infection in 1914 in a woman bitten by an African squirrel, *Taraxerus cepapi*. The disease was characterized by fever and also by nodules, which destroyed the sight of one eye. Another case was a man bitten by the same squirrel, and from the pus of this case Schottmüller obtained a nocardia which he called *Streptothrix taraxeri cepapi*. The nocardia infection is probably a complication, possibly also introduced at the time of the bite, as its presence has been confirmed by numerous observers, and species of nocardia are well known to live in the human tonsil, and may well exist in the mouth of rats, squirrels, and other animals.

ADDENDUM.

Weasels are also said to cause similar symptoms by their bites, and it is likely that many other animals do the same, and it is possible that they inoculate the bitten person or animal with various types of organisms, of which spirochætes appear to be more important as regards the causation of fever.

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CHAPTER LIII

THE ENTEROIDEA GROUP OF TROPICAL FEVERS

General remarks—Enteroidea or intestinal fevers—Enteric—Parenteric—References.

GENERAL REMARKS.

We use the word *enteroidea*, or intestinal fevers, for all those fevers which are caused by any of the intestinal bacteria, while the term *enteric fever* denotes those which are called *typhoid* and *paratyphoid A and B fevers*. By *parenteric fever* we mean those febrile conditions which, though clinically resembling 'enteric fever,' are caused by intestinal bacilli specifically different from *B. typhosus* and *B paratyphosus A and B*. These parenteric germs may be closely related to the enteric germs or may be widely separated therefrom (*vide* Chapter XXXVI., p. 934).

ENTEROIDEA OR INTESTINAL FEVERS.

The term *enteroidea* covers both the enteric and the parenteric groups, and applies to any fever caused by intestinal germs in the widest sense of the word (p. 934). These fevers may be classified as follows.

- ENTEROIDE FEVERS:—Synonyms: Enteroidea, Intestinal fevers, Enterica *sensu lato*
  - *Enteric Fevers:* Synonym: Enterica *sensu stricto*
    - Typhoid.
    - Paratyphoid A.
    - Paratyphoid B.
  - *Parenteric Fevers:*—Synonym: Parenterica
    - A, due to germs of genus Eberthus and Alcaligenes.
    - B, due to germs of genus Salmonella.
    - C, due to germs of genus Enteroides.
    - D, due to germs of genus Lankoides.
    - E, due to germs of genus Balkanella and Wesenbergus.
    - F, due to germs of genus Escherichia.

ENTERIC.

Synonyms.—Typhoid Fever, Abdominal Typhus, Gastric Fever, Pythogenic Fever, Endemic Fever, Autumnal or Fall Fever, Remittent Fever of many writers, Common Continued Fever, Slow or Lent Fever, Nervous Fever, Little Fever, Irregular Low Fever, Low Fever, Bilious Fever, Bilio-gastric Fever, Bilious Continued Fever, Night-soil Fever, Cesspool Fever.

French Synonyms.- Fièvre Typhoide, Dothienenterite, Fièvre Continue, Fièvre gastrique, Fièvre nerveuse, Enterite septicemique, Adéno-meningee, Fièvre meningogastrique.

Italian Synonyms.--Febbre tifoide, Tifo addominale.

German Synonyms. — Abdominaltyphus, Nervenfieber, Darmtyphus, Gastriches Fieber.

The Latin synonyms are very numerous, and have been classified by Murchison into:--

(*a*) From supposed resemblance to typhus: Typhus nervosus, T. mitior; T. gangliaris vel entericus, Ileo-typhus; Typhos, Typhus (of many old writers).

(*b*) From mode of prevalence: Febris non pestilens

(*c*) From its remittent character: Febris semitertianæ seu composita; Tritæophya typhodes.

(*d*) From its length: Febris lenta.

(*e*) From septic symptoms: Febris putrida, Febris putrida quæ vulgo lenta appelatur; Febris putrida aut biliosa; Febris a putredine orta

(*f*) Resemblance to hectic fever: Febris hetica.

(*g*) Occurrence of gastric symptoms: Febris gastrica, Febris acuta stomachica aut intestinalis; Synochus biliosis.

(*h*) From intestinal symptoms: Febris mucosa, Febris pituitosa, Febris mesenterica maligna, Febris intestinalis

(*i*) From supposed origin from worms: Febris verminosa, Typhus verminosus.

With regard to the nomenclature, we have adopted the term Enteric Fever, used by Ritchie in 1840, because we describe under the term three distinct diseases caused by distinct micro-organisms, all of which produce symptoms either identical with or so closely resembling one another as to be nearly impossible of clinical separation at the present time.

Definition. – The term 'enteric fever' is used at the present time to indicate three clinically similar fevers, typhoid fever due to *Bacillus typhosus* Eberth, 1880, the paratyphoid fevers due to *B. paratyphosus A* Schottmuller, 1901, and *B. paratyphosus B* Schottmüller, 1901, and varieties of these bacilli.

History. - The history of enteric fever may be considered under two headings viz., the general history of the disease, and the special history of its occurrence in the tropics.

It is quite impossible to recognize it with any degree of certainty in the meagre descriptions written by Hippocrates and the ancient physicians, which may or may not have referred to this disease. In the Middle Ages enteric fever, typhus fever, and relapsing fever were always confused with plague until Fracastorius, in the sixteenth century, distinguished typhus (which included enteric fever and relapsing fever), or febris pestilens, from plague, or febris vere pestilens. Spigelius, in 1624, is probably the first writer to clearly recognize the symptoms of enteric fever, because he described in Padua a disease characterized by fever, abdominal pain and tenderness, diarrhœa and delirium, having remissions and relapses, and associated with the post-mortem appearances of inflammation in the ileo-cæcal region. Similar descriptions can be found in the writings of Willis in 1659, who drew a distinction between febris pestilens and a febris lenta, the latter being associated with the enlargement of the mesenteric glands. Sydenham, in 1685, described a fever lasting fourteen to thirty days, and associated with diarrhœa, vomiting, epistaxis, etc., as distinct from febris pestilens. In 1715 Baglivi of Rome described the hemitritæus of older writers under the term 'febris mesenterica.' This fever was characterized by being irregularly remittent, lasting from fourteen to twenty-one days, and associated with inflammation of the intestines and mesenteric glands. Lancisi thought that the enteric ulcers were caused by round worms. Hoffman's febris petechizans vel spuria, Strother's lent fever, Gilchrist's nervous fever, Huxham's slow nervous fever, Riedel's febris intestinalis, and Manningham's febricula, are all synonyms of enteric fever. In 1810 Hildenbrand distinguished between contagious typhus and a non-contagious nervous fever, which were respectively named typhus exanthematicus and typhus abdominalis by German authors.

In 1813 Bretonneau of Tours associated this fever with hyperplasia of the solitary and agminated glands of the ileum, and gave it the name 'dothienenteric' (from *δοθιήν*, a tumour, and *ἔντερον*, the intestine).

In 1829 Louis gave the fever the name 'fièvre typhoïde,' and the work of Gerhard of Philadelphia in 1837, Shattuck of Boston in 1839, Barlow in 1840, Bartlett in 1842, Ritchie in 1846 (who introduced the term 'enteric fever'), Jenner in 1849-51, completed the clinical differentiation of enteric fever from typhus, from which relapsing fever was also being separated. Thus arose the clinical conception of enteric fever, but in the meanwhile many theories had been promulgated as to its causation; thus Bretonneau held the view that it was spread by means of contagion, but this opinion was slow in gaining definite support. In 1847 Canstatt pointed out '*that truly the exhalations of the sick man, his excrements, and possibly the typhus eruption in the skin, are the carriers of the contagion.*'

In 1850 Riecke recorded outbreaks due to drinking-water becoming contaminated with sewage; Murchison implicated milk.

In 1880 Eberth discovered the *B. typhosus* in the mesenteric glands and spleens of persons dying from enteric fever, and in 1884 Gaffkey cultivated the bacillus so discovered.

In 1885 Fraenkel and Simmonds obtained definite animal reactions in guinea-pigs, mice, and rabbits; and more recently Grünbaum, Metchnikoff, and Besredka reproduced the typical characters of the disease in chimpanzees: and Bland-Sutton described deaths of lemurs and monkeys in London which were associated with post mortem appearances resembling enteric fever.

The diagnosis of the disease was greatly facilitated by Grüber and Durham's, Widal and Grunbaum's, works on agglutinins and specific agglutination reactions. Later, the cultivation of the bacilli from blood obtained by splenic puncture, and by the dilution method as devised by Castellani from the circulating blood, assisted the diagnosis; while the bile enrichment method and the Conradi-Drigalski's, MacConkey's, and other media generally aided the investigation of the disease. Chantemesse has devised an ophthalmo-diagnostic method. The diagnosis of a mixed infection has been rendered easier by the absorption test as introduced by Castellani in 1902, which is of use also in the determination of closely allied bacteria. The *B. typhosus* has been found to be capable of living for weeks in the spleen, and for years in the gall-bladder, of people who are designated 'typhoid-carriers,' as the bacilli escape in the fæces in the latter case. The bacilli have been shown to occur naturally in water-supplies, earth, dust, fomites, flies, shellfish, and milk, etc. The subject of relapses has been studied by Chantemesse and Widal in 1892, Wright and Lamb in 1899, and Durham in 1901.

Attempts to obtain an antityphoid serum by Macfadyen, Hewlett, and Chantemesse, have not been successful, but Wright and Semple devised a vaccine in 1897 which was perfected by Leishman, and has been much used and has rendered great service: later Castellani brought forward vaccination with a mixed typhoid + paratyphoid A + paratyphoid B vaccine dead or living (attenuated) as a method of prophylaxis, while more recently Besredka and Metchnikoff have advised a living, not attenuated, sensitized vaccine.

The subject of variation of the *B typhosus* has been studied by Twort, Horrocks, and Penfold.

In 1895 Gilbert gave the name '*para-colon*' to bacilli occupying an intermediate position between *B. coli* and *B. typhosus*. In 1896 Archard and Bensaude used the term '*paratyphoid*' as a name for such organisms when capable of producing the symptoms of enteric fever, but this name dropped into oblivion, only to be revived by Schottmüller in 1901, when he clearly demonstrated his *B. paratyphosus A* and *B. paratyphosus B* as the cause of two forms of enteric fever, the diagnosis of such cases being obtained by the specific agglutinative reactions, or, better, by cultivation from the circulating blood. This is the reason why the symptoms characteristic of enteric fever are ascribed to three allied organisms—viz., *B. typhosus* Eberth, *B. paratyphosus A* Schottmüller, and *B. paratyphosus B* Schottmüller.

The presence of typhoid fever in the tropics has, even in recent times, been much debated, and apparently the view has been held that it was overlooked by the older tropical physicians. This, however, is quite erroneous, for typhoid fever was early recognized in the tropics after its separation as a clinical entity by the workers in the Temperate Zone. Thus Scott and Milley, in 1830, showed that it existed in Tasmania; Levacher, in 1840, in St. Lucia; while it was recognized in 1841 on the Niger River, in West Africa, and in Martinique, and somewhat later in Sierra Leone and Gaboon. In 1842 an epidemic is mentioned as occurring in Rio di Janeiro in Brazil, and others in Tahiti in 1847, 1849, 1853-54, and also in Damascus in 1852, and in Cayenne in 1852-53. Other epidemics were recorded in Cuba in 1853-54, while in the latter year Scriven definitely proved its existence in India by demonstrating the typhoid ulcers found by post-mortem examination. In the same year Thomson described enteric fever in New Zealand, and Ripley about the same time in Fiji. In 1865 Massey recognized it in Newera Eliya, in Ceylon, while its occurrence in Trinidad and the Bermudas was known in 1866, and Davidson, in 1868, described it in Madagascar. In 1877 Defant said it was common in Senegambia.

Notwithstanding all this early work, the fact of its prevalence in the tropics was not generally recognized, the disease being concealed under the terms 'remittent fever' and 'malarial fever' with ulcers, which latter became the so-called 'typho-malarial fever,' which we now know to be a mixed infection -enteric fever complicated by malaria. The cause of this long delay in the general diagnosis appears to have been the slow recognition of the disease by the profession as a whole in England, which reflected itself upon India and the British Colonies; while the authority of Morehead, who in the first edition of his book, 'Researches on Disease in India,' stated that typhoid fever was unknown in that country, is also believed to have had a deterrent effect upon the diagnosis of enteric fever therein. He, however, soon doubted the correctness of his original statement, for in 1860 he writes that in 1856 he recognized the disease in Bombay, and he quotes a lecture given by Goodeve on seven cases of undoubted typhoid fever: still, he is of the opinion that typhoid fever will be found in extra-tropical India or in inter-tropical provinces in the near proximity of the tropics.

Another point which prevented the general recognition of enteric fever was the supposed antagonism of malaria to it, and the immunity of malarial districts from its attacks. These views were simply based upon the opinion that all remittent fevers were malarial, and that swelling and ulcerations of Peyer's patches could take place in these fevers: and the practitioner in the tropics was carefully warned that he was not justified in asserting the existence of typhoid fever from the mere character of the post-mortem appearances, and that the so-called 'typhoid symptoms' were not peculiar to one form of fever, but might occur in all.

Such teaching probably had a marked effect upon the diagnosis of enteric fever in the tropics until the recent establishment of bacteriological institutions, wherein a bacteriological diagnosis could be made.

Still more recent is the general recognition of the fact that the disease may be prevalent among the natives: in Ceylon, however, the fact that the malady is common among natives has been recognized for several years, and typhoid wards for natives have been established, as well as a special typhoid hospital.

It may now be said that it is well known that enteric fever is prevalent in many, if not most, tropical countries, and that it occurs, not merely in Europeans, but in natives also.

Ætiology.—Enteric fever is caused by the *B. typhosus* Eberth, *B. paratyphosus A* Schottmuller, *B. paratyphosus B* Schottmüller. The description of these germs may be found in any manual of bacteriology. It is probable that there are several varieties of each of these germs, and certain characters have been given in Chapter XXXVI., p. 934. Of the *B. typhosus*, for instance, two varieties can be easily differentiated—one rendering milk alkaline after an initial acidity; the other making milk *permanently acid*.

Of *B. paratyphosus B* several varieties have been described by Castellani, Alcock, and others. As regards the so-called *B. paratyphosus C*, this term, used by several observers, among whom recently Hirschfeld, covers different germs, one of which is serologically identical with *B. aertryke*.

With regard to the *B. typhosus* of Eberth, it is found in the intestine, not merely during the attack of fever, but during the incubation, and for a period extending perhaps as long as thirty years after an attack—that is to say, the bacillus has been grown from the fæces of a person thirty years after an attack of enteric fever; but whether it had existed in the bowels for the whole period is naturally not known, but it is possible. In other words, the bacillus can live in the bodies of people for years after an attack. These people are reservoirs or carriers of the bacillus, and may be called *intestinal carriers*. People who pass the bacilli in their fæces during the period of incubation are called *precocious intestinal carriers*; the patients passing the bacilli during the attack and convalescence are called *acute intestinal carriers*; while people who continue to pass the bacilli in their fæces for a year or less than a year after an attack of enteric fever are called *temporary or transitory intestinal carriers*; and those in whose fæces the bacilli are found after an interval of longer than a year are called *chronic intestinal carriers*.

In addition, there are carriers who are not known to have had an attack of typhoid; that is to say, there may be people in whom the *B. typhosus* Eberth may live for an unknown period without showing any pathological signs at any time. These are known as *paradoxical intestinal carriers*. This is possible, but it is also probable that some of the carriers in question may have been cases of ambulatory typhoid, and therefore really belonged to the class of *chronic intestinal carriers*. As to the habitat of the bacilli while in the carrier, it seems that the gall-bladder is of the greatest importance, while during the actual attack of fever the bacilli are to be found not merely in the intestinal contents, but also in the mesenteric glands, the spleen, and the circulating blood. Now, the proportion of female carriers to male carriers is as five is to one. This is a curious fact, and, moreover, the bacillus is often found in the gall-bladder. Now, the frequency of gall-stones in women as compared with men is as three is to one; further, it is a well-known fact that gall-stones are often discovered for the first time at an autopsy; in fact, it is believed that only 10 per cent. of the persons suffering from gall-stones show any sign of the disease during life, and it is a curious fact that the percentage of persons showing signs of gall-stones after an attack of enteric fever is 14 per cent.

All these factors considered together, along with the known fact that *B. typhosus* has been isolated on several occasions from the centre of gall-stones removed by surgical operations, tend to support the view that the gall-bladder is, at all events in some cases, the home of the *B. typhosus* in a chronic carrier. Fornet, in 1909, has, however, stated that he believes the bacilli found in the fæces of a carrier are not descended from those which caused the attack of fever, but are derived from a reinfection which does not produce any clinical symptoms, because the human host has attained a tolerance to the parasite, which therefore leads a saprophytic existence, presumably in the lumen of the intestines.

The discharge of bacilli by means of the fæces appears to be intermittent, and not continuous, which is a most important fact, as the duration of the possible intermission is not positively known, and therefore it is difficult to say definitely when the carrier is really clear of the parasite.

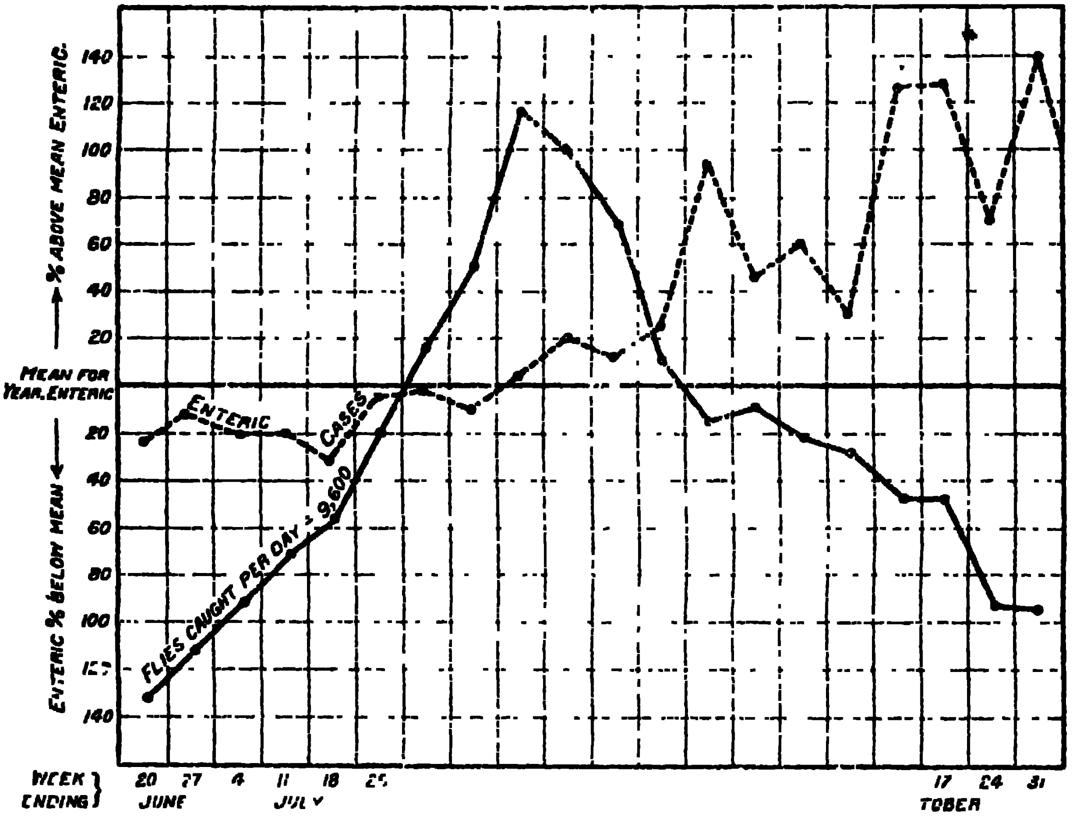

FIG. 658.—CURVES ILLUSTRATING NUMBER OF FLIES AND CASES OF ENTERIC FEVER. (After C. J. Martin.)

The reason why women are more commonly carriers than men is said to be due to the loss of resisting power brought about by the decrease in the alexins of the blood during the menstrual and puerperal periods, and this is supported by the fact that, while the incidence of enteric fever is greater in females from fifteen to twenty years of age, the possibility of becoming a chronic intestinal carrier increases steadily from the fifteenth to the forty-fifth year. A more probable reason seems to us to be that women are more liable than men to affections of the gall-bladder.

With regard to age, it appears that the transitory carriers are generally young—five to twenty years of age—while the chronic carriers are usually old—thirty to forty-five years of age.

The greatest infectivity of a carrier is during the incubation period, and the first weeks of the attack of fever; but chronic carriers are important in producing the endemicity of enteric fever in houses, groups of houses, and streets, as well as in institutions, etc.

As to the method of infection of the healthy by the carrier, evidence is being produced in favour of food contamination. So far, the evidence produced in favour of milk contamination by carriers is very strong, and it is quite possible that water, dust, fomites, etc., will all in course of time be shown to often obtain their infectivity from carriers.

The question of the infection of the house-fly (*Musca domestica*) by means of the bacilli in the fæces of carriers is most important, because the fly may take the bacilli into its crop or alimentary canal, where they not merely increase in amount, but also increase in virulence. Moreover, according to Nicoll's work, it is probable that larvæ may become infected, and thus infection pass to the adult insect. The mouth-part of the fly consists of a proboscis (*vide* Fig. 469) with oral lobes provided with tubules, so that solid particles and liquids pass up readily. It is a matter of everyday observation that the house-fly apparently tastes everything on which it settles that is to say, it extends its proboscis and presses on the substance on which it is standing by means of its oral lobes. When this proceeding is carefully examined, it is seen that the fly is regurgitating a little fluid from its crop via the pseudo-tracheæ of the oral lobes on to the solid substance, with the view of attempting to dissolve some of the solid substance so that it may be able to pass readily along the minute pseudo-tracheæ. This simple act is of the greatest importance pathologically, because the house-fly is an exceedingly foul feeder, and may absorb the liquid from the fæces of a case of enteric fever or from those of a carrier.

In this way the bacilli enter its crop, only to be extruded on to sugar, bread, milk, meat, the rim of a cup, etc., and in this way to gain entrance to the human victim. Naturally, the presence of carriers increases greatly the opportunity for the infection of flies. But it is not merely by the mouth that the fly can infect food materials and utensils, but also by means of its fæces; for the fly defæcates very frequently, and the typhoid bacilli can pass from its alimentary canal in an enhanced condition of virulence—according to some authors—on to food, drink, or utensils, and so reach the human host.

Intestinal carriers are not the sole carriers of the enteric germs, for, though more rarely, the bacilli can escape in the urine of people who have recovered from enteric: these people are called ***urinary carriers***. It is not uncommon to find bacilli in both the fæces and the urine in the case of transitory carriers, but it is much more uncommon to find them in the fæces and the urine in the case of chronic carriers if precautions are taken to prevent the contamination of the urine during or after micturition.

In urinary carriers the *B. typhosus* has its habitat generally in the renal pelvis, which is usually chronically inflamed or cystic, and it has also a secondary habitat in the chronically inflamed bladder; but it appears possible that it may also live in recesses in the pelvis of the kidney, the bladder, the urethra, the prostate, and the vesiculæ seminales, from which bacilli pass into the urine. The methods of urine infectivity are the same as fæcal infectivity.

To summarize, the reservoir or carrier of the *B. typhosus* Eberth is a human host who has suffered from enteric fever, and who affords food and protection for the bacilli in the gall-bladder in the case of intestinal carriers, or in some recess or recesses in the urinary tract from the pelvis of the kidney downwards, and in the male in the prostate and vesiculæ seminales in the case of urinary carriers. This carrier passes the bacilli into the exterior in the fæces and urine, and these may, in cases of defective hygienic surroundings, directly infect air, food, or drinking-water, or may be conveyed by fomites or by flies to the victim's hands, or food, or food utensils.

The problem of the carriers of the paratyphoid bacilli is a similar one. *B. paratyphosus B* is commonly met with in Europe, where it is disseminated by means of intestinal carriers when it lives in the gall-bladder; but its urinary carriers have so far not been recognized. It has, however, been found in the common house-fly in 1911 by Nicoll. Its infectivity and its auto-infectivity are well known. *B. paratyphosus A* is prevalent in India and Ceylon, where precocious and acute carriers are frequently met with. The germ, however, during the war has now become common also in Europe. It is known that it can live in the gall-bladder for a considerable time and pass out in the fæces, and several outbreaks of enteric fever have been traced to this source.

With regard to the general question of carriers, the persons most liable to be carriers are first of all those who have had attacks of enteric fever, and, secondly, nurses and other attendants upon these patients; while the carrier who is likely to prove most dangerous in spreading the infection is a person who is in any way engaged in the preparation or the handling of food intended for other people to consume, because the infection of the hands is a prolific source of infection for healthy people.

So far we have merely referred to *Musca domestica* Linnæus as an important intermediary host for these bacilli, but the fruit-fly, *Drosophila ampelophila* Loew, has been definitely implicated by Dutton in 1909. With regard to the accusations against the bug, *Clinocoris lectularius* Linnæus, and the flea, it can only be said that there is as yet no definite proof that they play an active part in the spread of enteric fever.

To summarize, it may be stated that *B. typhosus*, *B. paratyphosus A*, and *B. paratyphosus B* can escape from the bodies of precocious, acute, temporary, chronic, or paradoxical carriers by means of the fæces or the urine, and can infect food and drink directly or indirectly through the agency of flies, and by means of this infected food or infected hands the bacilli can gain entrance into another human host, and set up the infection anew. Of the foods and drinks which are of importance, the first and most important is milk, while water, shellfish, fish, and dried fish, may also be mentioned as of great importance. Attacks have also been traced to ice, and, indeed, no food or cooking utensil can be considered free from possible infection. Of great importance in the tropics are uncooked green vegetables, which are grown in gardens often manured by means of human excrement. Fæcally polluted dust and fæcally polluted clothes must also be assigned a prominent place in connection with the spread of the disease.

With regard to the *epidemicity* of enteric fever, it will be clearly understood that the basis of the epidemic as the basis of the endemic is the carrier, but the characters of the epidemic will largely depend upon the means by which the bacilli are introduced into the new non-immune hosts. Often this is by flies; hence the name 'autumnal fever' sometimes applied to the disease, because the local epidemic takes place after the time of their greatest prevalence. Epidemics due to milk will be found to agree with the distribution of this food by, generally, one dairy. The present writers once, during an outbreak of enteric fever and dysentery in a tropical town, bought by chance a sample of milk which, on investigation, was found to contain the *B. coli*—a sure proof of human fæcal contamination, which might have arisen from watering the milk, because water is often added by the seller to the milk of *Bos indicus*, and this escapes the notice of the buyer, because the milk is much richer than that of *Bos taurus*, and therefore does not appear to be diluted. As the water may have come from some polluted source—*e.g.*, a well or a roadside drain—this is very dangerous. Epidemics due to oysters and other shellfish will agree with the seasonal use of these shellfish, and may even be traced to certain breeding-grounds which may be situate near the mouth of a sewer, or in which the oyster-bed itself has become infected with bacilli. Another good instance of the cause of small epidemics is the tracing of the infection by Hamer to the fried-fish shops so common in London. But the infection of food materials will not give rise to the sudden widespread epidemic which will arise if the water-supply is contaminated. Maidstone, in 1896, had 35,000 inhabitants, of whom 1,900 persons suffered from enteric fever during the months of September, October, and November, due to contamination of the town's water-supply. In the tropics polluted wells are a prevalent cause of endemic and epidemic enteric fever. The present writers were acquainted with a town in which so-called 'remittent,' really typhoid, fever was very prevalent, and where in a certain area the wells and the cesspits, which always contained water, were only separated by a wall one brick thick.

The bacilli do not live when dried; still, it is probable that they can live, attached to particles of dust, long enough to contaminate food, which in certain tropical regions may become covered with dust.

Predisposing Causes.—With regard to predisposing causes, it was long considered that the native of the tropics enjoyed a partial or, as some said, an absolute immunity against enteric fever. This cannot be maintained, as we know definitely that enteric fever is quite common in all races. The position at the present time is that, while certain authorities consider that a considerable number of cases of enteric fever still lie hidden under the terms 'remittent fever' and 'simple continued fever,' and perhaps 'febricula,' as applied to natives, and especially to native children, who are not often treated by physicians trained in modern methods, still, there are others who maintain that there is a partial immunity in some races—*e.g.*, such an immunity is said to exist among the native Egyptians, Sudanese, and Japanese, which is believed to be due to racial inheritance. This question has been investigated by the Board for the Study of Tropical Diseases in the Philippine Islands, and ably reported by Chamberlain, who finds that epidemics of great severity among Filippinos are rare or unnoticed; that Widal reactions performed on the blood of 591 healthy Filippinos suggest a comparatively recent attack of enteric fever in about 6 per cent. of adults, but do not indicate that the disease is prevalent in childhood; that the native Filippino scouts show a lower typhoid rate than the white troops, possibly due to failure to diagnose the atypical cases; that more than one-third of the cases of enteric fever, whether among Americans or Filippinos, are entirely atypical, and cannot be diagnosed without laboratory methods. One-half of the total number of cases can, however, be diagnosed clinically, and do not differ from enteric fever as seen in the Temperate Zone. He concludes that much work still needs to be done among the natives to estimate the actual amount of mild and atypical enteric fever which is occurring, and to determine why extensive and destructive epidemics are not more often seen.

Our own experience in Ceylon causes us to believe that the disease is very prevalent among the natives of that island, and as dangerous among them as in Europeans. When the causes of death in the races of Ceylon were considered by us some years ago, it was noted that the total deaths contained the following percentages:

Race.	*Enteric Fever.*	*Simple Fever.*	*Remittent Fever.*
	Per Cent.	Per Cent.	Per Cent.
European	10·1	1·7	1·5
Sinhalese	7·6	12·0	0·3
Tamils	0·7	17·3	3·8

Added together, these give—Europeans, 13·3 per cent.; Sinhalese, 19·9 per cent.; Tamils, 21·8 per cent. The incidence of enteric fever among these peoples is probably more nearly approximating the conjoint figures than those given solely under Enteric Fever. Tamils are labourers on estates, and cases of fever among them are generally lumped together under the heading of Malaria.

Age is another predisposing cause, for there appears to be a general consensus of opinion that twenty to twenty-five years of age is a period more susceptible to the disease than the other periods of life, but no age period is free from attacks.

During the first journey from the Temperate Zone to the tropics the metabolism of the young resident in the Temperate Zone is possibly somewhat disturbed, leading to a weakening in the antibacterial and phagocytic reactions, as some authorities maintain; and hence, perhaps, his great liability to attacks of enteric fever and other complaints. It must not be forgotten that the young new arrival is apt to eat too much, to drink too much, and, being stimulated by the heat—the bad effects of which at first he does not notice—is apt to work too hard and play too hard, or, in other words, to attempt to exhaust his system in every possible way, and to thoroughly disregard the evil effects of the sun; and we consider these indiscretions play a certain rôle in the relative frequency with which these young new arrivals become infected.

Young people often live together in what are called '*chummeries*' —*i.e.*, several of them live together in a house, while one of them runs the messing. These houses, having no proper supervision, are allowed to become most insanitary, especially with regard to the servants' quarters, which are naturally the nearest to the kitchen and the places in which food is stored. The pollution of food in these places is often self-evident to the naked eye, while the whole place teems with flies. Moreover, the weakening of the system by venereal disease may play a part in producing the heavy incidence of enteric fever in new arrivals. In Bengal 50 per cent. of the cases in Europeans occurred within one year of arrival from Europe.

In India the disease is believed to be common among native children and among Europeans born in India; thus it was noticed by Rogers that 41·67 per cent. of the cases were under fifteen years of age, whereas in Europe and America only 9·45 of cases are under fifteen years of age.

As regards sex, we have already drawn attention to the apparently special incidence upon women between fifteen to forty-five years of age.

With regard to the conditions of life, the poor whites living in insanitary conditions are very liable to be attacked, and this may account for the prevalence of the disease among Europeans born and living in India, as may the natural habits of children playing among earth and rubbish, which are often more or less fæcally polluted. But of all predisposing causes, that of bad sanitation stands out pre-eminently first; thus Europeans are apt to get the disease most commonly in the dry season, when it is spread by dust and flies, and the natives in the wet season, when it may be due to water contamination.

With regard to meteorological conditions, we have observed that anything which prevents the heavy rainfall at the proper season tends to an increase in the enteric, dysentery, etc., rates; and, absurd though it may read, certain observations which we made some years ago led us to believe that the eruption of Mount Pelée may have had a disturbing effect upon the meteorological conditions, producing less rainfall, and preventing the filthy drains and other places being properly flushed, and thus indirectly causing an increased incidence of epidemic intestinal diseases.

Pathology.—Enteric fever is a septicæmia which is produced by the bacilli already mentioned entering the body by the mouth, and passing into the small intestine and colon, the lymphoid tissue of which they invade. In this tissue they increase in number, and pass via the lymphatics to the abdominal lymphatic glands and spleen, in all of which they multiply. No doubt they very soon reach the blood, but are probably quickly destroyed and their toxins neutralized, and so long as this continues the patient is without definite signs of the disease. This constitutes 'the period of incubation' or latency, and may possibly be the explanation of those persons who, though chronic carriers of virulent typhoidal germs, maintain that they themselves have never had any illness.

If the quantity of antitoxin substances produced are only sufficient barely to neutralize the toxins, then an ambulatory or an abortive attack may ensue.

When, however, the bacilli multiply in such numbers that, though still largely destroyed by the bacteriolysins of the blood, there is insufficient antitoxin to neutralize their liberated toxins, then the fever begins. The possible explanation of the intermittent type of the fastigium of the tropics is that the supply of antitoxic substances in the blood waxes and wanes. The evidence in favour of the above theory is the presence of the bacilli in the fæces in the incubation period, the presence of enlarged Peyer's patches, mesenteric glands and spleen found accidentally in post-mortem examinations of people who have died from other causes, and in whom enteric fever was not suspected: the possibility of cultivating the bacilli from specimens of the circulating blood obtained during the first week of the fever; and the constant necessity for immediate dilution of this blood if a successful culture is to be obtained.

Relapses can be explained as being due to any cause which so disturbs the metabolism of the body that the antitoxin production decreases, and the germs again gain entrance to the blood in such quantity as to produce fever.

The endotoxin contained in the bacilli has a markedly stimulant effect upon endothelial cells, causing them to swell and to block small lymph capillaries, thus causing patches of focal necrosis in the liver.

The bacilli can occur in any part of the body, but they have a predilection for the lymphatic system. When arrested in the lymphatics of the skin, they give rise to the rose-coloured maculo-papules so characteristic of the disease. The appearance and distribution of these red maculo-papules in the skin of the anterior abdominal wall, chest, and back is believed by Greenhalgh to agree with the cutaneous distribution of the nerves which supply the small intestine, the mesenteric lymph nodules, and the spleen. But this seems hardly possible, as papules can appear on the arms, legs, and other regions. It would appear as though local heat was a more important factor in their production than nerve-supply. The bacilli may attack the respiratory system, giving rise to bronchitis, pneumonia, etc., and they are commonly found in the gall-bladder, in which they cause cholecystitis, and may give rise to gall-stones. They also pass through the kidney into the urinary passages, and at times appear in large quantities in the urine (bacilluria).

They are also capable of living locally in the tissues, giving rise to inflammation, abscess formation, and local death of the tissue.

It has already been noted that they can live for years in the gall-bladder and the pelvis of the kidney, producing the chronic intestinal and urinary carriers, who are liable to infect, not merely themselves, but others also.

Auto-infection may possibly be the explanation of such cases as have second or even third attacks, within a short period after the first attack.

The typical gradual onset of the disease may be explained by the struggle between the antitoxins of the body and the bacterial toxins.

The occasional sudden onset seen especially in the tropics may be due to lowered resistance, owing to many causes—*e.g.*, climatic influences, other infections, etc.

Immunity is generally acquired after an attack, but second attacks are by no means rare; moreover, the immunity is homologous—viz., an attack of typhoid fever will protect against *B. typhosus*, but not against the paratyphoid bacilli.

The fever is due to a lessened loss of heat rather than to an increased production of heat, and this is the reason why, in ordinary cases, there may not be marked emaciation.

Morbid Anatomy.—On opening the abdomen in a typical post-mortem, the bowels will usually be seen to be distended with gas, and the small intestine will be noticed to present marked areas of congestion, especially near the ileo-cæcal junction.

The mesenteric glands will be observed to be enlarged and congested, as will the spleen and at times the liver. If there has been a perforation, a fæcal odour will be perceived on opening the abdomen, and there may be gas, fæcal matter, round worms, or pus in the peritoneal cavity, while careful search will reveal the perforation; but care must be taken not to artificially perforate the gangrenous, or almost gangrenous, intestinal wall by manipulation.

On opening the intestines, it will be noted that the most important site of disease is, as already stated, in the ileum near the ileo-cæcal valve; while the contents of the bowel will be noted to be of a yellowish colour, unless there has been a hæmorrhage, when blood will be seen, or unless medicines have been administered which alter the colour of the motions. The Peyer's patches in the lower few feet of the ileum will be enlarged, prominent, and whitish in colour, and covered, perhaps, with yellowish sloughs, or perhaps containing ulcers, which may be in the form of one large central or several small ulcers.

On inspection, a typical ulcer will be noted to have its long axis in the same direction as the long axis of the bowel, to be of oval form, with thin and undermined edges, and a base formed from the muscularis mucosæ, the infiltrated submucosa, or from the muscular or even the peritoneal coats of the bowel; while in cases of perforation a rent may be noticed through this last coat, permitting communication between the lumen of the bowel and the cavity of the peritoneum. In cases of extensive hæmorrhage injection of water into the carefully dissected out mesenteric artery may demonstrate more or less correctly the source of the bleeding. The solitary glands will also be seen to be enlarged and congested with sloughs or roundish ulcers, while the mucosa around these and the Peyer's patches will be seen to be intensely congested and red in colour. This congestion may be traced for a considerable distance along the ileum and into the jejunum, but it is rare to find the duodenum or the gastric mucosa in a state of acute congestion.

Tracing the bowel downwards into the ascending colon, it will be noticed that the mucosa of the cæcum and ascending colon is often congested, and at times the solitary glands will be seen to be swollen; but as a rule they are not ulcerated.

These typical appearances may be varied by finding only one or two Peyer's patches enlarged, and perhaps only one or two small ulcers, and very rarely there may be no signs beyond a catarrhal inflammation of the mucosa of the bowel. On the other hand, the ulceration in the region of the ileo-cæcal junction may be so extensive that there are only ridges and islands of intensely congested mucosa left, while at other times pieces of the bowel may be black and almost or quite gangrenous.

The mesenteric glands will be seen to be swollen and congested, and on section they will show marked congestion and perhaps pus.

The spleen is enlarged and swollen, dark red in colour, friable, with a tense capsule, while the liver may also be enlarged and congested, and may even on rare occasions show multiple abscesses brought about by a septic pylephlebitis. The gall-bladder and bile-ducts may be congested, or more rarely may contain pus, while the bile is usually light-coloured and watery, but may be inspissated. The pancreas is usually normal, but we have seen it congested and even hæmorrhagic. The suprarenal capsules are generally normal in uncomplicated cases. The kidneys are usually enlarged and congested, with a capsule which strips off readily. On section, both cortex and medulla are seen to be congested, with often fatty degeneration, and more rarely small abscesses or infarcts. The pelvis is congested, but the ureter and bladder are usually normal, though signs of cystitis may be found at times.

With regard to the thorax, if there is much meteorism, the diaphragm may be noted to be pushed up considerably higher than usual. The trachea and bronchi may show signs of inflammation, and in the lung pneumonia, hæmorrhagic infarcts, pyæmic abscesses, and purulent infarcts may be seen. The heart is usually flabby and without any sign of rigor mortis, and is often pale, soft, and friable, from fatty degeneration. Rarely will vegetative or ulcerative endocarditis or aortitis be found.

In the neck the thyroid gland may in cases of great rarity be seen to be enlarged, and even to have abscesses. There may be congestion and ulceration of the larynx and tonsils, but they are not common in our experience. The tongue will be seen to be covered with sordes, and may, perhaps, show fissures.

The brain is often congested, as are the meninges, but meningitis and other naked-eye signs are rarely met with. Venous and, much more rarely, arterial thrombosis may be seen, while Zenker's vitreous degeneration may be found, especially in the adductors of the thigh, the rectus muscles of the abdomen, the pectoralis, and the diaphragm, and very rarely one of these degenerated muscles may be found ruptured and surrounded by hæmorrhages. The bone-marrow may also be congested and show signs of focal necrosis.

Finally, there may be the signs of the complications or sequelæ—as, for example, the arthritis of the joints, the abscesses in various parts of the body, etc.

The pathological history of these post-mortem appearances may now be briefly related, beginning with the history of the lesions of the Peyer's patches.

At first a Peyer's patch or lymphoid follicle is hyperæmic, but this is followed by a proliferation of the lymphoid and epithelioid cells of the follicles, together with a swelling of the endothelial cells of the capillary vessels, and these together produce a more or less definite blocking of the capillary vessels, which causes an anæmia, and produces the whitish colour of the hyperplastic Peyer's patches, to which attention has already been drawn. The typical bacilli can be found lying in the centre of the follicle, and also in the lymphatic vessels, not merely of the follicle, but also of the submucosa. Such is the condition of the follicle about the eighth to the tenth day, and now one of two things may happen: either the excess of lymphoid cells undergo fatty degeneration and absorption, with the result that the blood-flow returns, and the follicle becomes normal; or the blockage of the bloodvessels is increased by fibrinous thrombosis, with the result that the superficial portion of the swollen follicle dies and forms a slough, which, separating from the edges towards the centre, becomes an ulcer some time during the second week. These ulcers may increase in depth by an extension of the necrosis, and may lead to perforation; on the other hand, there may be a formation of granulation tissue over the base, which subsequently leads to fibrous tissue formation, and thus eventually to the healing of the ulcer, which process is completed by the growth of the mucosa over the young fibrous tissue. The site of a previous typhoid ulcer is often clearly visible as a depressed pigmented area, which, on microscopical examination, is seen to consist of atrophic mucosa covering a fibrous submucosa, which is also often atrophic.

The mesenteric glands show at first hyperæmia and cell proliferation, among which the typical bacilli can be found. Pus formation may also be found at times.

The spleen early becomes hyperæmic, and swells considerably, remaining enlarged until the third or fourth week. The capsule becomes tense, and the pulp assumes a dark red colour. The swelling is due to the hyperæmia and cellular infiltration with leucocytes, endothelial cells, and macrophages, among which the typhoid bacilli may be found. During the third week the pulp becomes softer, and the Malpighian bodies become prominent, and absorption begins to take place, which produces a paler colour in the pulp, and eventually leads to an increase in the amount of fibrous tissue.

The liver shows cloudy swelling and fatty degeneration of the cells and spots of focal necrosis, which may be produced by accumulations of epithelioid cells in the lymphatic spaces of the portal system, or to small areas of necrosis of liver cells owing to occlusion of adjacent capillaries. These foci are associated with clumps of the specific bacilli.

The kidneys show cloudy swelling of the cells of the convoluted tubules, but in the cases when the kidney is specially involved there may be considerable hyperæmia, together with perivascular cellular exudation and granular degeneration of the cells of the convoluted tubules.

The heart muscle may show fatty or, rarely, waxy degeneration, while endarteritis obliterans in the small arteries is said to be seen in cases of sudden death without obvious cause.

In the nervous system there are no very marked changes, but pigmentation of the ganglion cells and leucocytic infiltration of the perivascular spaces may be seen, as well as fatty degeneration of the nerve fibres.

The bone-marrow is generally congested, and may show signs of focal necrosis, with hyperplasia of lymphoid cells and clumps of typhoid bacilli.

Symptomatology.—Enteric fever is a very protean disease, the description of which is usually divided into incubation period, onset, course, subdivided into weeks, relapses, and terminations in death or convalescence. In general terms, it may be stated that the fever presents physical signs and symptoms not unlike those seen in the Temperate Zone, but a number of cases are atypical.

These atypical cases may have a slight and short attack of fever presenting but few symptoms, and very liable to be overlooked, or the attack may be ushered in by some other fever—as, for example, malaria or dengue. We will first describe a typical attack with mild or severe symptoms.

Incubation.—The incubation period of enteric fever ranges in its known extremes from three days to twenty-three days, or much longer. The shortest known period—that is to say, the one with three days' incubation—was exceptional, the infection being due to swallowing a culture of virulent bacilli, and therefore it may be excluded for ordinary purposes. It is by no means easy as a rule to define the incubation period, and it is usual to agree with Murchison, and to state that it is most commonly about two weeks (ten to fourteen days), but that it is often less than this, and may possibly be as short as four or five days; while, on the other hand, it is often longer, and no definite maximal limit can be mentioned, because the study of typhoid carriers has demonstrated that persons, apparently in good health, may be infected with the bacillus, and it has further been shown that these people may suffer from auto-infection, all of which naturally complicate the question of the duration of the period of incubation.

We therefore conclude that the usual incubation period for enteric fever is about two weeks.

During this period the patient may apparently show no signs or symptoms of the disease, though at times headache and general malaise may be felt.

Onset.—Typically the onset is gradual, the patient attending to his ordinary duties, though suffering more markedly from the feeling of malaise and lassitude and from headache than during the period of incubation, and associated with these symptoms there may be constipation, or there may be diarrhœa with pains in various parts of the body, but especially in the back, the iliac regions, or the legs. At times there is a troublesome cough. The disinclination for exertion, mental or bodily, increases, as does the headache and the pains, until the patient feels so ill that he consults his medical attendant, when it is found that the temperature is raised above normal (100° to 101° F. in the morning); that it is higher in the evening (103° to 104° F.) than in the morning; that the pulse, though accelerated (80 to 90 per minute), is relatively slow as compared with the temperature, and may be dicrotic; while the tongue is coated on the dorsum, though red at the tip and along the margins; the headache is generally frontal, and there may be thirst, vomiting, or epistaxis, as well as abdominal tenderness and slight distension, especially in the right iliac region. If the case is observed early, a step-like rise of the temperature may be noted—that is to say, the evening temperature is always slightly higher than that of the preceding evening—while the morning remission is less, until about the third or fourth day, when the temperature reaches 103° to 105° F. at night.

The onset, however, is often atypical in the tropics, the symptoms being but little marked, and the patient, though feeling wretched and ill, perseveres with his work, and may never consult a doctor until well into the second week of the fever, and in some cases may even advance farther in the illness than this before the complaint is diagnosed.

With regard to the other atypical onsets, it is well to remember that the disease is a septicæmia, and that, following the account of the pathology given above, any organ or system of the body may be specially attacked. Thus, for example, the nervous system may be specially attacked, with the result that the most urgent symptom is a neuralgia, an earache, a backache, or pains resembling those of pleurisy; or, again, there may be signs as though cerebro-spinal meningitis were coming on, or there may be early delirium. If the respiratory system is specially attacked, the signs will be those of bronchitis, pneumonia, or suggestive of acute tuberculosis. If the alimentary canal is selected, there will be symptoms indicating irritant poisoning or appendicitis; if the renal system is marked out for attack, they will resemble the signs of acute nephritis. The above remarks do not by any means cover all the possibilities of the onset, but enough has been said to indicate the remarkably protean nature of the signs and symptoms of enteric fever, and of the way in which it imitates other diseases.

The First Week.—The early days of this week are as a rule occupied by the onset of the fever, as described above, and often the medical attendant does not see the patient until about the end of the third or fourth day of the illness. In the tropics, however, the attack is at times ushered in by some other fever—as, for example, malaria, by which its symptoms are more or less masked. It is, however, possible, even at this early stage, to observe, associated with the symptoms of the predominant disease, signs and symptoms which arouse suspicion of enteric fever. This suspicion is presently converted into certainty as these signs increase in evidence, while the symptoms of the original ailment decrease and finally disappear. The signs and symptoms to which we specially refer are the alteration of the temperature chart from one of remittent or intermittent fever in malaria to one of more continued fever, with more marked headache, slowing the pulse, the appearance of dicrotism, the signs of abdominal distension, the local pains, the tenderness, and perhaps the gurgling in the right iliac region, and the altered condition of the tongue.

During this first week the facies of the patient becomes at times typical—*i.e.*, the cheeks are flushed and the eyes bright, and there may be some photophobia. The decubitus is almost always dorsal. As the week proceeds, the patient becomes more or less apathetic, listless, and drowsy. Headache, noises in the ears, and pains in various parts of the body are the marked symptoms of this week, while sleeplessness is often another marked symptom. Delirium is, however, rare. The temperature continues high, being usually from 103° to 104° F. in the evening, with a remission of a degree or so in the morning; but in our experience a much greater remission than a degree or so is by no means unusual, and the temperature, as already mentioned, may assume an intermittent character. The pulse is about 80 to 100 beats per minute, often with more or less dicrotism, while the blood-pressure varies, the systolic being about 120 millimetres, and the diastolic about 90 millimetres of mercury. At this stage of the disease there is usually little or no change in the blood, though slight leucopenia may be present. The specific agglutinin reaction is not available, but the bacilli can be cultivated from the blood. In uncomplicated cases the spleen is more or less normal at the commencement, but enlarges distinctly towards the end of the week. The respiratory symptoms may cause the patient much annoyance, especially the dry, hacking cough, and there may be signs of mild tonsillitis, pharyngitis, laryngitis, or bronchitis. Pneumonia must be looked upon rather as a complication than as a symptom of the disease. The gastro-intestinal symptoms present much variability. The mouth is often dry, and the patient may be worried by thirst. The lips and teeth are normal, but the tongue, which is moist, is generally coated by a white fur on the dorsum, while the tip and edges are red. There is little or no desire for food; the stomach is irritable, and vomiting may occur, especially if indiscretions in feeding are allowed. The abdomen is more or less distended, especially in the region of the right iliac fossa, where it is often painful and tender, as, indeed, it may be in other places. There may be constipation or there may be diarrhœa; the motions may be of an ordinary colour, but more typically they are ochre-yellow. It is not often that hæmorrhage is seen during this week, and is then generally small in amount: but its presence is, in our opinion, a relatively serious symptom. The urine is generally diminished in quantity, high in specific gravity, dark in colour, with a markedly acid reaction, but there is usually no albumen, no casts, and the diazo-reaction cannot be obtained.

The skin is hot and dry, with, however, paroxysms of greater or lesser amount of perspiration, followed by the presence of more or less sudamina. The typical rose spots do not as a rule appear before the seventh day, and therefore will not be described under this week. At times a bluish subcuticular mottling is to be observed, especially on the abdominal wall, towards the end of this week of quite a different nature to the bluish spots (*taches bleuâtres*), which are generally assigned to the action of lice. There is often a yellowish coloration of the palms of the hands, the lateral aspects of the fingers, and the soles of the feet, sometimes called 'Philipowicz's sign,' which, however, is by no means characteristic of enteric fever.

The most marked feature of the week is the gradual increase in severity of the disease as marked by the growing apathy and dulness of the patient; the aggravation of the symptoms, with the exception of the pains, which tend rather to abate towards the end of the week; the enlargement of the spleen; the possible occurrence of the typical spots; and the continued fever.

The Second Week.—The signs and symptoms described in the first week continue to increase, with the exception of the headache and local pains, which usually diminish and disappear by about the middle of the week. The tendency to hæmorrhage is, however, more marked, and the danger of perforation of the bowels has now to be considered, while the typical rose-coloured rash should appear to a greater or lesser extent; the specific agglutinin reaction should be obtainable, as well as the diazo-reaction in the urine, while the specific bacilli are much more difficult to obtain from the circulating blood, but can still be recovered from the spleen, the fæces, the rose spots, and often from the urine. Liver or gall-bladder symptoms and other complications may appear. With this introduction the signs and symptoms of the second week may be considered in slightly more detail.

During this week the patient, who may have been up and about, is generally confined to bed, and may be seen for the first time by the physician. The facies is dull, apathetic, and listless; the reaction time is prolonged for answering questions; the hearing may be diminished; and the patient is drowsy. At night there may be sleeplessness and mild delirium. There may be slight subsultus tendinum. The decubitus is dorsal. The temperature continues high, varying from about 102° to 105° F., while the pulse is generally relatively slow (90 to 100 beats per minute), although it may reach to 120. The dicrotism may have disappeared, but the blood-pressure has generally diminished somewhat, and the first sound of the heart is not as appreciable as normal. The circulation is as a rule not good; the extremities are apt to be cool, or even cold; and the hands and feet, or more usually the tips of the fingers and toes, may be of a bluish colour. The nails often show signs of lack of vitality, and transverse ridges may be observed. Philipowicz's sign may disappear, or may persist through the week, and even later. The typical rose-red or pink maculo-papules appear in successive crops on the front of the abdomen or chest, beginning about the seventh to twelfth days, though in exceptional cases they may occur as early as the fifth day, or they may be delayed as late as the twentieth day, while they may be entirely absent. Their number and presence depends upon some unknown secondary cause and not upon the severity of the attack, to which they bear no reference. They are pinkish or rose-red, circular, slightly elevated, isolated maculo-papules about 4 millimetres in diameter, usually few in number, which disappear temporarily on pressure, but reappear as soon as the pressure is removed. They usually last three to five days, more rarely as long as ten days, and as a rule undergo no change until they fade and disappear, leaving occasionally a brownish stain. They are not associated with any subcuticular mottling, and are but rarely met with on the face, though they may at times be found on the arms and legs. They continue to appear until the end

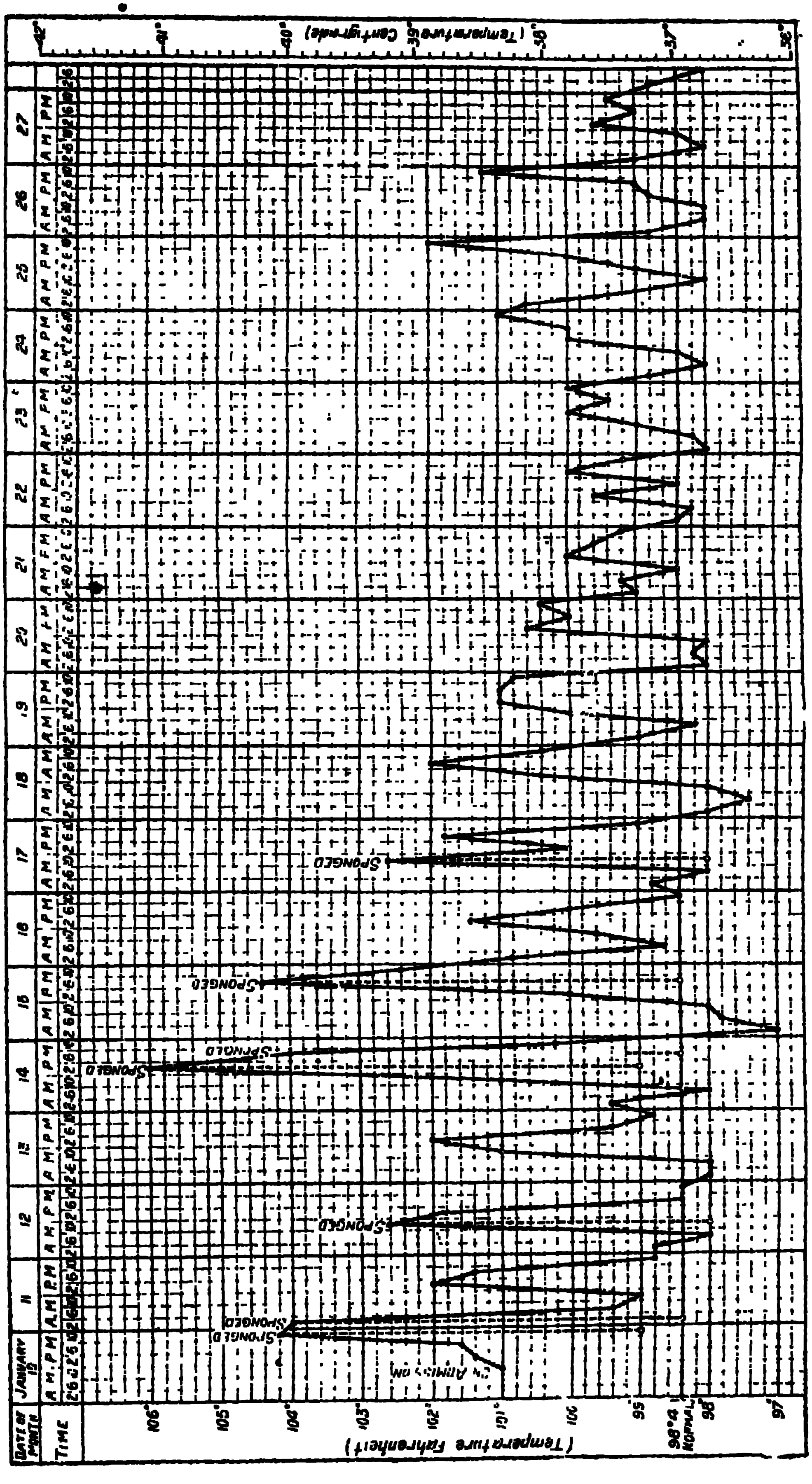

Fig. 659a.—Temperature Chart of the Intermittent Type of Enteric Fever.

of the second week, during the third week, or even during convalescence.

The lips and tongue at the commencement of the second week are in much the same condition as at the end of the first week, and if the attack is of mild or medium virulence, they may remain in this condition during the whole week: but if the attack is severe, and if the patient passes into the typhoid state, they alter in appearance; for in this condition the patient lies on his back, breathing through the partially open mouth, with the lips and teeth covered with the dark brown scabs, formed from epithelial débris, micro-organisms, and food, which are called 'sordes.' The tongue becomes dry, and is covered with a brown or brownish-black fur or crust, and may have painful cracks: but this condition is largely due to oral sepsis, and is not part of the disease, and may be more or less avoided by careful nursing and oral antisepsis. The pharynx is generally more or less inflamed, and may be ulcerated, as may the tonsils. Gastric disturbance, if present in the first week, is not continued into the second week as a rule, and it is rare to observe vomiting in this week unless there is some complication. There may be constipation or there may be diarrhœa, and the motions are often of a yellowish colour, with alkaline reaction and somewhat offensive odour, and may contain sloughs, which will be recognized as greyish-yellow fragments of tissue about an inch in length.

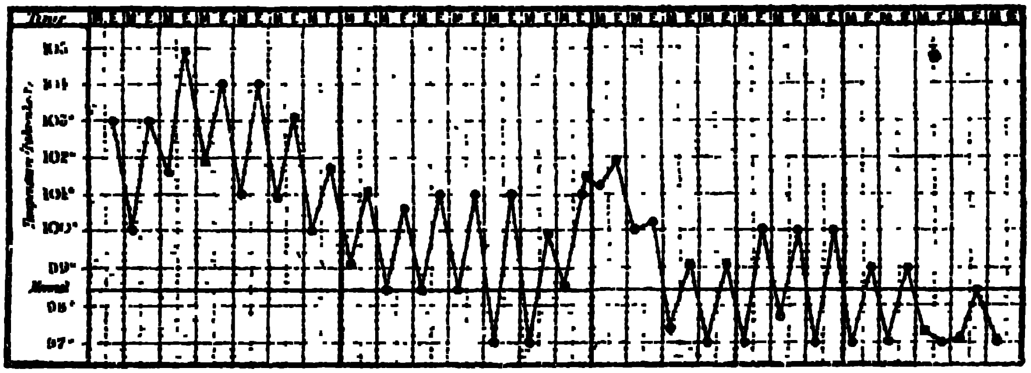

FIG. 659B.—TEMPERATURE CHART OF A CASE OF PARATYPHOID A FEVER.
(Chart made by Major Archibald.)

Hæmorrhage is said to occur in about 10 per cent. of cases, but our experience would indicate that it is more frequent than this. It varies from a mere trace to a serious haemorrhage, and most usually occurs from the end of the second to the end of the third week—that is to say, during the period of separation of the sloughs.

Often there are little or no signs or symptoms to mark a slight hæmorrhage, but a profuse hæmorrhage produces serious symptoms. Often a hæmorrhage takes place without warning, but as it is known to be possible, the attendants will be on the outlook for signs; and our experience is that there often is warning given by the presence of a trace of blood in the motions, by the slight increase of the pulse-rate, or by a slight drop in the temperature. In sudden severe cases of hæmorrhage the facies alters, becoming pinched and pallid; the pulse increases in frequency, and the temperature drops perhaps quite suddenly. In very severe cases a sudden fatal collapse may take place before any sign of blood has been visible in the motions.

More or less meteorism is always present during this week, and at times this becomes a great trouble to the patient, and very rarely may reach to such a degree that it embarrasses the heart's action. It is dangerous in that it favours perforation, which may occur in this week, but is more commonly met with in the third week, under which heading it will be described.

Usually the spleen is distinctly enlarged during this week, and the blood shows an anæmia due to the reduction of red blood cells, while the hæmoglobin and the leucocytes are also reduced. The leucopenia is due to a reduction of the polymorphonuclear leucocytes and eosinophiles, while the mononuclear leucocytes are usually increased in numbers. The presence of a marked leucocytosis would indicate the occurrence of some complication. The coagulability of the blood is reduced.

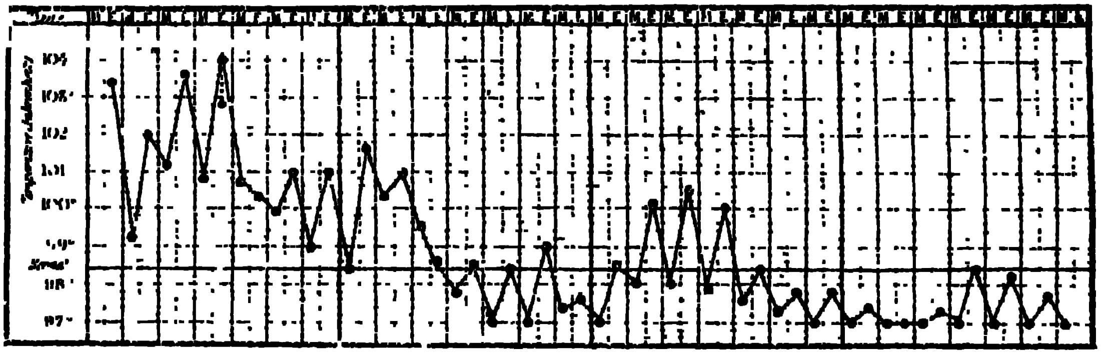

Fig. 650c.—Temperature Chart of a Case of Paratyphoid B Fever.
(Chart made by Major Archibald.)

Pain and tenderness may occur in the right hypochondrium over the area of the gall-bladder, and is often due to a slight attack of cholecystitis, which may also be indicated by slight enlargement of the liver, slight jaundice, and rigidity of the abdominal muscles.

The lungs should be carefully watched during this period, as lobar pneumonia may occur, and as the symptoms are not marked, and rusty sputum is rare, it may be overlooked.

Rarer symptoms during this week are local neuritis, tetany, eye troubles, and ear complications; but muscular cramp is by no means rare, and may cause great inconvenience to the patient.

The urine is febrile, and may contain albumen. The diazo-reaction may appear before the rash, or may be deferred as late as the end of the third week. Bacilluria is found in about one-third of the cases, while urobilin and indicanuria are also fairly frequently met with. Acetone and diacetic acid occur, but may be due to the starvation. In mild cases the patient may show marked improvement during this week, and the temperature may decline gradually, and reach normal about the fourteenth day. This, however, is rare, and usually the temperature keeps high during the whole week, and the patient enters the third week with all the signs and symptoms of the fully developed attack.

The Third Week. During the third week the temperature may gradually fall to normal about the twenty-first day in typical cases, and with this the various symptoms may subside and convalescence begin. In moderately severe cases all the symptoms described in the second week may continue, but the fever may be less, and may gradually remit towards the end of the week. In the severer cases the fever continues, and the patient passes into a condition commonly called the 'status typhosus.' This is the week in which there is a great danger of hæmorrhage and perforation of the intestine.

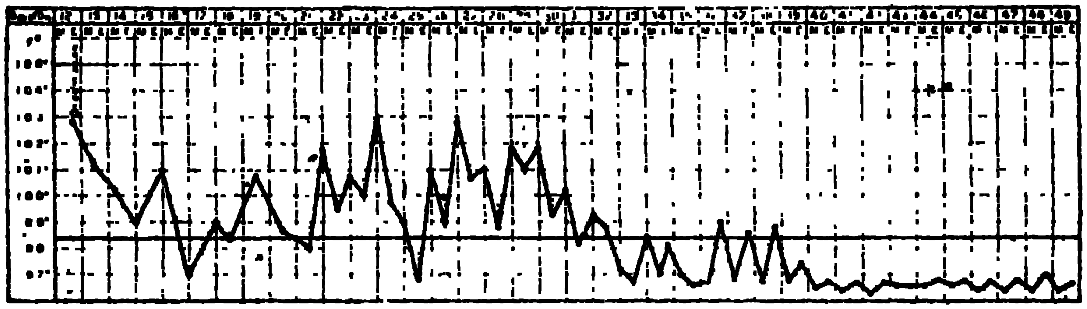

FIG. 660.—TEMPERATURE CHART OF A DOUBLE INFECTION OF TYPHOID AND PARATYPHOID B FEVERS

In the severe cases the temperature remains high; the pulse becomes quick; the tongue, teeth, and lips become covered with sordes; the diarrhœa and abdominal distension become worse; and the toxæmia produces delirium, at first mainly at night, but later more or less continuously; or the patient may develop a quiet state of delirium, lying quietly in the bed with the eyes open and staring, and quite unconscious of the surroundings. The muscles are markedly irritable, and show fibrillar contractions, tremblings, and twitchings, with or without subsultus tendinum. Emaciation now progresses, and the anæmia is more marked. This is the time for the pharyngo-typhoid ulcer to appear, and tympanites develops.

The great danger of the third week is perforation, which is said to occur in about 3 per cent. of cases. It may take place in the mildest of cases, and we have seen it in one in which only two small ulcers could be found at the post-mortem examination, so that no case can be said to be free from this danger.

The symptoms are often sudden, severe, stabbing pain in some part of the abdomen, and often referred to the region of the right iliac fossa, but may also be referred to the left iliac fossa. This sharp pain disappears, but is replaced by a more general pain all over the abdomen, which may be persistent or intermittent. At times this general pain may be absent. Sometimes, but by no means always, there is vomiting. Usually there is more or less collapse, as indicated by the pinched features and the quick, small, thready pulse. The temperature generally falls, but quickly rises again; the abdomen becomes distended: the liver dulness is encroached upon by the tympanites, and the breathing becomes thoracic; while the urine may be suppressed. The prostration increases, and the patient may gradually sink and die. In other cases peritonitis may intervene before death. A small perforation may not present the above typical symptoms, and may be only suspected at first by the fall of temperature and the rise of the pulse-rate.

The Fourth Week.—In typical cases the temperature has fallen to normal by the commencement of this week, and the tongue has begun to clean and all the symptoms abate and gradually disappear, and convalescence begins. Now comes the danger of a relapse, as towards the end of this week the patient begins to get hungry.

In severe cases the symptoms may continue unabated, and complications may occur.

In protracted cases the patient lies in the status typhosus with a high temperature, passing urine and fæces involuntarily, and may die from cardiac failure, from perforation, or some other complication.

The Fifth and Sixth Weeks.—These should be weeks of convalescence, but at any time a relapse may take place, while complications and sequelæ may occur.

Varieties.—The various types of typhoid fever may be classified in the following sequence: Ambulatory, abortive, mild, typical, severe, and the masked.

The ambulatory is typically presented by a person who feels ill for some days or weeks, but goes about his usual work, feeling exceedingly wretched, until, perhaps, someone, noticing how ill he looks, may take his temperature, and perhaps find it over 104° F.; thereupon the patient seeks advice for the first time, and may be well into the second or even third week of the disease. More rarely a patient may go through the whole attack without medical assistance. Often, however, the illness may begin with the ambulatory variety and end with an exceedingly severe attack.

The mild, the typical, and the severe, have been included in our general or typical account given above, and these are estimated to be about two-thirds of all cases of enteric fever.

The masked type of fever is that in which one special group of symptoms is pronounced, as, for example, the nervous, with the severe headaches, neuralgias, early delirium, and other marked mental symptoms—*e.g.*, mania or the signs of meningitis. Another example is that in which the pulmonary symptoms are specially marked—*e.g.*, the early bronchitis or the pneumonia. Other examples are the severe gastro-intestinal symptoms, imitating poisoning, or the signs of an acute nephritis. Lastly, the type in which hæmorrhages begin early and are persistent is often spoken of as the hæmorrhagic type.

One curious form may be just mentioned, as, for example, the spleno-typhoid, in which the spleen is very markedly enlarged, without signs of malaria or relapsing fever.

Complications and Sequelæ.—The most important complication is malaria, but dengue and certain unclassified fevers of intestinal origin are occasionally met with during the first week, and complicate the diagnosis. Bedsores and boils are not infrequent complications, and loss of hair is a frequent sequel. Venous thrombosis in the femoral vein is a frequent complication, and infarction may occur in various organs. Arterial thrombosis is much rarer. Acute ascending myelitis is noted, while joints may be attacked, giving rise to a typhoidal arthritis, and the spine to a typhoidal spondylitis. Periostitis of various bones is not rare. Inflammation of the thyroid gland may also occur. Hæmorrhage and perforation have been noted. Iritis, orbital cellulitis, and purulent choroiditis have been recorded as due to typhoid fever, but purulent otitis media and mastoiditis, described as associated with typhoid fever, are generally due to other causes than the typhoid bacilli. Appendicitis and meningitis may also occur.

Relapse.—One of the most important sequels to an attack of enteric fever is the relapse which may occur at any time during the three or four weeks following the fall of temperature to normal. It usually resembles an ordinary attack of typhoid fever.

Diagnosis.—The diagnosis of enteric in typical cases is not difficult, being based principally on the slow onset of the fever, the enlargement of the spleen, the presence of roseola at the beginning of the second week, the apathetic appearance of the patient, the leucopenia. Every medical man, however, practising in the tropics has noticed that enteric fever there, much more frequently than in temperate climates, presents an atypical course. The temperature chart may be very irregular, sometimes of a well-marked remittent or intermittent type (Fig. 659); the enlargement of the spleen may be absent during the whole course of the disease, or in other cases it may be much more enlarged and harder than is usually the case; roseola, invisible, of course, in natives, may be absent in Europeans, while at times these may present a profuse rash. In a few cases some of the peculiarities met with, especially the very irregular type of temperature, are explained by the presence of two infections—typhoid and malaria. Individuals who have had an attack of malaria may harbour in their spleen Laveran's parasites for a long time without any symptoms, but as soon as the resistance of the organism is diminished by any cause like a chill, a disorder in dietetics, or the onset of some disease, an attack of malarial fever ensues. When these malarial carriers develop enteric, the malarial infection breaks out again, and probably modifies the course of the temperature. It must be admitted, however, that in the largest number of cases no such explanation can be found. As regards a clinical differentiation of the three varieties of enteric—typhoid, para B, para A—this is impossible, at least in

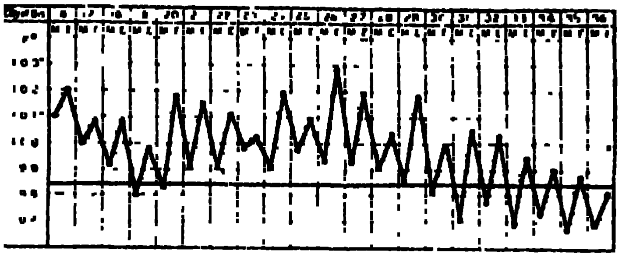

Fig. 1.—Temperature Chart of a Triple Infection of Typhoid, Paratyphoid A and B Fevers.

the tropics. With these clinical difficulties the bacteriological diagnosis of enteric fever acquires in the tropics even more importance than in temperate climates.

The bacteriological diagnosis of enteric is based on the following methods:—

1. Agglutination test.
2. Hæmocultures.
3. Search for the enteric bacilli (*B. typhosus*, *B. paratyphosus A*, *B. paratyphosus B*) in stools and urine.
4. Splenic puncture.
5. Ophthalmo-reaction and cuti-reaction.
6. Subcutaneous inoculations of dead cultures and Vincent's splenic diagnosis.
7. Complement fixation, etc.

The first two processes are really the only ones of practical importance, but a few words may be said also on some of the others.

Agglutination Test (Widal Reaction). This test is based on the work of Grüber, Durham, Widal, and Grünbaum. Either the microscopical or the macroscopic method may be used. The simplest way to perform the microscopical test is to place on a slide 19 loopfuls of broth and 1 of blood, and mix the whole gently together. A loopful of this dilution is then mixed with a loopful of a young typhoid broth culture, a hanging-drop made, and the preparation examined microscopically for agglutination after one hour. The technical details may be found in any textbook on bacteriology. It suffices here to say that the blood should be sufficiently diluted—at least 1 in 40—and the agglutination should be first tried, using the typhoid bacillus, and if this is negative, the paratyphoid A and the paratyphoid B bacilli. If the medical man in attendance cannot perform the test himself, he should send the blood to a bacteriological institute. The sample of blood is obtained by pricking the finger and collecting a few drops of blood in a capillary tube. After closing both ends in the flame, the tube is packed in cotton-wool, and despatched to the bacteriological institute.

Macroscopic tests (sedimentation test) are also in use, and various forms of apparatus (agglutinometers) can be obtained, which enable the general practitioner to carry out the test himself without using a microscope. A convenient rapid method is Alcock's, the blood being diluted very little and examined after only a few minutes. Dreyer's method, using specially standardized emulsions, is useful, as this method renders much easier the making of agglutination curves, which are of great practical importance in the diagnosis of enteric in inoculated individuals. Technical details may be found in any modern textbook on bacteriology.

In the tropics, even at the present time, one is apt to be asked what value is to be placed on the result of the agglutination reaction. Some medical practitioners are inclined to be sceptical, while others tend to base their diagnosis solely on the result of the test. We would emphasize the fact that in enteric fever, as in any other bacterial disease, in order to come to a definite diagnosis the results of the clinical examination and those of the laboratory must not be dissociated.

The practitioner should give his attention to the following points:—

Reaction Negative.—(1) The reaction is generally absent during the first week of the disease

(2) In some very rare cases—in our experience generally of very malignant type—the test may remain negative during the whole course of the malady.

(3) The reaction with the *B. typhosus*—which in certain tropical laboratories is still the only bacillus of the typhoid group used for the test—is negative in two varieties of enteric fever—paratyphoid A and paratyphoid B.

Reaction Positive.—(1) When the reaction is positive, it should be remembered that the blood may contain specific agglutinins many years after an attack of typhoid is over. In the event of fever in such a case the medical man who would solely rely on the Widal test would easily fall into error.

(2) The reaction is not rarely positive in cases of jaundice, but recent researches have demonstrated the fact that these cases are in reality often due to the colecystitis caused by *B. typhosus*.

(3) The reaction is positive in vaccinated persons for a variable period of time after inoculation.

(4) One must be sure that the test has been carried out with sufficiently diluted blood. A dilution of 1 in 40 is sufficient for ordinary purposes.

HÆMOCULTURES.—Two methods may be used—the so-called 'dilution method,' introduced by Castellani in 1898, and the 'bile-enrichment method,' introduced by Drigalski and Conradi, and modified by many authors. The latter is at the present time to be preferred, being simpler. The former is still of use when a mixed infection is suspected, as, for instance, a typhoid-pneumococcus infection. The pneumococcus and many other germs would grow very badly, or not at all, in bile media.

Castellani's Dilution Method.—The region of the bend of the elbow is cleaned with spirit or ether, then disinfected with perchloride lotion (1 in 1,000), then a little spirit or ether is poured again on the skin, or the region may be simply painted with tincture of iodine. When this has become dry, a few c.c. (2 to 5) of blood, by means of a sterile all-glass syringe, are taken aseptically from a vein of the region, generally the median basilic. The blood is immediately added to several large sterile flasks (at least three), each containing

200 or 300 c.c. of faintly alkaline broth. A dilution of about 1 in 100 to 1 in 200 is generally sufficient. The flasks are incubated at 37° C. Generally, after twelve to twenty-four hours in positive cases, the broth becomes cloudy, and shows a growth of the germ.

The germ, of course, must be further identified in the usual way by cultivation in milk, various sugar broths, and by the agglutination test. The method gives satisfactory results, the *B. typhosus* having been found by Schottmuller, Auerbach, Widal, Pinot, Vegrès, and others, in a percentage varying from 70 to 100 per cent. The novelty of the method is the dilution of the blood in a very large amount of broth instead of employing the usual small quantities of the medium. This simple innovation makes all the difference in the result. With the old methods the majority of observers failed to detect the germ. These satisfactory results are probably due to the fact that the blood being greatly diluted, the agglutinins are also diluted, and any bactericidal properties of the blood serum greatly weakened.

Gildemeister recommends dilution in sterile water, while Cummins and Cumming consider a solution of 0·5 per cent. taurocholate of soda to be a very efficient medium.

Drigalski and Conradi's Bile-Enrichment Method.- We use the following modification: 2 to 5 c.c. of blood are withdrawn from a vein by means of a sterile syringe (see above), or if a vein puncture is objected to, a deep prick is made in a finger, and the blood collected and dropped in Coleman and Buxton's glycerine-ox-bile medium, which consists of ox-bile 90 c.c., glycerine 10 c.c., peptone 2 grammes, distributed in small flasks, each containing 20 c.c. of the medium. If the blood is taken in the evening the percentage of positive results seems to be larger.

OPHTHALMO-DIAGNOSIS. -Chantemesse has introduced a method of diagnosis similar to the ophthalmo-diagnosis of tuberculosis. An extract of typhoid bacilli, specially prepared, is used. A drop is instilled into the conjunctival sac; after two to three hours, if the case is typhoid, the conjunctiva becomes very red, and the inflammation persists for two or three days.

CUTI-REACTION. Attempts have been made by several authors to evolve a method of cuti-reaction for enteric in analogy to that which has been done in tuberculosis. The results have not been very satisfactory.

SILVESTRINI'S TEST. -A small amount of broth typhoid culture killed by heat is injected subcutaneously. If the case is typhoid, this procedure induces a sharp rise of the temperature for a day or two.

COMPLEMENT FIXATION.- -A complement fixation test has been worked out for typhoid, para A and para B, by several authors, but its use has not become general.

VINCENT'S SPLENO-REACTION.- Vincent has noticed that in many cases after the subcutaneous injection of dead vaccine the spleen becomes temporarily distinctly larger. The reaction is specific viz., a patient suffering from typhoid shows an enlargement of the spleen if he is injected with typhoid vaccine, but not if injected with paratyphoid A or paratyphoid B vaccines.

SPLEEN PUNCTURE.- The point of maximum spleen dulness is found, the skin is disinfected by painting with tincture of iodine, and the puncture made by using a sterile syringe supplied with a long, strong needle. A few drops of splenic blood and juice are obtained with facility, and should be immediately sown in bile-glycerine medium. The method gives good results, but is not advised as a routine procedure.

Bacteriological Examination of Stools for B. typhosus and Paratyphosus A and B.—A small portion of the stool recently passed and collected into a sterile vessel is smeared on several large MacConkey's agar plates. These are incubated for twenty-four to forty-eight hours at 35° to 37° C., and then any suspicious white colonies further investigated. As is well known, on MacConkey's medium the colonies of coli like bacteria are red, while those of the typhoid and dysentery group appear whitish. Instead of MacConkey's agar, the Drigalski medium may be used, or Holt-Harris and Teague's methylene blue-eosin medium, the inoculation of which may be done from a growth of the fæces in Douglas' peptone-free broth.

Castellani's Contemporaneous Gas-Agglutination Test.—Twenty tubes of salicin (or raffinose) peptone water, each containing a small fermentation tube, are used, and to each tube 1-2 drops of trivalent typhoid and para A and para B agglutinating serum are added, or 1 drop of each monoserum may be added instead of the trivalent one. Each tube is inoculated from one of the lactose non-fermenting white colonies present on the MacConkey plates made from the suspected fæcal matter. The tubes are placed in the incubator at 35°-37° C. for twelve to twenty-four hours and then examined. All tubes showing diffuse turbidity or gas, or both, are discarded. If one (or several) of the tubes shows agglutinated growth as well as absence of gas a diagnosis of enteric may be made, at once, for practical purposes.

If the search is limited only to typhoid and not para A or para B, it is better to use glucose-peptone-water tubes slightly tinged with litmus, to which 1-2 drops of typhoid agglutinating monoserum have been added. If one of the tubes (or several) shows agglutination and absence of gas while the medium has taken a reddish colour (acidity), the diagnosis of typhoid may be made.

Castellani's Poliserum Method. This is an application of Castellani's general method to isolate a bacterium from a mixture of other bacteria by using a multivalent serum which will agglutinate and delay the growth of all or most of the bacteria present, while it does not influence the growth of the germ or group of germs one desires to isolate. Great difficulty, however, is found in practice in preparing such a serum, the best method of preparation being that of mixing several plurivalent sera. The poliserum method may be carried out in various ways. Two may be mentioned:—

1. (*a*) Inoculate with the fæcal matter to be investigated several tubes of taurocholate of soda peptone water, or Browning, Gilmore, and Mackie's telluric acid peptone water may be used.

(*b*) Immediately after, or better immediately before, the inoculation, add 3 drops polyvalent lactose-fermenting intestinal-bacteria serum, 3 drops polyvalent non-lactose fermenting fæcal bacteria serum (*B. proteus* group, etc.), taking care to use serums containing only a very small amount of typhoid coagglutinin; or serums can be used from which the typhoid coagglutinin has been removed by absorption

(*c*) Incubate for twelve or twenty-four hours, then make plates on MacConkey, Conradi Drigalski, or similar media, from the most superficial portion of the liquid medium, and investigate further any suspicious colonies which may develop, testing them with typhoid, paratyphoid A, and paratyphoid B serums, etc. When there are many flocculi of agglutinated bacilli also in the upper portion of the tube, these may be got rid of by a short centrifugation. A short centrifugation with an ordinary electric centrifuge will cause the agglutinated bacilli to fall to the bottom, while it has practically no effect on the non-agglutinated germs in young cultures.

2. Instead of inoculating the suspected fæcal matter direct in taurocholate peptone water and poliserum, the stool is plated on MacConkey's medium. After fifteen to twenty-four hours' incubation at 35°-37° C. all the white colonies (lactose non-fermenters) are inoculated in a tube of peptone water, to which has been added 2-3 drops of the poliserum for lactose non-fermenters apart from enteric group. After fifteen to twenty-four hours' incubation the growth from the top of the tube is further investigated.

Bacteriological Examination of Urine.—The urine should be collected aseptically. In women a catheter should be used. In males this is not necessary. It is sufficient, after purifying the glans and meatus first with a disinfecting lotion, and then with boiled water, to make the patient pass his urine. Any germs of the anterior portion of the urethra will probably pass with the first portion of urine, which is thrown away, while the last portion is collected into a sterile vessel, and immediately sown in tubes containing Coleman and Buxton's bile-glycerine medium. These are incubated at 35° to 37° C. for twenty-four to thirty-six hours, and then the further bacteriological investigation is carried out in the usual manner by making plates, etc.

Diazo-Reaction.—A chemical laboratory test often used is Ehrlich's diazo-reaction, which, however, is positive in several other febrile conditions.

Marris's Atropine Test.—Marris found out that the injection of $\frac{1}{33}$ grain of atropine sulphate in fevers of the enteric group hardly accelerated the pulse-rate, while in patients suffering from other diseases such an injection will increase the rate of the heart by some twenty to forty beats per minute in the same manner as in normal individuals.

Marris's technique is as follows:—The patient should lie horizontally, perfectly quiet, and the test should be carried out at least one hour after meals. The pulse-rate is taken and recorded minute by minute until found to be steady. This usually takes ten minutes. An injection of $\frac{1}{33}$ grain of atropine sulphate is then given in the deltoid region. The patient remains absolutely quiet, and after twenty-five minutes the pulse-rate is taken and recorded minute by minute. An increase of the pulse-rate by about twenty or more per minute indicates that the patient is not suffering from enteric. If the increase in the pulse-rate is only ten beats or less, the reaction is suggestive of enteric.

Diagnosis of Enteric in Inoculated Persons.—The diagnosis of enteric in inoculated persons may be very difficult, the symptoms being often most atypical. Moreover, the commonest laboratory test—agglutination—is of little use unless carried out according to certain methods.

It is well known that in individuals inoculated with the triple vaccine typhoid and para A and para B, specific agglutinins develop for the three germs, as was shown by one of us long ago. The maximum agglutination titre is reached two to three weeks after the first inoculation, then the titre falls at first—for a few weeks—rapidly, but later on in an extremely slow, gradual manner, so slow as to remain practically constant for months and years. After two months from inoculation only very exceptionally one finds an agglutination limit greater than 1 in 320 for *B. typhosus* and *B. paratyphosus B*, and for *B. paratyphosus A* greater than 1 in 180. Therefore, in a person inoculated longer than two months, if the agglutination limit is higher than 1 in 300 for *B. typhosus* or *para B*, or more than 1 in 180 for *B. para A*, and there is fever, a provisional diagnosis of enteric may be made. It is always advisable, however, as emphasized especially by Dreyer, Walker, and Gibbon, to take the agglutination titre at intervals of three to five days several times during the course of the suspected fever and make an agglutination curve for *B. typhosus*, *B. paratyphosus B*, and *B. paratyphosus A*.

If the agglutination for *B. typhosus* exhibits a regular rise, with a maximum of even 100 per cent. in the third or fourth week from onset of fever, and then a subsequent regular fall, as seen in non-inoculated subjects, but starting from and returning towards the higher base line of inoculated persons, while there is little or no rise in the agglutination titre for *B. paratyphosus B* or *A*, a diagnosis of typhoid fever may be suggested with great probability.

If there is a regular rise and subsequent fall in the agglutination for *B. paratyphosus B*, while the agglutination titres for *B. typhosus* and *B. paratyphosus A* show only a slight or no increase, the diagnosis of paratyphoid B may be suggested.

If there is a regular rise and later fall in the agglutination titre for *B. paratyphosus A*, while the titre for *B. typhosus* and *B. paratyphosus B* is only slightly raised or not at all, a diagnosis of paratyphoid A fever may be made with a certain degree of probability.

If there is a very distinct rise in the agglutination for all three germs or any one of them, there is the possibility of the patient suffering from one of the three fevers with non-specific agglutinins for one or both the germs producing the other two, or there is the possibility of the patient suffering from a mixed infection. In the first case the agglutination curves are generally synchronous, and the germ for which the agglutination is highest is often the infective germ.

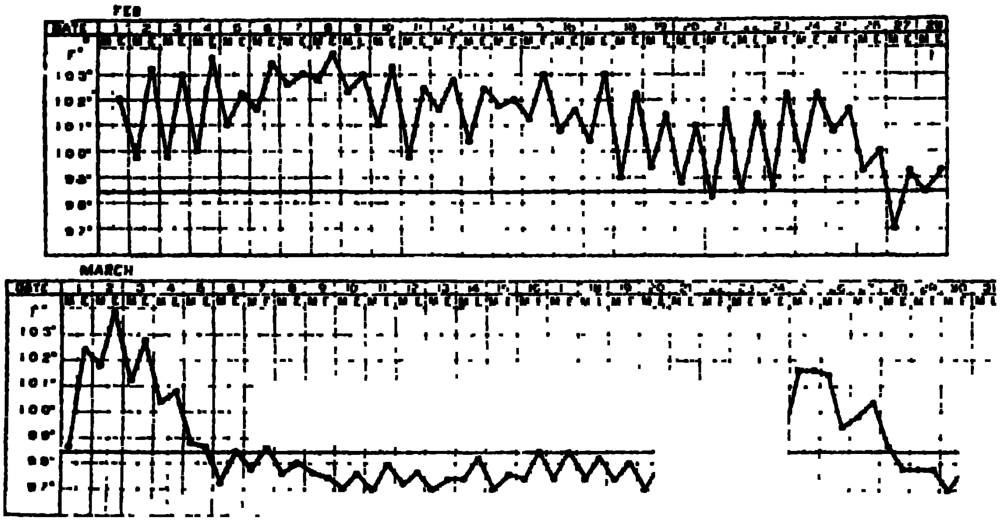

Fig. 662.—Temperature Chart of a Triple Infection: Typhoid and Paratyphoid A and B Fever.

In *mixed infections*, whether in inoculated or non-inoculated subjects, the agglutination curves for the various infecting germs are as a rule not synchronous, and follow their ordinary course independently of each other.

To carry out the above tests it is necessary to have recourse to an accurate quantitative method, and we recommend for the purpose Dreyer's standard agglutination method, using standard agglutinable emulsions. Details will be found in any modern manual of bacteriology, such as Hewlett's seventh edition.

Of course, in inoculated persons the search for the infecting organisms in the blood, stools, and urine, as already described, is even of greater importance than in non-inoculated individuals. Marris's atropine test may also at times help the diagnosis of enteric in inoculated people, the test apparently not being affected by previous vaccination.

Differential Diagnosis.—The term 'enteric fever,' as already stated, is used to cover three infections—typhoid fever, paratyphoid fever A, and paratyphoid fever B, which clinically, at least in the tropics, cannot be distinguished from one another, except by bacteriological methods. Enteric fever imitates many diseases, and many diseases resemble enteric fever, and this renders the differential diagnosis complicated and difficult. Of the many fevers which may possibly be mistaken for some usual or unusual attack of enteric fever, we have chosen the following for differential diagnosis—viz., malaria, the relapsing fevers, dengue, undulant fever, plague, yellow fever, typhus, influenza, trichiniasis, acute miliary tuberculosis, appendicitis, pneumonia, rat-bite disease, psittacosis, parenteric fevers, ulcerative endocarditis, and pyæmia.

Malaria.—Intermittent fevers are hardly likely to be confused with enteric fever, but remittent fevers are liable to cause difficulty, and may be recognized by the presence of the parasites in the peripheral blood, by the presence of pigment in the leucocytes, by the enlargement of the spleen, and the reaction to quinine. Moreover, the attack of fever is usually sudden, the temperature quickly rising to 105° F., while the pulse is, as a rule, not dicrotic, and if the fever has lasted a few days, there is generally some sign of anæmia. It must, however, be remembered that malaria is a not infrequent complication of the first week of an attack of enteric fever in the tropics, as malarial carriers are very apt to develop this fever when commencing an attack of enteric fever.

Relapsing Fevers.—In these fevers the onset is sudden, and characterized by chills and severe pains in some region of the body, while a careful examination of the blood in a first attack should reveal the spirochætes.

Dengue.—Dengue begins suddenly with often severe pain in some part of the body, and often congestion of the conjunctiva, and perhaps a sensation of chilliness. It must not be forgotten that typical cases of dengue fever sometimes develop enteric fever.

Undulant Fever.—This disease may very closely resemble enteric fever, and during the first week can only be definitely recognized in a locality in which both diseases occur by cultivation of the specific germ from the blood, while later sweating and the undulating type of fever, together with the articular symptoms, are characteristic.

Plague.—The ordinary severe type of plague may be recognized by the sudden onset, the severity of the symptoms, the mental dulness, and the full development of the typical symptoms and bubo in a few hours.

The milder forms of plague are more difficult to recognize, because there is little fever; but the enlargement of a group of lymphatic glands will arouse suspicion as to the true nature of the disease.

Plague pneumonia may be distinguished from the pneumonic form of enteric fever by an examination of the sputum.

Yellow Fever.—Mistakes are most apt to occur at the commencement of a yellow-fever outbreak before the disease is recognized. The diagnosis may be effected by the rapid onset of the fever, the tenderness in the region of the pylorus, and by the albuminuria which is often present on the first day, and later by the vomit. But in such an important point as the diagnosis between yellow fever and typhoid fever, bacteriological examination of the blood and motions should not be neglected.

Typhus.—This fever may be distinguished by its sudden onset, and by the early appearance of mental symptoms, and especially by the early appearance of delirium and coma, while the macular petechial eruption appearing on the fourth day materially assists the diagnosis. Brill's disease is merely a mild form of typhus, and may be differentiated by the appearance on the fifth or sixth day of a maculo-papular eruption, which does not disappear on pressure, and does not appear in crops.

Influenza.—The diagnosis between influenza and enteric fever can be made by the presence of catarrhal symptoms in the former.

Trichiniasis.—The presence of œdema of the eyelids, together with swelling and painful tension of the muscles, associated with dyspnœa, are in favour of trichiniasis. The blood should be examined for any signs of eosinophilia, while the worms may be discovered in the motions.

Acute Miliary Tuberculosis.—The differential diagnosis here is very difficult, and is complicated by the fact that the two diseases may occur together. The fever in acute miliary tuberculosis is irregular, and the pulse and respiration are rapid, and there is embarrassment of the breathing, often leading to cyanosis; but the diagnosis is very difficult, and may have to depend entirely upon bacteriological research.

Appendicitis.—In appendicitis the onset is usually abrupt, and the pain in the right iliac fossa is distinctive, but there are cases which closely resemble enteric; and it must be remembered that the typhoid bacillus can cause appendicitis.

Pneumonia.—Enteric fever may, though very rarely, begin with a typical attack of pneumonia, when the specific organisms may be found in the sputum; otherwise, a diagnosis must be made by the examination of the blood, or later clinically, when the more typical symptoms of enteric arise in the second week.

Rat-Bite Disease.—This may be recognized by the history, by the blotchy, measly eruption, and by the fact that the fever ends for the first time after a few days, only to reappear again later.

Psittacosis.—This enteric-like fever may be suspected by the history of there having been sick parrots in the house in which the patient has been residing, and this can be confirmed by the isolation of the specific bacilli from the blood.

Parenteric Fevers.—These can only be diagnosed by the bacteriological examination of the blood and fæces.

Ulcerative Endocarditis.—Usually in this complaint there are recurring chills, irregular fever, substernal pains, and endocardial murmurs, while bacteriological examination of the blood may not merely differentiate it from enteric fever, but may indicate the germ which is causing the endocarditis.

Pyæmia.—In the first week this may be difficult, and depend upon the bacteriological examination, but the usually intermittent fever, the prostration, and the sweats, may give rise to suspicion. The marked leucocytosis may also arouse suspicion.

Weil's Disease.—This may be recognized by the early onset of jaundice.

Diagnosis of Mixed Infections.—As already stated, mixed infections, especially typhoid and malaria, typhoid and paratyphoid, typhoid or paratyphoid and coli-like germs, are not rare. In the typho-malarial-infection cases the microscopical examination of the blood will reveal Laveran's parasites. As regards the diagnosis of the second group of mixed infections—viz., typhoid + paratyphoid, or typhoid + coli infections—the diagnosis is based on:—

1. Hæmocultures.
2. Castellani's absorption test.

The technique for hæmocultures has already been given. We may here remind our readers that the finding in the blood of some other organism besides the *B. typhosus* does not mean always that the case is a real mixed infection. The organism found may play only a saprophytic rôle, especially if the blood does not contain *specific* agglutinins for the germ.

Castellani's Absorption Test.—The usual agglutination tests are not, as a rule, sufficient to make a diagnosis of mixed infection, because coagglutination does not always mean multiple infection. If the blood of a typhoid patient agglutinates the *B. paratyphosus,* besides the *B. typhosus,* one is not justified in coming to the diagnosis of a mixed infection brought about by the *B. typhosus* and the *B. paratyphosus B,* because it is well known that the blood of a typhoid patient may contain, besides the specific, primary or homologous agglutinins for the typhoid bacillus, secondary or non-specific or heterologous agglutinins for *B. paratyphosus B* and many other bacilli, such as many strains of coli. This has been demonstrated by many authors. Grüber and Durham, as long ago as 1896, demonstrated that the typhoid sera may agglutinate Gaertner bacilli. Zupnik and Poser later found out that 89 per cent. of typhoid sera reacted with paratyphoid B, and 40 per cent. with paratyphoid A.

Boycott, who has made a very complete investigation of the subject, has noted that 59 per cent. of typhoid sera present coagglutinations; 55 per cent. reacted with Gaertner, or Brion and Kayser; 41 per cent. with Schottmüller B; 33 per cent. with Aertrycke; and 12 per cent. with Schottmüller A.

The greater the quantity of typhoid agglutinin, the greater, as a rule, the subsidiary agglutination.

To distinguish between primary and secondary agglutinins, and to facilitate the diagnosis of closely allied organisms and mixed infections, the absorption test, discovered by Castellani in 1902, is useful. This test has been further studied, and the technique improved, by Boycott, Bainbridge, O'Brien, Cummins and Cumming, Alcock, and others. An excellent monograph on the absorption test is the very recent one by Frank E. Taylor.

Castellani found out that in rabbits immunized for typhoid only, whose serum agglutinated besides the typhoid bacillus, also certain 'coli' germs, the saturation with an excess of typhoid bacilli would remove not only the primary (specific, homologous) typhoid agglutinin, but also the secondary (heterologous, non-specific) coli agglutinin; while in a serum derived from rabbits immunized both for typhoid and coli bacilli, neither saturation with typhoid alone nor coli alone, but only both together, simultaneously or successively, would remove the whole of the agglutinins present in the serum.

He experimented with various other germs, and applied the method to the differentiation of closely allied bacilli and mixed infections in man. For practical clinical purposes it may be said that if the blood of a typhoid patient presents, besides agglutination for the *B. typhosus*, also agglutination for, say, *B. paratyphosus B* or *A*, or a coli-like germ, and if this agglutination for the *B. paratyphosus B* or *A*, or coli-like, persists to a great extent after saturation with *B. typhosus*, the case is very probably one of true mixed infection: typhoid + paratyphoid B, or paratyphoid A, or coli-like, as the case may be.

Of course, as with every other biological test, the results obtained cannot be accepted as absolute, but are only of relative value.

To remove the typhoid agglutinin from the typhoid serum, this is diluted, and an excess of typhoid bacilli from young agar cultures added and kept in contact for two hours. The serum is then tested for agglutination for the various germs. A similar technique is used for removing the specific paratyphoid B, paratyphoid A agglutinins, etc.; by adding to the serum an excess of paratyphoid B or paratyphoid A, etc., bacilli. For technical details one should consult books on advanced bacteriology, or Taylor's excellent monograph on the absorption test.

Prognosis.—The typhoid mortality is, in the tropics, about 20 to 25 per cent. for ordinary hospital practice, and rather lower for private practice. The mortality from paratyphoid A and paratyphoid B is lower. Unfavourable symptoms are the early appearance of hæmorrhage, severe nervous symptoms, considerable meteorism, and severe diarrhœa. A bad sign, pointing to a probable relapse, is the temperature falling while the pulse remains rapid.

Severe hæmorrhages are of grave import, as is perforation. Sudden death may occur at any stage of illness and during the convalescence, but is, fortunately, very rare.

Treatment.—The treatment of enteric fever may be divided into:—

A. The treatment during the attack.
B. The treatment during the convalescence.

A. **The Treatment during the Attack.**—This may be subdivided into:—

I. Treatment of a simple uncomplicated case.
II. Treatment of special symptoms.

I. The treatment of a SIMPLE UNCOMPLICATED CASE may be considered under the following headings: (1) General hygiene; (2) nursing; (3) diet; (4) medicines.

1. *General Hygiene.*—A well-ventilated, airy, and well-lighted room should be chosen, and all superfluous furniture, hangings, belongings, etc., removed, except such few things as may be desirable to render the general appearance cheerful. Special attention should be paid to the bed, because the patient is to remain in bed for about one month after reaching a permanently normal temperature. The bed should not be too broad or too narrow, and should have a wire-woven mattress, which is part of the bed. Over this a soft horsehair mattress should be placed, and a reserve mattress should be kept handy. Over the horsehair mattress two folds of blankets should be placed, and then the sheet, and in the middle third there should be the draw-sheet, with its waterproof sheeting. The bed should be provided with an easily movable mosquito-net. The whole room should be thoroughly cleansed once a day by means of damp cloths dipped in Jeyes' fluid. All motions and urine should be protected against flies, and, after being inspected by the physician, should be disinfected with Jeyes' fluid or crude carbolic acid, which is allowed time to act before the contents are thrown away. A separate set of feeding appliances should be reserved for the patient, and these should be sterilized after use. All fomites should be soaked in Jeyes' fluid or carbolic lotion for some hours immediately after use and before being washed. A large piece of ice is very useful to keep down the temperature of the room in the tropics.

2. *Nursing.*—The most important feature of the treatment of a case of enteric fever is the nursing. Two nurses, one for the day and one for the night, are absolutely necessary, and their work may be rendered easier, and the patient considerably benefited, especially if he is over the average weight, by the use of a Skeffington lifter, or, failing this, by some simple apparatus based upon the plan of this ingenious lifter. The temperature should be recorded every four hours, and as hæmorrhage is so common in the tropics, both nurses should be warned, and should be instructed to be on the watch for the slightest suspicion of this symptom. Moreover,

they should be instructed how to act when it occurs, in order that there may be no delay. The nurse should also be warned to be careful as to the disinfection of her own hands. Nurses who are to attend enteric fever cases should be selected from among those who have been vaccinated, in order to prevent the possibility of infection; failing this, a course of intestinal disinfection at the end of nursing a case of enteric fever is not without its benefits, as many nurses contract the disease.

The patient should be sponged all over with tepid water twice a day, in the morning and in the evening, and this may be repeated if the temperature rises above 103° F. An excellent plan is to add to the water a little of a lotion of thymol 40 grains, spirits of lavender 2 ounces, rectified spirits of wine 3 ounces, dilute acetic acid 3 ounces, in 16 ounces of rose-water. The patient generally finds this admixture to be most refreshing.

From the first the back should be carefully inspected and dried, and dusted with a powder composed of boric acid, zinc oxide, and starch, or some similar powder. Any irritated region should be bathed with rectified spirits.

The mouth must be carefully attended to, and a mouth-wash of glycothymoline, listerine, or other antiseptic mouth-wash, must be used, while the teeth should be carefully cleaned by the nurse by means of a small stick carrying a little cotton-wool.

The bed-pan or slipper and the urine-bottle must be used throughout the illness and the early part of the convalescence.

When the temperature is high, a *light* ice-bag to the head is useful.

3. *Diet.*—With regard to the diet, the patient should not be unduly starved, but should be given liquid food in small quantities at stated intervals. The best basis for the dietary is good chicken-broth and milk, and special attention should be paid to the fact that the liquid actually given to the patient is chicken-broth, and not some greyish warm water, with yellow fat floating on the surface. To this broth some Plasmon may be added, if desired. With regard to the milk, it should be boiled and diluted in the proportion of 1 to 2 with either soda-water, Perrier-water, lime-water, or barley-water, and attention should be paid as to whether it is properly digested or not by examining the fæces. If it is not digested, it must be replaced by malted milk, zymonized or peptonized milk, or by whey. Junket and weak tea may also be used. The patient should be given plenty of water to drink, either plain or as albumen-water, and it is very soothing to occasionally rinse out the mouth with soda-water. But no very warm or very cold foods or drinks should be given.

4. *Medical Treatment.*—The less medicine given to a person suffering from uncomplicated and mild enteric fever the better for the patient.

Some mild medicine—*e.g.*, an intestinal antiseptic, or quinine in some form—is often given—*e.g.*, the quinine and chlorine made by pouring about 30 minims of strong hydrochloric acid upon 30 grains of chlorate of potash.

and dissolving the chlorine gas so evolved in 12 ounces of water, which constitutes the first bottle, and should be dispensed in a non-actinic bottle with a glass stopper. The second bottle contains quinine bihydrochloride 36 grains, syrup of lemons 1 ounce, also dissolved into 12 ounces of water. One tablespoonful from each bottle is mixed and taken three times a day. A thin slice of orange is sucked after each dose to remove the unpleasant taste. Some authorities prefer giving tincture of iodine 2 to 3 minims in an ounce of water every three to four hours; others prefer β-naphthol 2 to 3 grains mixed with bicarbonate of soda 2 to 3 grains, or eucalyptus oil or cinnamon oil 2 to 3 minims in a suspension.

Constipation must be counteracted by a simple enema or an enema with a little turpentine if there is some tympanites every other day.

After the second week urotropine may be given in 10-grain doses three times daily in order to disinfect the urine and gall-bladder.

Serums and Vaccines.—Serums have not been successful: somewhat better results have been recorded by a number of authorities by the use of vaccines. We do not use the vaccine treatment except in some protracted cases with low fever and fairly good general condition.

Tchikana, Fagiuoli, Micheli, Quarelli, and others, give the enteric vaccines by intravenous injection. Kraus, De Castello, and Lucksh, claim to have had good results in enteric by the intravenous injection of heterologous vaccines, as, for example, a *B. coli* vaccine. Intravenous injections of a peptone solution have also been used.

II. The Treatment of Special Symptoms.—The special symptoms which require treatment may be considered under the following headings:—

1. Tympanites.
2. Hæmorrhages.
3. Perforation.
4. Diarrhœa.
5. Cholecystitis.
6. Hyperpyrexia.
7. Delirium.
8. Cardiac failure.
9. Phlebitis.
10. Bedsores.
11. Abscesses.
12. Bone lesions.

1. *Tympanites.*—Tympanites is to be treated by fomentations, turpentine stupes, by the administration of 15 minims of turpentine every three hours, or 3 to 5 minims of cinnamon oil at the same intervals, or by a hypodermic injection of $\frac{1}{50}$ grain of eserine.

2. *Intestinal Hæmorrhage.*—The nurse should be prepared on the onset of this complication to stop all food and drink except a few sips of cold water, to apply an ice-bag to the abdomen, and to raise the bedclothes on a cradle and to administer either the enema mentioned above or to give a capsule of 3 minims of turpentine, or both. This is of the utmost importance, as then time is not wasted in getting the treatment under way. When the physician is certain that a perforation has not occurred, a hypodermic injection of morphia is very useful, but this should not be given so as to hide the signs of a perforation. The turpentine capsules may be continued three or more times a day, and calcium lactate in 10-grain doses may also be given.

3. *Perforation.*—The only chance is to perform a laparotomy, and deal with the perforation surgically; but this must be done as soon as possible. After the operation the Fowler-Murphy after-treatment should be carried out, and the patient placed as nearly in an upright sitting position as compatible with comfort. This position is maintained for four days. At the same time a continuous administration of salt solution *per rectum* is carried out, and so arranged that the patient obtains 2 to 6 litres per diem for a week, and Wainwright's special apparatus for this purpose may be employed.

4. *Diarrhœa.*—This may be checked by tannalbin, 10 to 20 grains, three times a day, or tannigen in the same dose. A very useful adjunct is an enema containing Dover's powder, 5 grains; tannin, 10 grains; mucilage of gum, 1 ounce; and thin starch solution, 1 ounce. Bismuth preparations should, if possible, be avoided, as they are apt to obscure traces of blood, which may be valuable hints of a possible hæmorrhage.

5. *Cholecystitis.*—This should be treated by urotropine, and when chronic by antityphoidal vaccination, or a surgical treatment may be advisable.

6. *Hyperpyrexia* must be combated by tepid, cool, or even iced sponging, by immersion in baths of a temperature between 75° to 85° F. Antipyretic drugs should not be given.

7. *Delirium.*—Acute mental symptoms require sedatives or relief of intracranial pressure by lumbar puncture.

8. *Cardiac Failure.*—This may require to be combated by hypodermic injections of digitalin or camphor in ether, or by strychnine and by saline injections.

9. *Phlebitis.*—This usually occurs in one of the legs, which must be wrapped in cotton-wool after applying ichthyol in lanoline (2 per cent.).

10. *Bedsores.*—These are usually quite preventable, but great care is necessary to dry and to disinfect the back and to harden the skin with spirit lotion. When the sores have developed they should be disinfected twice daily with hydrogen peroxide, and a xeroform or zinc oxide powder applied. In some cases a protargol ointment (5 per cent.) or a balsam of Peru ointment (1 to 2 per cent.) are useful.

11. *Abscesses.*—Local inflammations should be treated with ice-bags, and when pus has formed incisions must be made.

12. *Bone Lesions.*—A stiff jacket may be necessary to relieve the pain of a typhoid spine, and the osteitis or periostitis may require surgical treatment.

B. **The Treatment of Convalescence.**—This may be subdivided into—(I.) The treatment of a simple case; (II.) the treatment of sequelæ; (III.) the treatment of the acute carrier.

I. THE SIMPLE CASE.—The most important factor is to keep the patient in bed without any change of diet until twenty-one days after the temperature has permanently reached normal, and then to gradually increase and modify the dietary. The patient should not be allowed to sit up or to get out of bed until the temperature has remained normal for about four weeks. In the meanwhile the urotropine treatment should be carried out, and, if possible, a bacteriological examination of the urine and fæces should be made six weeks after the permanent return to a normal temperature.

II. THE TREATMENT OF THE SEQUELÆ.—The phlebitis has been mentioned, and as it is followed by œdema will require a bandage or elastic stocking. Post-typhoidal neuritis requires massage and electricity. Nervous sequelæ are not very uncommon, giving rise to a temporary form of mental weakness, or to types resembling disseminated sclerosis, myelitis, etc.

III. THE TREATMENT OF THE ACUTE CARRIER.— If a patient has become an acute carrier, he should be treated by antityphoid vaccination, as already described, and urotropine should also be administered, for this drug, in addition to its action on the kidney, is excreted during twenty-four hours by the liver cells and by those of the gall-bladder. A dose of 15 grains per diem is said to be sufficient to destroy the *B. typhosus* in a gall-bladder in ten days, but the complete cure of carriers is very difficult, even having recourse to surgical measures.

Prophylaxis.—The essential features in the prophylaxis of enteric fever are a pure water-supply, a good system of drainage, and sewage and dust disposal, a pure food and milk supply, the destruction and prevention of fly-breeding grounds.

Another essential feature is the watering of the streets with antiseptic solutions when there is much dust, and lastly, and by no means least, the search for, discovery, isolation when possible, and treatment of the typhoid carriers.

VACCINATION.—At the present time Castellani's triple vaccination (typhoid, para A and para B) has come into general use. The triple vaccine can be prepared according to various methods: broth cultures killed by heat, carbolic salt solution emulsions, oily emulsions, sensitized vaccines, etc. In a general way, it may be stated that, whatever the method of preparation, the results are satisfactory. We generally use a vaccine consisting of an emulsion of typhoid, para A and para B bacilli in normal salt solution, to which ½ per cent. carbolic acid has been added. The details of preparation may be found in various papers by one of us. Each cubic centimetre contains typhoid 500 millions, para A 250 millions, para B 250 millions. Half a cubic centimetre is inoculated the first time and 1 cubic centimetre a week later. Certain authorities recommend a double dose, 1 c.c. the first time and 2 c.c. the second. The triple vaccine gives a certain amount of immunity for the three varieties of enteric—viz., typhoid, para B, and para A; the immunity for typhoid and para B seems to be more marked than that for para A.

The inoculation of the triple vaccine gives rise to a local and general reaction, which is not more marked than after the old typhoid monovaccine: some infiltration and pain at the point of inoculation; fever with headache and rheumatoid pains. The inoculated persons are generally fit to resume their duties twenty-four to forty-eight hours after inoculation.

In countries where cholera is endemic in addition to enteric, the tetravaccine, typhoid, para A, para B, cholera, should be used. Certain observers describe a 'vaccine disease' in analogy to a 'serum disease,' and state that the human organism becomes sensitized by a previous injection of vaccine. This phenomenon, however—at least with marked features—is, in our experience, extremely rare.

Until 1916, in the British Army and practically in every other army—with exception of the Serbian Army, which adopted Castellani's tetravaccine (TABC) in 1915—the vaccine used was the Wright-Leishman typhoid monovaccine, which, as regards prevention of typhoid, gave good results, but naturally was of no efficacy in the prevention of the paratyphoid fevers.

Vaccination by a Single Inoculation.—This has been attempted with a certain degree of success by using oil emulsions of the various bacteria (lipovaccines), as done by Le Moignic and Pinoy, or by using 2 per cent. glycerin emulsions, as done by Castellani.

As regards the results of simple typhoid vaccination, Firth's figures worked out by Pearson's methods showed that out of 55,368 inoculated persons in the army in India, 61 were attacked by typhoid, and out of 12,074 non-inoculated 45 were attacked; while another series of figures showed 58,481 inoculated and 34 attacked, as against 10,927 non-inoculated and 22 attacks.

The vaccine used in the army was the Wright-Leishman, made from cultures not more than forty-eight hours old, which were sterilized at 53° C., and to which, when cold, 0·4 per cent. of lysol was added. This vaccine was to be used during the period extending from three weeks to three months after its preparation, and was to be injected under the skin opposite the insertion of the left deltoid.

The first dose was 500 million bacilli, and the second, given ten days after, was 1,000 million bacilli, and sometimes a third dose of 1,000 million was also given. Inoculation takes place at 4 p.m., and the soldier goes to bed at 8 p.m., when the reaction begins, and is on light duty for two days. There is practically no negative phase, and the reaction consists of a localized hyperæmia with œdema and some slight fever, malaise, and chilliness. Occasionally the symptoms are more severe, but usually disappear in forty-eight hours. The typhoid monovaccine was prepared according to many other methods: the Pfeiffer-Kolle vaccine, the Vincent vaccine, the nucleo-proteid vaccine of Lustig and Galeotti, etc. An attenuated live vaccine was prepared by one of us, and a non-attenuated sensitized live vaccine was prepared by Metchnikoff and Besredka, and extensively used by Alcock.

PARENTERIC.

Synonyms.—Typhoid-like and paratyphoid-like fevers; Enteric-like fevers; Fevers due to intermediate germs.

Definition.—The term 'parenteric' indicates a group of fevers clinically hardly distinguishable from one another, and from enteric, but due to intestinal bacteria specifically different from *B. typhosus* Eberth, *B. paratyphosus B* Schottmüller, and *B. paratyphosus A* Schottmüller.

Historical.—Since the discovery of the paratyphoid bacilli cases of clinical enteric, but apparently due to germs different from those of the enteric group (typhoid, para A, para B), were placed on record by a few observers. These cases were generally viewed with much scepticism, which was to a certain extent justified, as in a number of cases the germ believed to be the cause of the fever represented in reality merely a secondary infection. After our work, that of Balfour, and of Archibald, the fact that there is a group of fevers due to so-called intermediate intestinal germs began to attract more general attention, and is now accepted by most authorities.

Geographical Distribution.—Parenteric occurs apparently in every climate, but is of much more frequent occurrence in tropical and subtropical countries. Cases have been reported from Ceylon, India, Egypt, the Sudan, the Balkans, Southern and Central Europe.

Ætiology and Classification.—Parenteric is caused by a large number of intestinal bacteria, excluding *B. typhosus*, *B. paratyphosus A*, and *B. paratyphosus B*. Ætiologically one might differentiate a variety of parenteric for each species of intestinal germ capable of becoming the ætiological agent of a fever, but such a procedure would differentiate several scores of parenteric fevers, and we therefore consider it simpler, for the time being, to classify parenteric according to six types, corresponding to the six principal groups in our classification of intestinal bacteria (Chapter XXXVI., p. 932), as follows:—

A. Parenteric due to bacteria of genus *Eberthus* Castellani and Chalmers, excluding *B. typhosus*, and of genus *Alkaligenes* Castellani and Chalmers.

These cases do not seem to be very rare. Among the germs found we may mention *B. fæcalis alkaligenes* Petrowsky, *B. fæcaloides* Castellani, *B. meta-alkaligenes* Castellani, *B. para-alkaligenes* Castellani, *B. vivax* Archibald, *B. pritnitzi* Castellani, *B. kandiensis* Castellani, etc. It would appear that these germs are usually non-pathogenic, but under certain circumstances, of which very little is known, may become so.

B. Parenteric due to intestinal bacteria of genus *Salmonella* Lignières *emend.* Castellani and Chalmers, apart from *B. paratyphosus A* and *B*. These cases seem to be the most frequently met with. Among the bacteria found we may mention *B. psittacosis* Nocard, *B. columbensis* Castellani, *B. archibaldi* Castellani and Chalmers. These three germs seem to be constantly pathogenic, while many other members of the group are often non-pathogenic, representing when found only secondary infections, although it is not excluded that at times they may become pathogenic.

Two very important germs of the genus Salmonella are *B. aertryke* De Nobele (= *B. suipestifer*) and *B. enteritidis* Gaertner, but these two germs very seldom give rise to an enteric-like fever; usually they give rise to acute enteritis.

C. Parenteric due to germs of genus *Enteroides* Castellani and Chalmers. Cases of parenteric seem occasionally to be caused under certain circumstances by such germs, which as a rule are not pathogenic fæcal bacteria. The following germs have been found capable at times of becoming pathogenic: *B. entericus* Castellani: *B. khartoumensis* Chalmers and MacDonald; *B. parentericus* Castellani.

D. Parenteric due to germs of genus *Lankoides* Castellani and Chalmers. These seem to be rare, though a few cases have been recorded due to *B. ceylonensis A* Castellani and *B. ceylonensis B* Castellani.

E. Parenteric due to germs of genus *Balkanella* Castellani and Chalmers and genus *Wesenbergus* Castellani and Chalmers. These cases appear to be very rare, the germs of this group apparently seldom becoming pathogenic.

F. Parenteric due to bacteria of genus *Escherichia* Castellani and Chalmers. Cases of parenteric due to bacteria of this group (so-called coli group) are in our experience very rare. True, germs of this group are comparatively often found in the blood of cases of fever, and, moreover, are often agglutinated by the blood of the patient, but repeated bacteriological examinations very frequently show that these germs play only the rôle of secondary or associated infections, and that the cases are often true cases of enteric (typhoid, para A, or para B), the coliform germs having entered the general circulation through the intestinal ulcers. One should also keep in mind the frequent invasion of germs of this group in the pre-agonic period.

Parenteric due to germs of the tribe *Proteæ*, such as *B. cloacæ*, *B. pyocyaneus*, *B. proteus vulgaris*, etc., is rare, these germs generally acting as secondary infective agents.

Morbid Anatomy.—Very little is known. Intestinal ulcers do not seem to be present. The mesenteric lymph glands may be larger than normal, and the spleen and liver may be enlarged, and the latter organ may show cloudy swelling and fatty degeneration. The heart is flabby, and may be in a condition of fatty degeneration.

Pathology.—This seems to be somewhat similar to the pathology of enteric.

Symptomatology.—Parenteric is clinically very similar to enteric, the onset being at times slow, the fever subcontinuous or continuous, ending by lysis.

At times, however, the onset is sudden, and the fever may have a most irregular course. The duration varies between ten days and several weeks, or occasionally months. The patient in some cases takes the 'typhoid look,' being apathetic and expressionless; at other times he does not appear to be very ill. Intestinal symptoms may be present or totally absent, but a certain amount of meteorism is often noticeable. The spleen may be palpable, but this is of much less frequent occurrence than in enteric. Roseola is extremely rare and intestinal hæmorrhages practically unknown, the germs of the parenteric group giving rise very seldom to intestinal ulcers.

Frequency of Parenteric.—It is well to keep in mind that parenteric is on the whole much less frequent than true enteric (typhoid, para A, para B). The observation has been made that persons inoculated against enteric (typhoid, para A, para B) seem occasionally to become more prone to contract parenteric, in the same manner that persons inoculated against typhoid only, seem at times to develop a tendency to contract paratyphoid A and paratyphoid B more frequently than non-vaccinated individuals. This, however, cannot be used as an argument against vaccination by the enteric or triple vaccine (typhoid, para A, para B), because, although individuals vaccinated therewith may develop a slight tendency to contract parenteric, still the total number of enteroidea fevers (enterica and parenterica) observed in such individuals is greatly less than in non-vaccinated people or in people vaccinated only with typhoid monovaccine.

Diagnosis.—When a patient is suffering from enteric-like symptoms, while all serological and bacteriological investigations for enteric remain constantly negative, the practitioner is justified in suggesting the possibility of parenteric. The diagnosis, however, should always be confirmed by a complete and repeated bacteriological examination of the blood, stools, and urine, with the object of isolating the causative organism and of determining from what variety of parenteric the patient is affected. We should like to emphasize here that the mere presence of an intestinal germ in the blood is not sufficient to come to the conclusion that this fever is due to that germ. Repeated examinations may show that it is present in association with true *B. typhosus*, *B. paratyphosus A*, or *B. paratyphosus B*, and may have little or no part in the causation of the symptoms, quite a number of fæcal bacteria being capable of entering the general circulation through intestinal ulcers. If, however, the germ not only is found in the blood, but the blood contains specific agglutinins for it, while hæmocultures and serum reactions are constantly negative for enteric, the probabilities are that the germ isolated is the real ætiological agent of the fever.

Prognosis.—This is, on the whole, much more favourable than in enteric (typhoid, paratyphoid A, paratyphoid B).

Treatment.—This should be on the same lines as for enteric. Complete rest in bed and fluid diet are necessary. Drugs are of little or no use except occasionally. Urotropine may be given in doses of 10 grains three or four times a day. The vaccine treatment with autogenous vaccines seems to give better results than in enteric.

Prophylaxis.—As regards general prophylactic measures (sanitary improvements, destruction of flies), these are the same as for enteric. The usual enteric vaccination (TAB) does not, of course, protect against parenteric, and when certain forms of parenteric become frequent the bacteria causing them may be added to the enteric bacilli in the preparation of a prophylactic vaccine.

VARIETIES OF PARENTERIC.

In the general account we have given of parenteric we have stated (see Ætiology) that ætiologically very numerous varieties might be differentiated, but we have limited ourselves to distinguish six chief types in relation to the six principal groups of intestinal bacilli which may cause the condition. We consider, however, it advisable to give a brief separate description of certain varieties of parenteric which have been more completely worked out. These are:—

- Psittacosis parenteric.
- Alkaligenes parenteric.
- Columbensis parenteric.
- Archibaldi parenteric.
- Asiaticus parenteric.
- Khartoumensis parenteric.

PSITTACOSIS PARENTERIC.

Definition.—A very fatal specific epizoötic among parrots, which is capable of spreading to man and causing a febrile condition resembling typhoid fever in its characters, and which is very liable to be complicated with severe pneumonia.

History.—Ritter, in 1879, was the first to suspect that there was a connection between small epidemics of pneumonia limited to certain houses and an illness among parrots in the same houses. In 1880 Eberth obtained large numbers of micrococci from the bodies of grey parrots. Ritter's observations were confirmed by Ost of Berne, in 1882, and by Wagner of Leipsic, in 1885. In 1892, 500 parrots were shipped from South America for Paris, but no less than 300 died *en route* from enteritis. On arrival in Paris the surviving birds were divided into two lots, and sold to various people, with a result that within twenty-six days of their arrival an epidemic of psittacosis broke out, which resulted in forty-nine cases, with sixteen deaths. The epidemic was characterized by being of the *house type*, by which is meant that several persons in the same house were attacked by the complaint.

Smaller epidemics occurred in 1893 and 1894, and in the same year Banti, Malenchini, and Palamidessi reported an epidemic in Florence. In 1895 there were outbreaks at Prato, Cologne, and Paris; in 1897 at Genoa; in 1898 at Cologne; in 1901 at South Elpidio, Ancona, and Hull; in 1904 at New Hampshire, one of the Eastern United States of America. Beddoes in 1914 reported several cases in England. We have seen epidemic enteritis of this nature develop in parrots in the Sudan, but prophylactic measures being immediately instituted it did not spread to man.

Ætiology.—The disease is apparently due to a bacillus belonging to the genus *Salmonella* Lignières of our classification, first isolated from the wings of parrots which had died from the disease by Nocard in 1893, and subsequently found by Gilbert and Fournier in 1897 in the intestine of the sick birds, and also in the heart-blood of a man who died from the disease. The bacillus in question is pathogenic for parrots and other birds. It is possible that this bacillus exists normally in parrots, and only becomes pathogenic under circumstances of bad hygiene, when it causes an enteritis. The feathers, becoming contaminated with fæcal matter, are cleaned by the parrot with its tongue in the usual way, so that its mouth and bill become infected, and by this means the disease is spread to persons who feed or caress the bird. Very rarely the disease spreads from man to man. According to Bainbridge, *Bacillus psittacosis* is identical with *B. aertryke* (p. 954).

Pathology.—In parrots the disease causes a very fatal form of enteritis. In man it produces a septicæmia, often complicated by a pneumonia, brought about as a rule by the pneumococcus.

The post-mortem reveals lobular pneumonia in the lungs, fatty degeneration of the heart-muscle and liver, enlargement and softening of the spleen, and congestion of the kidneys, with swelling of the tubular epithelium.

Symptomatology.—The incubation period varies from seven to twelve days, after which the disease may begin suddenly with a chill, but more usually commences insidiously, like typhoid fever, with headache, malaise, etc., and a rise of temperature from 102° to 104° F., with a pulse-rate of 100 to 120 per minute, quickened respirations, cough, and muco-purulent expectoration. Râles may be heard over the lungs, while the spleen is enlarged, the tongue dry and furred, and diarrhœa or constipation may be present. Rose-coloured spots appear on the skin, and the patient becomes dull and stupid, in which condition he may remain for several days, and as a rule will recover in about fifteen to twenty days if no pneumonic complication intervenes. If, however, pneumonia sets in, the patient becomes much worse, and as a rule dies.

Diagnosis.—The diagnosis is to be made by the discovery of sick parrots in houses in which people are suffering from typhoid-like fevers and pneumonia. Bacteriologically, attempts may be made to obtain cultures of the bacilli from the blood.

Prognosis.—The prognosis is grave in old people and when pneumonia sets in, the mortality being stated to be about 35 to 40 per cent.

Treatment.—The treatment must be conducted on the lines usually laid down for typhoid fever and pneumonia.

Prophylaxis.—Th[illegible]ted parrots appear always to come from South America; therefore [illegible] should be taken that only healthy birds are allowed to be shipped, and that these are kept in good hygienic conditions during the voyage. On arrival at their destination, they should be quarantined for about a couple of weeks, and, if found to be infected, should be destroyed, and their dead bodies and cages burnt. The places in which they were kept should also be thoroughly disinfected. Parrots should not be allowed to take food out of people's mouths, and should always be kept in good hygienic conditions.

ALKALIGENES PARENTERIC.

Remarks.—*B. fæcalis alkaligenes* Petruschky—which belongs to the genus *Alkaligenes* of our classification—is generally a harmless fæcal germ, but researches by various observers have demonstrated that it may occasionally become pathogenic for man, and produce fever. Cases have been recorded by Straub and Krais (1914), by Rochaix and Marode (1916), by Shearman (1916), by Hirst (1917), and others.

Symptomatology.—The fever often resembles a mild type of enteric, and is generally of short duration, twelve to fifteen days, though protracted cases are occasionally met with. At times the temperature is very irregular, subcontinuous or intermittent, and even a tertian periodicity is said to be occasionally present, though possibly some of these cases may have been associated with malaria. The spleen is seldom enlarged, roseola is not present, and intestinal hæmorrhages have never been recorded.

Diagnosis.—This is based on the isolation of *B. fæcalis alkaligenes* from the blood, and the presence of specific agglutinins for this germ, while all bacteriological tests for enteric and other intestinal germs are negative. The bacteriological examination of the blood is carried out as in enteric, either using Castellani's dilution method, details of which have been given when discussing the bacteriological diagnosis of enteric, or one of the modifications of Drigalski-Conradi's bile method. The technique which, in the hands of Shearman, has given good results is the following:—5 c.c. of blood drawn aseptically from a vein is placed in 50 c.c. of a 2 per cent. solution of taurocholate of soda in distilled water, incubated at 35° C. for twenty-four hours, and then plated out on MacConkey's plates. These are incubated for twenty-four hours, and any white colony present is further investigated.

Prognosis.—This is favourable.

Treatment.—The treatment is symptomatic. Vaccines have been tried in a few cases, but no definite results have been so far obtained.

COLUMBENSIS PARENTERIC.

Synonym.—*Febris columbensis.*

Historical and Geographical Distribution.—The disease and its causative germ were described by Castellani in Ceylon in 1905. Spaar published a case in 1914. Recently cases have been recorded in India by De Mello, in Europe, in the Balcanic Zone by Lurie, and in the South of Europe by Conte. It also occurs in the Anglo-Egyptian Sudan.

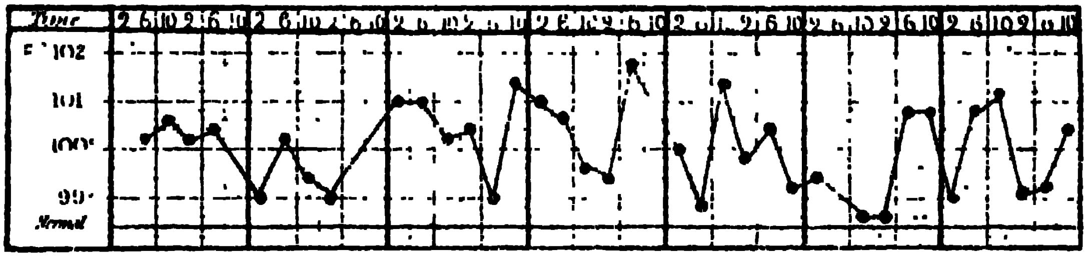

FIG. 663.—TEMPERATURE CHART OF COLUMBENSIS PARENTERIC.

Ætiology.—The causative germ is *B. columbensis* Castellani, 1905. This germ is somewhat peculiar in that occasionally when recently isolated its action on lactose may not be constant, the same strain having at times no action whatever on lactose, at other times slightly fermenting it. After several subcultures all the strains become non-lactose fermenters. It is not agglutinated by typhoid, paratyphoid A and paratyphoid B sera. Its biochemical characters can be found in the table of intestinal bacteria on p. 946. It differs from *B. paratyphosus A* and *B* in producing gas in glycerine and other

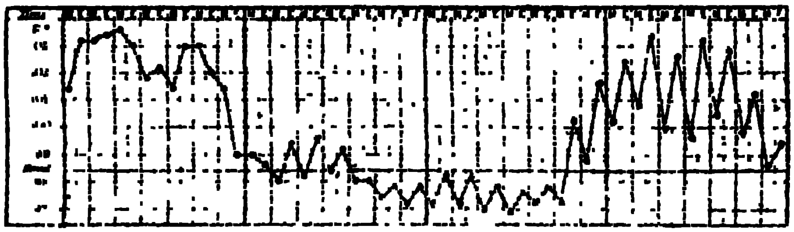

FIG. 664.—TEMPERATURE CHART OF COLUMBENSIS PARENTERIC FEVER.

minor characters. It is not agglutinated by either paratyphoid B or paratyphoid A serum.

Symptomatology.—Two types of the fever may be differentiated, one closely resembling typhoid, the other characterized by numerous relapses. Enlargement of the spleen and meteorism may be present, but are not constant symptoms. Roseola has not been recorded, nor intestinal hæmorrhages. Urinary complications (cystitis, etc.) are not rarely met with. All the cases recorded have ended in recovery.

Prognosis.—Appears to be favourable *quoad vitam*, but in the relapsing type the disease may last for four to six months, the patient having several attacks of fever, each lasting a couple of weeks.

Treatment.—This is on the same lines as for enteric, including complete rest in bed and fluid diet. Urotropine is useful, especially when there are urinary complications.

Prophylaxis.—Castellani has used in Ceylon a *B. columbensis* vaccine in the form of a combined *B. columbensis*, *B. typhosus*, *B. paratyphosus A* and *B. paratyphosus B* vaccine.

ARCHIBALDI PARENTERIC.

This fever and its ætiological agent were described by Archibald in the Sudan in 1912. The bacillus was believed by Archibald at one time to belong to the *B. cloacæ* group. It seems to us probable that the germ belongs to the genus Salmonella of our classification, and that it is related to *B. columbensis* Castellani.

Symptomatology.—As a rule the symptoms presented by the patient are not unlike those of the second week of enteric fever. There is high fever, ranging from 101° to 103° F., associated with drowsiness and perhaps delirium, but this is often absent, with furred dry tongue, but without diarrhœa or tympanites, and with or without some very slight enlargement of the spleen. Sometimes the temperature falls to normal after a week, but this intermission is followed by a prolonged fever of a remittent type, or, instead, the fever may be more or less remittent from the commencement.

Complications.—Complications in the form of pneumonia, abscesses, femoral thrombosis, etc., may occur.

ASIATICUS PARENTERIC.

This fever was differentiated by Castellani in Ceylon by obtaining the specific bacillus from the blood and motions. There are two varieties of the bacillus, which may be called *B. asiaticus* Nos. 1 and 2. (For the specific characters see table in Chapter XXXVI., p. 944.) Culturally these bacilli are identical, but the biological reactions are slightly different. The possibility of a double infection of one of these bacilli or other parenteric germs with those of enteric fever must not be forgotten. The diagnosis will then depend upon the absorption test.

Symptomatology.—*B. asiaticus* No. 1 is associated with a long, protracted, rather low fever of medium severity, which shows usually a remittent or an intermittent character (*vide* Fig. 665). *B. asiaticus* No. 2 produced a fever resembling certain types of protracted enteric fever, but without any enlargement of the spleen, without roseolæ, but associated with rather severe abdominal pains of long duration, though as a rule there is no diarrhœa and the stools never contain blood or mucus.

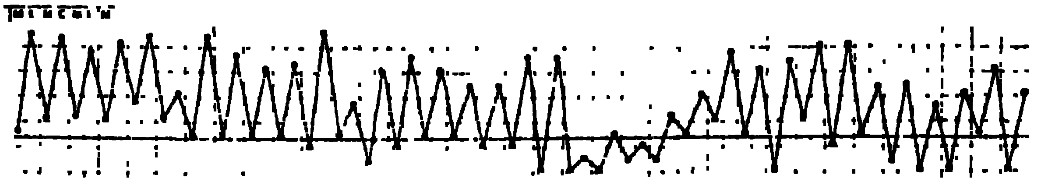

FIG. 665.—PORTION OF TEMPERATURE CHART OF A CASE OF ASIATICUS PARENTERIC FEVER.

One case due to *B. asiaticus* No. 1 was associated with a severe ancylostome infection, while one due to *B. asiaticus* No. 2 was associated with a heavy ascaris infection. The fever did not stop when the patients got rid of the parasites.

Diagnosis.—The only possible method of diagnosis is the early bacteriological examination of 5 to 10 c.c. of the blood taken aseptically from the median basilic vein, and examined as already described for enteric fever, while an attempt may also be made to isolate the bacillus from the fæces. The specific bacillus will be agglutinated by the patient's serum in high degrees of dilution.

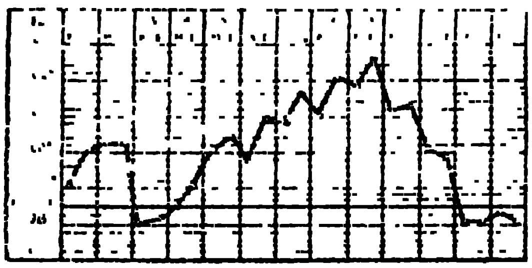

FIG. 666.—TEMPERATURE CHART OF KHARTOUMENSIS PARENTERIC.

Treatment.—The cases must be treated on the lines already laid down for enteric fever, but the most suitable special treatment is the injection of autogenous vaccines prepared like the typhoid vaccines, provided the acute symptoms are over and the fever is of very low type.

KHARTOUMENSIS PARENTERIC.

This fever and its ætiological agent have been described by Chalmers and MacDonald in the Sudan. The germ *B. khartoumensis* Chalmers and MacDonald, 1915, belongs to our genus Enteroides of intestinal bacteria, and is closely related to *B. entericus* Castellani, 1911, and *B. parentericus* Castellani, 1914.

Symptomatology.—After a preliminary period of one to three days, during which the patient suffers from headache, constipation, and malaise, with marked or slight fever, the febrile attack sets in with constipation, headache, and a disinclination for mental or bodily work. The heart, lungs, liver, and spleen remained normal, and, except for the usual febrile changes, the urine was also normal. Except for headache, the nervous system was normal, and no skin eruptions were noticed. The cardinal features of the illness were constipation, fever, relatively slow pulse, headache, malaise, and a general feeling of illness.

After about seven days from the commencement of the true rise of temperature the fever, which had gradually risen to a maximum lying between 101° and 103° F., subsided quickly, and in about another three days fell to normal, when the disease ended, or to nearly normal, and was followed by a relapse of a more irregular and prolonged nature. When the temperature subsided all symptoms gradually disappeared and the patient felt quite well, but if the relapse occurred the headache, lassitude, constipation, etc., returned. At no time was any patient seriously ill, and at no time did a purgative produce other than good effects.

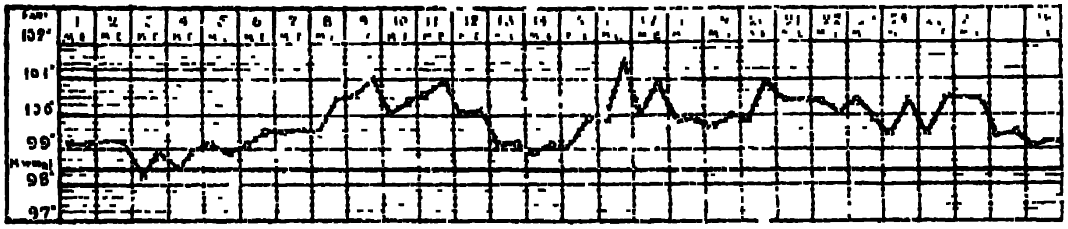

FIG. 667.—TEMPERATURE CHART OF KHARTOUMENSIS PARENTERIC.

The condition somewhat resembles a case of enteric, but the spleen is not enlarged and roseola is not present.

The **diagnosis** is made on finding *B. khartoumensis* in the fæces and by the serological reactions, while all the tests for enteric are negative.

The **prognosis** is favourable.

The **treatment** is symptomatic, but vaccines might be tried.

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CHAPTER LIV

PLAGUE

Synonyms — Definition — History — Climatology — Ætiology — Pathology — Symptomatology — Diagnosis — Prognosis — Treatment — Prophylaxis — References.

Synonyms.—Black Death, Pestis, Lues. *French*, La Peste; *Italian*, Peste Bubbonica; *German*, Die Peste; *India*, Mahamari; *Japan*, Yeki; *China*, Kota-wen; *Uganda*, Kaumpuli.

Definition.—Plague is a septicæmia caused by *Pasteurella pestis* Kitasato and Yersin 1894 (usual name *Bacillus pestis*), which produces an epizootic in rats, from which it spreads to man and other animals by the agency of fleas.

In man it causes an acute specific fever, characterized by an inflammation of the lymphatic glands; a secondary septicæmia, with hæmorrhages, skin necrosis, and often a secondary pneumonia; or it may give rise to a primary pneumonia or a primary septicæmia. The pneumonic forms are highly infectious, spreading from man to man by aerial convection.

History and Epidemiology.—Plague, because of its epidemicity and its high mortality, is much feared and has been noticed from early times to be associated with a mortality among rats. Thus, the Bible contains an account of an epidemic disease in the Philistine country which produced buboes in human beings and killed rats ('mice of the field'), and there is also reference in Simpson's work on plague to the fact that Sennacherib's army was attacked by a pestilence in which field-mice were in some way concerned.

But it was not until the outbreak in Pelusium, a great Egyptian market, in A.D. 542, that the disease was seriously considered, for it spread to Byzantium, at that time the city of the world and then passed into Asia, and through North Africa into Western Europe as far as Ireland, lasting in epidemic form for about 200 years.

The next outbreak is in the eleventh century, when it spread as a pandemic, reaching a maximum in the fourteenth century, and gradually declining, until suddenly, in the seventeenth century, it left Western Europe, and in 1844 it vanished from Eastern Europe, and practically from Asia Minor, remaining, however, in the district of Assyr, in West Arabia.

This great pandemic stirred Governments to take prophylactic measures, and Count Bernabo, of Reggio, is found impressing stern quarantine laws in 1374, while the Venetians, in 1403 and subsequent years, laid the foundations of modern prophylaxis by erecting the first lazaretto, or depot for the isolation of the sick, by instituting the quarantine for forty days (hence the term), and by the disinfection of clothing and merchandise. Further, they compelled the ship coming from an infected port to hoist a yellow flag, and to allow an inspection of the crew and passengers before it was given pratique

In the meanwhile plague occurred in India, where the first records are t be found in a sacred Hindu book, the 'Bhâgavat Purana,' believed to be 800 years old, which describes a disease in man associated with death among rats, and advises the vacation of a house in which dead rats are found. Plague is known to have formed epidemics in the eleventh, twelfth, fourteenth, fifteenth, sixteenth, and seventeenth centuries, after which, apparently, it disappeared, only to reappear in Gujurat and Sindh in 1812. In 1823 it was discovered that plague existed in the districts of Garhwal and Kumaon, but no one has been able to determine from whence it came, or how long it had existed in those places. It is now said to be endemic there, and to form the focus for the epidemic of Delhi in 1825, and Rohilcund in 1836. In 1836 plague broke out in Rajputana—the so-called Pali Plague, from the place first infected—and lasted two years. Since then plague has been introduced into India from China, and has spread therein, as will be explained later. With regard to China, it is difficult to obtain any exact information, but it is possible that plague may have been introduced at some time by Mohammedans returning from Mecca via Burma to the province of Yunnan, where, according to Minakata, it was known some time between 1736 and 1809, for a Chinese author who lived during this period gives an account of a disease which caused death in men and rats. From that time plague has been endemic in Yunnan, from which it appears to have spread southwards, reaching Pakhoi on the southern coast, about 1867, where it disappears and reappears at intervals without apparently affecting other regions, until 1894 when, after an absence of ten years, it again reappears and, infecting the district of Kaochao, spre[illegible] Canton to Hong-Kong. In June, 1894, the causative bacillus was discovered by Kitasato in cases in Hong-Kong, and a little later by Yersin in the same town. In 1896 plague spread from China to Bombay, from which it has gradually extended over the larger portion of India, causing an enormous number of deaths.

In 1897 a most important international conference was held at Venice, when protective measures were agreed to, and regulations framed to combat the disease, based upon the view that the sick person and his personal effects were the chief source of danger, and a quarantine of ten days from the last infected port was placed upon healthy ships. In 1898 the pandemic spread from India to Madagascar, and from there to Lorenzo Marquez and Mauritius. In 1899 it affected the Malay States, the Philippine Islands, New Caledonia, the Sandwich Islands, Australia, San Francisco, New York, Asunçion, Rosario, Buenos Ayres, Rio de Janeiro, Oporto, Lisbon, and Alexandria. In 1900 it passed from Rosario to Cape Town, and also appeared in Glasgow.

In 1900 Clemow pointed out that the disease had existed endemically in Mongolia, Southern China, the Himalayas, Mesopotamia, Persia, Arabia, Uganda, Transbaikalia, Russian Central Asia, and Tripoli, between 1850 and 1894.

In 1903 a Second International Conference was held in Paris, which issued a series of regulations confirming those of the Venetian Conference, except that the quarantine of ships was reduced to five days, and that the agency of the rat in the disease was clearly recognized, and regulations for its destruction framed. Further, this Conference established an International Sanitary Office in Paris for the purpose of collecting and transmitting sanitary information to the different countries. In 1904 Johannesburg was attacked, in 1905 Persia and Russia, in 1906 Leigh, and in 1907 Accra, on the Gold Coast, in which year the disease was widespread throughout the world occurring in India, Persia, Arabia, Egypt, Tunisia, Algeria, West Africa, South Africa, East Africa, Russia, Glasgow, Argentina, Brazil, Chili, Paraguay, Peru, Uruguay, United States, Australia, New Zealand, Japan, China, and Indo-China.

Turning to Africa, which has already been mentioned to have been often infected, it is now known to possess two infected endemic areas—viz., Benghazi, in Tripoli, and Buddu, Koki, and Nkole, in Uganda, from the latter of which an epidemic is supposed to have spread into the Kissiba district of East Africa.

Such a pandemic as the one just described could hardly exist without numerous careful inquiries into its causation and spread, for Governments were interested in its prevention. Therefore Austrian, German, and Russian Commissions were appointed, and did excellent work. In 1898 the first Plague Commission of India was appointed, and was followed by an Advisory Committee of the India Office, Royal Society, and Lister Institute, appointed in 1904, and, finally, in conjunction with this committee, the Second Indian Commission was appointed in 1907, and has done excellent work in tracing the ætiology to the rat-flea.

In the meanwhile individual observers had also studied the disease—*e.g.*, Haffkine of India, and Lustig of Florence, had brought forward protective vaccines, while Verjbitski, of St. Petersburg, showed in 1908, the importance of the bug as a carrier of the disease.

Of great value have been the researches carried out in various colonies by Professor Simpson

According to Nicolas, plague is almost constantly present in New Caledonia, where the bacillus is believed to exist in a latent form.

During 1909-10 in Manchuria there was a very severe epidemic of pneumonic plague with a few cases of the bubonic type It was studied by Strong, Kitasato, Teague, Galeotti, and others

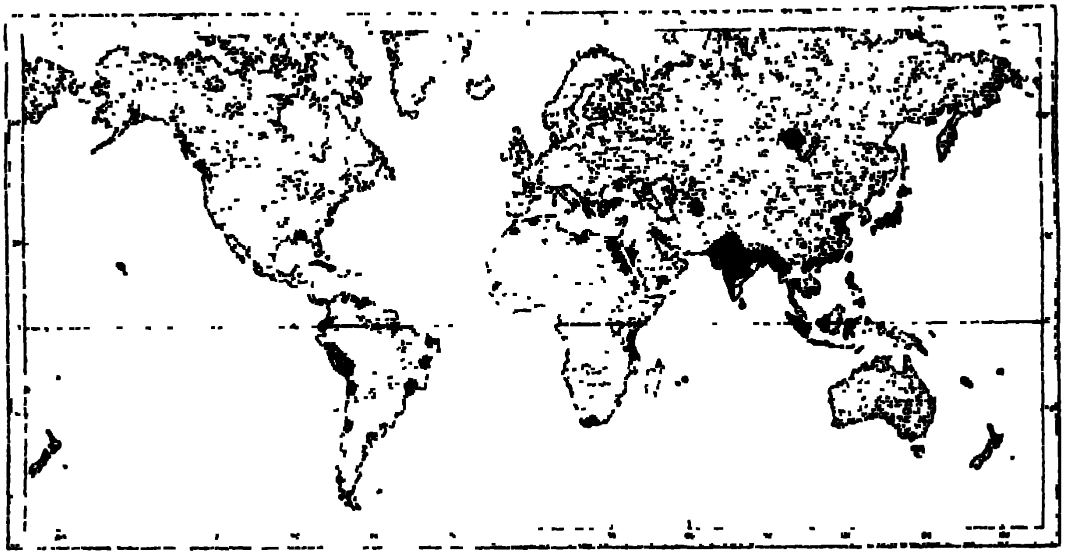

FIG. 608.—DISTRIBUTION OF PLAGUE IN 1914

In 1914 plague appeared in Colombo, Ceylon, where the epidemic was studied by Castellani, who isolated the bacillus, Philip, and Hirst. Several features of the onset were of interest:—

1. The human epidemic was certainly not preceded by a diffuse rat epizoötic, as for years the bacteriological examination of rats had been carried out by the Municipal Health Office with negative results, and it was several weeks after the onset of the human epidemic that the first infected rats were discovered.

2. Practically all the cases were of the acute septicæmic type, and were associated with an extremely high mortality without distinctive features, either clinically or post-mortem; and it is interesting to note that when infection was found in the rats it was also of the septicæmic type, and in them also the post-mortem findings were non-characteristic of plague, there being no buboes, no mottled appearance of the liver, no pleural effusion.

3. The strain of plague bacillus isolated (*B. pestis* Yersin-Kitasato *var. metapestis* Castellani) differed in some minor points from the typical one.

4. The commonest rat flea, as noted by Hirst, was different from that found on rats in the majority of plague-infested areas, such as Bombay, but it is the same as that found in Madras and Rangoon.

Climatology.—At the present moment the so-called endemic regions are an area in the Kurdistan Hills, with a secondary area in Irak, in Mesopotamia; another area about the Himalayas—*i.e.*, Kumaon and Garhwal, in India, Thibet and Yunnan, in China—and four lesser areas—viz., Benghazi, in Tripoli, Uganda, in Central Africa, Azeer, in Arabia, and the trans Baikal Province of Siberia—but only the first two are of real importance as far as we know. On the strength of these two different regions an attempt has been made to differentiate two distinct types of the disease: the first, the Western Asiatic, being mild, and pneumonic cases rare, while it is often self-limited, not capable of wide distribution, and not associated with an epizoötic in rats; the second is the Indo-Chinese plague, or the disease as it is known to-day. It seems, however, hardly likely that such a distinction will be supported when the disease in the first area is carefully studied. Climate appears to have but little influence on the distribution of the disease, and soil apparently none. In India an excessive rainfall seems to favour the spread and virulence of the malady. The hot season of the tropics and the winter season of the Temperate Zone are deleterious to the spread of the disease. The reason for this appears to be the effect of temperature on the bacilli in the flea, which disappear rapidly from its stomach above 85° F., and are very ineffectual at that temperature, while at 70° F. they are virulent. Moreover, as has already been stated in the chapter on Fleas, high temperatures restrain the adults from laying eggs and the larvæ from developing. When temperatures below 50° F. are reached, it is found that rats die before the bacilli pass into the blood, and therefore the fleas do not become infected when sucking the blood. A temperature of about 70° F. is therefore best for the propagation of an epidemic.

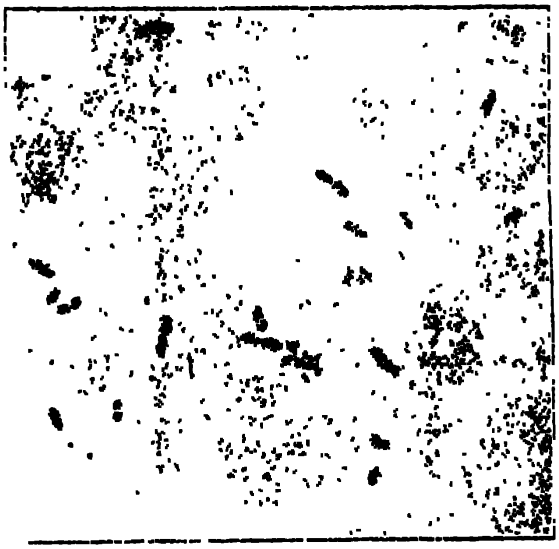

Fig. 669.—Plague Bacilli in the Blood. (× 1,000.)

(From a photograph by J. J. Bell.)

Ætiology (*vide* also pp. 909 and 913).—The ætiology of plague has been placed on a sure footing by the labours of Kitasato, Yersin, Cantlie, Simpson, Thompson, Ogata, Kolle, Martini, and the Special Committee already mentioned, together with the Second Indian Commission.

It is caused by the *Pasteurella pestis* (usual name, *Bacillus pestis*) of Kitasato and Yersin, which is found in the fluid of the initial cutaneous vesicle, the buboes, the spleen, the blood, and the sputum in cases of pneumonia. When inoculated into monkeys, cats, rats, guinea-pigs, squirrels, mongooses, bats, jerboas, etc., it causes the typical disease, while in bovines and equines it only causes local reactions, while camels are insusceptible. Canines, birds, and reptiles appear to be immune. It causes a natural epizoötic in rats which apparently is the true disease, from which that of man must be looked upon as an offshoot. In typical outbreaks there should be, firstly, the *enzoötic;* secondly, the *epizoötic;* then the *endemic*, followed by the *epidemic* in the affected country; and finally *pandemic*. In rats it produces either an acute or a chronic attack, the post-mortem appearances of which are different (*vide* Chapter XXXV.).

In the acute type a bubo is found in 85 per cent. of infected rats, being present usually in the neck or axilla. If the bubo is absent, a plague rat can often be recognized by the subcutaneous congestion, the purplish-red appearance of the muscles, the waxy, mottled, or finely granular appearance of the liver, the hæmorrhages, and the pleural effusions. The diagnosis can be confirmed by finding the bacilli in the bubo, the spleen, or the blood.

The chronic type of the disease consists of encapsuled caseous foci, or abscesses containing bacilli, and found in the spleen and other organs. This form plays no part in the spread of the disease.

The epizoötic does not continue with equal virulence all the year round, for it appears to be profoundly altered by the temperature, being diminished in the hot weather of the tropics and the cold weather of the Temperate Zone. Thus in Bombay the Plague Commission found 1,766 plague infected rats in one week in the season December to May, and only 20 to 30 in the season June to November. The cause of this variation has already been given.

But all rats are not equally infected, for it was found in Bombay that there were two principal species, *Epimys norvegicus* and *E. rattus*, and that during the epizootic period no less than 1,331 of the 1,766 belonged to the former species, while in the non-epizoötic period it alone carried on the disease. The reason assigned for this difference was that the numbers of the flea population of the two rats were very different, *E. norvegicus* possessing about double the number of *E. rattus*. Further, it was noticed that the curve of *E. norvegicus* infection began to rise about ten days before that of *E. rattus*, which points to the origin of the infection of the latter from the former in the first instance.

In Ceylon also the percentage of infected rats was higher in *E. norvegicus* than in *E. rufescens*, the local representative of *E. rattus*, but the septicæmic type was more frequent in the latter.

E. norvegicus, which is not nearly so numerous in Bombay as *E. rattus*, lives outside houses, for the most part in sewers, drains, and stables, and has a great facility for burrowing, and is a good climber. It, however, has never been found above the third floor of a house. It forms its nest in one of its burrows, and breeds all the year round, but has two special seasons, one in March and one from June to October, the average family being eight.

E. rattus is more common in Bombay than *E. norvegicus*, especially in houses, where it increases, relatively to the other, up to the third floor, but above that level it alone infects the house. It is not so common in gullies, compounds, stables, go-downs, and food and tea shops as *E. norvegicus*. The common meeting-ground of the two species appears to be the lower floors of houses, gullies, and go-downs. Though a domesticated rat, it can climb and burrow. It forms its nest in cupboards, heaps of firewood, etc., and breeds all the year round, but especially from June to October, the average family being five.

The spread of the plague from *E. norvegicus* to *E. rattus*, according to the experiments of the Commission, is neither by direct contact nor by air, soil, or food, but solely by the flea. Contact was excluded by placing healthy rats in the same room with plague-infected animals from which the fleas had been removed, when it was found that none of them developed plague. The experiment was kept up for a long time, replacing dead infected rats with freshly infected rats, and, further, the room was never cleaned out, so that the healthy animals lived in contact with the infected urine and fæces, and even ate food polluted therewith, and yet not one contracted plague, thus excluding transmission by contact, soil, and food.

Again, when healthy animals were suspended in cages 2 feet from the ground, so that the fleas could not get to them, or placed on the ground, and surrounded by 6 inches of tangle-foot, over which a flea cannot pass, as it is said to be incapable of jumping more than 4 inches, or surrounded by a curtain of wire gauze so fine that a flea could not penetrate it, and exposed to infection, they escaped, though others not so protected became infected, thus disproving aerial infection. Further, the transmission by the rat-flea was proved by constructing a glass box, inside which two wire cages were placed at a little distance, but side by side, each standing in a tray filled with sand. Each cage had a lid, through which rats, food, water, etc., could be introduced, and the whole apparatus was covered in with fine muslin to prevent the escape of the fleas. A plague-infected rat and a number of rat-fleas were placed in one cage. When this rat died, a healthy rat was placed in the other cage, and after some time the dead body of the infected rat was removed, when it was found that the new rat became infected with plague, and fleas containing bacilli were found upon it. This experiment was repeated many times, 15 per cent. of the exposed rats taking the disease. Further, fleas infected by biting plague rats, when placed upon healthy rats, produced the disease in 55 per cent. of the experiments.

The Commission calculated that the blood of an ordinary plague rat in two-thirds of the cases contains more than 100,000,000 bacilli per cubic centimetre, and that a flea's stomach could hold 0·5 cubic millimetre of blood. Therefore, when the flea gorged itself on the average plague-stricken rat it received at least 5,000 bacilli. These bacilli are found only in the stomach and in the alimentary canal posterior to that viscus, especially the rectum, and escape from the flea solely with the fæces. It was proved, however, that the bacilli multiplied in the body of the flea by allowing infected fleas to feed solely on uninfected rats, a fresh one being supplied each day, when abundant bacilli were found up to the twelfth, and once to the twentieth day, thus proving that multiplication must have taken place, otherwise the original number of bacilli would have become much diluted by the feeds with fresh blood. Further, it was discovered that the proportion of fleas in whose stomach multiplication took place was six times greater in the epidemic than in the non-epidemic season. In the former season the bacilli could be found easily up to the fourth and even to the twelfth day, while in the latter never after the seventh day. Infected fleas were found to transmit the disease for seven to fifteen days.

The method of infection probably is in one of two ways—either fæcal pollution of the proboscis, or else fæcal pollution of the wound made by the proboscis, which was found quite large enough for the purpose of introducing the bacilli into the skin. Martin's experiments tend to show that regurgitation often takes place, due to plugs of bacilli in the œsophagus (see Chapter XXXV.). Both males and females can transmit the disease, but it was found that one infected flea alone was unlikely to do so. The flea most commonly found on rats, and the one by which the infection in these experiments was usually spread, was *Xenopsylla cheopis* Rothschild, but others—*e.g.*, *Ceratophyllus fasciatus* and *Pulex irritans*—were found also capable of causing the disease.

With regard to the spread of the disease to man, the Commission believes that the infection generally comes from *Epimys rattus*, because the habits of that rodent bring it into close relationship with man, and because the curve of its epizoötic begins to rise ten to fourteen days before that of the epidemic. This period is calculated to be made up of three days, during which the flea leaves the dead rat, to which is added another three days, which is the incubation period of plague in man, and five and a half days, which is the average duration of the fatal illness in man.

Xenopsylla cheopis appears to be the flea by which plague is spread from *Epimys rattus* to man. This rat-flea will not merely bite man when it cannot get rat's blood, but is capable of living for three to four weeks on man's blood, and is often found on human beings after inspection of plague-stricken houses.

Further, it is believed that the spread of plague is due, not to migration of rats, but to the carriage of infected rats on ships, and of fleas in merchandise or on human beings. The Commission apparently consider the last to be the most important method.

In Ceylon, as observed by Hirst, the commonest rat-flea is *Xenopsylla astia* Rothschild, which seems to bite man with great reluctance at temperatures over 80° F.

Pneumonic plague, which occurs only in 2·5 per cent. of cases during bubonic epidemics, spreads from man to man by bacilli carried by the air, for Strong and Teague demonstrated that the sputum in invisible droplets containing viable plague bacilli was frequently to be found in the air near a patient. Teague and Barber have shown that the fine droplets of sputum disappear very quickly unless there is a considerable amount of aqueous vapour in the atmosphere, as is found in very cold climates, and hence the tendency for pneumonic plague to spread in those rather than in warm climates. On the other hand, the bubonic or septicæmic is not spread from man to man, but from rats to man. The epizoötic is the real disease, and the epidemic is only an offshoot.

The above ætiology explains fully the predisposing causes of sex, women staying more in the house than men; of house, of season, of climate, and also the carriage of the disease from one place to another by people, fodder, grain, bales of cotton, and clothing, rags, etc.

Verjbitski in 1908 showed that bugs could act as carriers of the bacilli, and this has been confirmed by Jordansky and Kladnitsky, while Walker considers *Clinocoris rotundatus* to be one of [illegible] carriers of plague [illegible] India, having found 22 per cent. infected with *B. pestis* when collected from infected native huts. Moreover, he successfully transmitted the disease from man to the rat by means of *Clinocorus rotundat*

The possibility of lice acting as occasional carriers should not be forgotten. Lice caught on patients suffering from plague have at times been found infected with *B. pestis*.

In California Wherry, McCay, and others have shown that the ground-squirrel (*Citellus beecheyi*) is subject to plague, and that its commonest flea, *Ceratophyllus acutus* Baker, is the vector from squirrel to squirrel, and, further, that this flea will bite man. Further, they record a subacute case of plague in a boy where the infection was believed to be acquired by contact with ground squirrels. With regard to the outbreak in Manchuria and North China, Gray has shown that it started among men who handled the tarbagan (*Arctomys bobak* Müller), which is susceptible to epizoötic plague, and that these men on returning to their homes introduced the disease into three provinces, as pneumonic and septicæmic plague, while it was spread by the agency of the breath and personal contact of clothes and belongings by coolies travelling in parties and sleeping together in overcrowded insanitary inns, especially as the cold of the winter induced an indoor existence. These travelling parties infected adult males who stayed at the inns or were travelling, and so it spread to the ordinary population. No infected rats could be found, in 20,000 examined, while isolation of the patients and their contacts, together with efficient disinfection, were sufficient to diminish the death-rate This shows how important the pneumonic form of plague may be in epidemics, especially in cold weather, but it is also to be noted that, although it starts from association with an epizoötic, it tends to die out without being succeeded by a bubonic outbreak, but it may infect rats and so cause a bubonic epidemic. There has been an epizoötic in Suffolk, in

England, but only a few cases of bubonic plague in man. The tarbagan suffers at times from plague, but the epizoötic is not extensive, and its direct relationship to human plague is negligible. *Spermophilus citellus*, the marmot, is susceptible to plague.

Attention may be called to epidemic diseases in the lower animals due to bipolar staining bacilli, somewhat resembling the plague germ. We have observed one such epidemic in cats in Ceylon in 1904 A bipolar staining bacillus was found to be the cause (*Bacillus felisepticus* Castellani), but the cultural characters were somewhat different from those of the true plague bacillus.

Pathology.- Plague is a hæmorrhagic septicæmia in the rat, which is communicated to the human being by flea-bites. The site of inoculation is sometimes marked by a vesicle, the contents of which contain the *Bacillus pestis* in considerable numbers. The bacilli then travel via the lymphatics to the nearest lymphatic glands, which they may traverse, and, passing through the thoracic duct, enter the blood stream, and cause a septicæmia. More usually they remain and grow in the peripheral lymph sinuses of those glands in which they or their toxins cause degenerations of the cells, periglandular serous infiltration, and, later, degeneration of the walls of the bloodvessels and hæmorrhage. The lymphatic glands are matted together by the exudation from the primary bubo. The glands usually affected are the femoral, inguinal, axillary, iliac, or cervical, which may briefly be classified into the groin, the axillary, and cervical glands.

The Indian Commission points out that the reason why the groin glands are so frequently attacked is simply because they drain the largest skin area, for they say that the areas drained by the glands of the neck, axillæ, and groin are in the proportions of 1 : 1·8 : 5, while the number of cervical, axillary, and inguinal buboes are in the proportion of 1 : 1·[illegible] : 5·[illegible], and that therefore there is no seat of election as to where the plague bacillus enters.

From the primary bubo the bacilli may travel along the lymphatic to the next chain of glands, in which they produce the secondary bubo, and from this they may enter the blood stream via the lymphatics. The bacilli, however, may gain direct access to the blood stream through the injuries to the walls of the veins in the primary bubo. Once the blood stream is reached the disease becomes a septicæmia, and affects the lymphatic glands, forming tertiary buboes: the lungs, causing bronchitis and secondary pneumonia; the spleen, liver, kidneys, skin, and other organs: and, finally, leaves the body through the kidneys, skin, and mucosæ, escaping in the urine, fæces, and sputum (if there is pneumonia), as well as by any discharges or hæmorrhages from the skin. The excretion, via the sputum and saliva, can proceed for a period of at least forty-eight days after the temperature is normal. Further, as in chronic plague in rats, the bacilli may be found in abscesses some two and a half months after an attack. The chemical pathology of the disease is not well known.

Strong, Crowell, and Teague, from a study of the pathology of Mukden plague, have concluded that epidemic pneumonic plague results from inhalation of the bacilli. The primary infection appears to be the bronchi, while it extends along the bronchioles by continuity into the infundibula and air-cells, or through the walls of bronchioles into the lung tissue, causing a peribronchial inflammation. From these centres the infection spreads to the adjacent pulmonary tissue and to the visceral pleura, the bacilli growing rapidly, and causing first a lobular pneumonia and later a lobar pneumonia, while the blood becomes quickly infected, causing a septicæmia. Secondary pathological changes take place in the spleen, bronchial glands, heart, bloodvessels, kidneys, liver, and tonsils, which may at times become primarily affected. No sign of any intestinal plague was found, although plague bacilli must have been repeatedly swallowed in the bronchial secretions and saliva by the patients.

Morbid Anatomy.—The characteristic features of a plague post-mortem are the hæmorrhages and the buboes, which have been studied in detail by Dürck. The skin in the region of buboes and on the head, arms, neck, and shoulders may show hæmorrhages, which arise from the action of the toxins upon the endothelial cells of the vessels. These cells increase in size, and perhaps in number, and some macrophages arise, after which they degenerate, and allow hæmorrhages by rhexis to take place. These hæmorrhages, therefore, may be petechial or diffuse, and will contain bacilli. Besides these, however, vesicles, pustules, or carbuncles, may be seen.

The vesicle arises from the irritation caused by the bacilli in the skin, producing inflammation with exudation, which may go on to pustulation, or, the vesicle drying up, the cutis may become much inflamed and degenerated, forming the so-called carbuncle, which in no respect resembles a true carbuncle.

The primary bubo shows a periglandular infiltration, which may spread from the site of the enlarged glands in all directions. When this gelatinous exudate is cut into, the enlarged glands can be seen matted together, grey or yellowish-grey in colour, with a soft centre and numerous hæmorrhagic spots, or perhaps large hæmorrhages. The secondary buboes are seen to consist of degenerated glands without the œdema, but with endo- and peri-glandular hæmorrhages. The tertiary buboes contain hard hyperæmic glands marked by hæmorrhages.

The muscles of the body, but especially those of the abdominal wall, will be seen to be hæmorrhagic. The spleen is enlarged and congested, and shows hæmorrhages and contains bacilli. The liver may be slightly enlarged and hæmorrhagic, with cloudy swelling and fatty degeneration of the cells. The lungs usually show some bronchitis, and often patches of secondary broncho-pneumonia. The right heart is usually dilated, and the musculature shows fatty degeneration, cloudy swelling, and hæmorrhage. Primary broncho-pneumonia may, however, exist, and be followed by a septicæmia and bubo formation. The stomach is hyperæmic and hæmorrhagic, while the solitary glands and Peyer's patches of the intestine are swollen and the mesenteric glands enlarged. The kidney may be normal, or show hæmorrhages. The nervous system seldom shows any changes, but hæmorrhages and meningitis may occur.

The post-mortem appearances of plague in rats are:—

Bubonic Type.—Lymphatic glands enlarged and hæmorrhagic, liver and spleen enlarged and congested; the former shows granular degeneration of a peculiar nature, and the latter is speckled with whitish spots as seen on section. There is often fluid in the pleural sacs. These features have been found useful in diagnosis of plague rats when microscopical examinations cannot be carried out.

Septicæmic Type.—There are no characteristic macroscopic features, and the diagnosis is solely based upon microscopic findings of the splenic juice and heart blood.

Doell and Warner have applied to the diagnosis of plague infection in rats Ascoli's thermoprecipitation method

In cases of *acute septicæmic type* there is no post-mortem characteristic feature on which the diagnosis of plague may be made or even suspected. The lymphatic glands are not enlarged, though the spleen may be of larger size than normal.

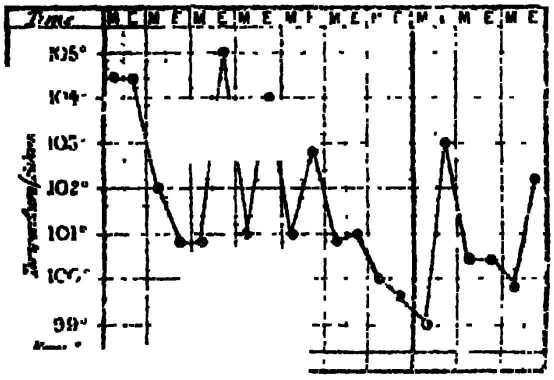

FIG. 670.—TEMPERATURE CHART OF PLAGUE.

Symptomatology—*Incubation.*—The incubation period varies from two to ten days, the average being three days. During this period there may be prodromal symptoms in the form of general malaise, headache, gastro-intestinal disturbance, pain, or feeling of discomfort in the site of the future bubo, chilliness, giddiness, and mental dulness.

Onset.—The onset is usually sudden, with rise of the temperature to 103° to 104° F., pulse of 120, and respirations 30 to 40, and marked prostration, with an aggravation of the prodromal symptoms—*i.e.*, severe headache, furred tongue, vomiting, at times diarrhœa, pains in the back and limbs, and at the site of the future bubo, marked chilliness or a rigor, staggering gait, and marked mental dulness.

Course.—In a few hours the disease becomes properly established, when the patient presents a typical facial expression of fear or anxiety, the eyes being bloodshot, bright, and staring, the face drawn and the nostrils dilated. The temperature rises during the first day, but may remit a degree or so on the second day, but if so, it rises quickly again to the same or a higher degree than at first. As a rule, however, the temperature is most irregular. Towards the end it may fall by lysis, if recovery is to take place, or fall rapidly to normal or subnormal, and then as rapidly to rise about 107° F., or may simply rise directly to about 107° F., and death ensue. There is much thirst, and the tongue is coated at first with a whitish fur, but later it becomes covered with sordes, as do the teeth and lips. Vomiting is frequently met with, as well as diarrhœa; but the abdomen is not tender, unless there are enlarged abdominal glands. The spleen is always, and the liver often, enlarged. Cardiac dilatation is an important feature of the disease, and systolic murmurs may be heard. The pulse is rapid, reaching 120 to 180 early in the disease, and later becoming, in bad cases, not countable. At first it is full and of moderate tension, but later it becomes small, weak, and intermittent.

The coagulation of the blood is diminished. Plague bacilli can be found culturally in about a third of the cases examined. The number of erythrocytes and the amount of hæmoglobin are distinctly increased above the normal, and there is a great leucocytosis—*i.e.*, 90,000 to 100,000 and more—but in the septicæmic form there may be a leucopenia. The leucocytosis is almost entirely due to an increase in the polymorphonuclear leucocytes.

The breathing is rapid, and the breath sounds harsh, with moist râles, but signs of lobular pneumonia and pleuritis may also occur. The sputum in this type of pneumonia is very hæmorrhagic and full of bacilli.

Buboes of varying sizes may be noted in the groin, the axilla, or the neck, and are very painful, respectively causing the patient to lie with the leg drawn up close to the chest wall, or the head bent towards the affected side. They usually appear during the first twenty-four hours, and they may decline or suppurate.

The skin is hot and dry, and may show vesicles, pustules, or areas of necrosis, often called 'carbuncles' (they are, of course, not true carbuncles). Hæmorrhages, in the form of petechiæ or ecchymoses, may be seen under the skin, and epistaxis, hæmatemesis, melæna, and hæmaturia may occur.

The quantity of urine is usually diminished, the specific gravity is high, and plague bacilli may be found. If hæmorrhages have occurred in the urinary tract, there will be erythrocytes and leucocytes, with albumen and globulin, though, apart from this, there is often a trace of albumin present, while anuria is generally present before death. Pregnant women always abort.

Termination.—As the disease progresses the patient becomes weaker and weaker, the mind wanders, and a wild delirium may occur; but later a low muttering delirium passes into coma, and death ensues from the third to the fifth day. In favourable cases the tongue becomes moist and clean, the temperature declines by lysis, the pulse-rate diminishes, and convalescence begins, but may be much prolonged by suppuration of the buboes or by a secondary septicæmia. Even now death may occur from cardiac failure, suppuration, septic infection, or secondary hæmorrhage.

Varieties.—Four variations of the disease are recognized: (1) The ambulatory type; (2) the bubonic type; (3) the acute septicæmic type; and (4) the pneumonic type.

The Ambulatory Type.—This is the mildest form of the disease, and is characterized by but little fever, with slight enlargement and tenderness of a group of lymphatic glands. If the area of skin drained by these glands is carefully investigated, a primary vesicle will often be seen at the site of the inoculation, and considerably helps in the diagnosis, for its fluid contains typical bacilli. The symptoms of this type resemble those already described as prodromata.

The Bubonic Type.—This type agrees with the general description, the bubo being usually in the groin, less commonly in the axilla, and least commonly in the neck. The fever reaches its maximum on the fourth to fifth day, and lasts till the seventh to tenth day, when it falls by lysis, though it may rise again if suppuration is taking place in the buboes. The attitude of the patient depends upon the position of the bubo, as described above.

The Acute Septicæmic Type.—Here the onset is sudden, and the temperature very high, with very rapid pulse, marked prostration, and delirium. There may be severe vomiting, and occasionally diarrhœa. No enlarged lymphatic glands are found, and the diagnosis on clinical grounds may be impossible. Hæmorrhages may at times occur in the skin and from the regions indicated above, and death rapidly takes place in from eighteen hours to three days. This type of the disease is often common at the onset of an epidemic.

The Pneumonic Type.—There are two distinct types of pneumonia in plague—a pneumonia secondary to bubonic plague and a primary pneumonia. This latter begins suddenly without prodromata, after an incubation of two to five days, with chilliness, high fever, headache, anorexia, and rapid pulse. Within twenty-four to thirty-six hours the temperature is 103 to 104 F., and the pulse 110 to 130 beats per minute. Cough and dyspnœa appear within twenty-four hours, when the expectoration is at first scanty, but soon becomes abundant. At first it is only composed of mucus, but it soon becomes tinged with blood and later very hæmorrhagic, and is full of bacilli. The conjunctivæ become injected, and the tongue coated with a white or brownish fur. The breathing is very rapid, and dulness may or may not be present over the bases: the breath sounds are usually tubular and crepitant, and sibilant râles are heard, while the vocal fremitus may be increased. Dyspnœa and cyanosis are early marked features, as is the fluid bloody sputum which is found by the second or third day, and is full of bacilli. Pleuritis, with its usual symptoms, may also occur. Prostration is extreme: the heart becomes very weak and the pulse rapid, while the spleen is usually not palpable. A marked leucocytosis may occur. This is a very fatal type of the disease; delirium and coma appear, and cases die at the end of sixteen hours, two or three or, much more rarely, four days.

Sequelæ.—Cardiac weakness, with proneness to syncopal attacks, paralyses, septic infections of the buboes, or a general septic infection, or gangrene of the lung, may occur.

Diagnosis.—This, in the *bubonic type*, which is commonest, is based on the acute onset with high fever, great prostration, and the presence of a bubo. Difficulty may arise in the diagnosis between the bubonic type of plague and climatic, venereal, and symptomatic buboes; between pneumonic plague and ordinary pneumonia; and between septicæmic plague and various fevers.

In venereal bubo there will be found ulcers on the genital organs, or, at least, the patient will give a history of such. In climatic buboes and various symptomatic buboes due to small ulcerative lesions on the legs, etc., the general condition of the patient is usually far from being so grave as in plague. In any doubtful case bacteriological methods should be employed. A little of the fluid from the suspected bubo is withdrawn, under aseptic precautions, by means of a sterile syringe, and films are made and stained with methylene blue, diluted carbol-fuchsin, or Leishman's stain. The presence of bipolar staining bacilli is sufficient, for all practical purposes, to diagnose the case as one of plague, though it is desirable, whenever possible, to complete the investigation by cultural methods followed by inoculations into animals.

In *pneumonic plague* the expectoration is generally fluid and greatly hæmorrhagic, and is not purulent, as it frequently is in catarrhal bronchitis or in bronchial pneumonia, nor is it tenacious, as in croupous pneumonia: the examination of the sputum—instead of the sputum, the lung juice, obtained by puncture with a sterile syringe, may be examined—will reveal the presence of numerous plague bacilli, easily distinguishable from the pneumococcus by their being Gram-negative.

Acute Septicæmic Plague.—The diagnosis is most difficult, as there are no characteristic symptoms and no glandular enlargements. In a country where plague is endemic any case of sudden high fever, with extreme prostration and blood examinations negative as regards malaria and relapsing fever, should be viewed with suspicion. The fever is generally higher than in dengue or pappataci fevers, often reaching 105° F., while the prostration is much more marked. The microscopical examination of the blood for *B. pestis* is unfortunately often negative, and the cultural examination requires time, and hence the diagnosis may be made too late, as by that time the patient may be dead. It may be distinguished from malaria by the absence of Laveran's parasites, from relapsing fever by the absence of spirochætes, but it is to be noted that cases of mixed infection occur. In India, as observed by Polverini and others, cases of mixed infection of plague and relapsing fever are not rare. The diagnosis between septicæmic plague and cryptogenic septicæmias due to the pneumococcus and other germs, as well as occasionally the differential diagnosis from pernicious malaria, typhus and typhoid, may be impossible without a complete bacteriological examination of the blood.

The simple microscopical examination of thick films of blood (Manson-Ross method) for the presence of bipolar staining bacilli is often a failure. The so-called *dilution method* introduced by Castellani for the search of the *Bacillus* *typhosus* in the blood of typhoid patients is useful also for the search of the plague bacillus, as proved by Kolle and others: 10 c.c. of blood are collected, under aseptic precautions, with a sterile syringe from a vein, and immediately distributed into several flasks of slightly alkaline broth, each containing 300 cubic centimetres of the medium. In this way the bactericidal substances of the blood are greatly diluted, and the growth of the plague bacillus facilitated. Agglutination tests are not of much use in the diagnosis of plague.

In places far from bacteriological laboratories Broquet recommends that a gland or a portion of a gland obtained as soon after death as possible should be placed in a vial containing 125 to 175 c.c. of a mixture of neutral glycerine (30° B.) 20 c.c., distilled water 80 c.c., and carbonate of lime 2 grammes. The mouth of the vial or flask is flamed and sealed with paraffin. On arrival at the laboratory the glycerine is wiped off the gland, which is made into an emulsion with normal saline, and injected, half into a guinea-pig and half into a rat. It is stated that by this method virulence is maintained for thirteen days, which is of great importance in the tropics. A dead animal should be immersed in a solution of strong disinfectant, such as carbolic 5 per cent., in order to kill the fleas, and should then be placed in sawdust or other packing in a hermetically sealed air-tight metal case, and forwarded for examination, if the distance is not too far, to the laboratory.

Prognosis.—Simpson quotes Procopius of Cæsarea as saying, with regard to the plague in Byzantium, that many whose death the physicians predicted recovered, while those who were supposed to be about to recover often quickly died, from which it may be inferred that the prognosis in cases of plague has to be most guarded, for dangers are numerous even in convalescence—*e.g.*, cardiac failure.

The prognosis varies with the character of the epidemic, some being milder than others, and is better when the number of cases is declining. It also varies for the type of the disease, being best for the ambulatory and worst for the pneumonic. As 75 per cent. of the deaths occur before the sixth day, after that time the prognosis improves.

A good pulse, a clear mind, a normal quantity of chlorides and no albumen in the urine, are good signs. High fever, rapid, thready pulse, violent delirium, sudden fall in the temperature, disappearance of the buboes on the fourth or fifth day, and anuria, are bad signs. But in all cases be cautious about the prognosis, and remember the physicians of Byzantium. In pneumonic plague the prognosis is most unfavourable—*e.g.*, in the Manchurian epidemic of pneumonic plague no case in which the bacteriological diagnosis was positive was known to recover.

Treatment.—The treatment should aim at killing the bacillus and neutralizing its toxins, and naturally one hopes to find those requirements supplied by sera. Unfortunately no such serum has as yet been found, though encouraging reports have been recorded by Choksy and Polverini concerning Yersin's and Lustig's sera, and by others concerning Cruz's serum. Whatever the serum, it should be given in large doses (30 to 50 c.c., and even more) by subcutaneous injection. A second and a third injection can be given during the course of the disease, but one should keep in mind the possibility of anaphylactic symptoms in people previously inoculated with serum. Several such cases have been recorded by Darling. The serum may be given also by intravenous injection.

Yersin's serum is prepared by the inoculation of horses with fresh agar cultures, and is such that 0·1 c.c. should protect a mouse from a dose of bacilli, which otherwise would kill it in two to three days. The dose for man is 60 to 300 c.c., given intravenously and also subcutaneously near the buboes. Lustig and Galeotti's serum is prepared by injecting a horse with a vaccine which contains nucleo-proteid from cultures. The mode of action of these sera is said by some not to be bactericidal, but to encourage phagocytosis.

Though admitting that the serum treatment is far from being perfect, we advise its use at the very beginning, as it gives somewhat better results than the ordinary symptomatic treatment or the so-called antiseptic treatment, such as the internal administration of carbolic acid.

As regards the symptomatic treatment, the first indication is to keep the patient in bed, because of the danger of syncope, and to give him good nursing and fresh air. Fever must be treated by sponging and cool or cold applications; buboes by cold applications and ichthyol, and when they suppurate an incision must be made and the wound treated aseptically. Not much good is to be obtained by excising the glands even in an early stage, though several authors—*e.g.*, Terni—have recommended it. The heart's action must be maintained by digitalis, strophanthus, and strychnine. Restlessness may require a hypodermic of hyoscin; hæmorrhage will require treatment by calcium chloride; the so-called carbuncles must be treated antiseptically; pneumonia and bronchitis require the ordinary treatment; and if there is constipation, calomel and a saline purge may be given; while vomiting is to be treated as described under Malaria. A sufficiency of fluid should be given, so as to keep up the action of the kidneys.

The diet should consist of broths and milk, while stimulants are usually required.

Tincture of iodine has been recommended, and is given by oral administration, a few drops at a time, diluted with cinnamon water, and may be given also by intravenous injection, 5 to 7 minims once or twice daily. Eusol has been recommended by Brayne.

Prophylaxis.—*Bacillus pestis* being conveyed by the rat-bite from rats to man as a rule, and more rarely from man to man, it is obvious that prophylaxis must include methods directed against rats and fleas, and methods for the protection of human beings.

The spread of the disease from place to place is thought to be mainly by the flea being carried by human beings on their person, or in their clothing, or by means of the merchandise, or by rats.

The prophylaxis will be considered under two headings—Public Prophylaxis and Personal Prophylaxis.

PUBLIC PROPHYLAXIS.—It is necessary, in order to prevent a country from being infected with plague, to institute a Sanitary Service, which should consist of a central authority for collecting and dealing with information on a large scale, and to which will be attached bacteriologists, who will carry out the necessary bacteriological examinations and prepare prophylactics; and a Port Sanitary Branch, for investigating and disinfecting ships.

It is as well, if possible, to limit the communication with infected areas to as few ports as possible, and to provide isolation hospitals for the sick and for the healthy coming from infected areas. The length of quarantine is fixed at present at five days, but this appears to be too short, if the findings of the Indian Commission with regard to fleas are considered.

Attempts can be made to prevent the disease crossing land frontiers by the medical inspection of persons coming by rail, road, or river, but this method of prophylaxis is liable at any time to break down.

It would appear most necessary to disinfect the clothing and persons of all people coming from infected areas, as they may carry fleas, and this is most difficult to effect, but it is not so difficult to disinfect merchandise by the Clayton apparatus.

In addition, rats must be caught regularly in places situated in danger zones, and inspected to see if any are becoming diseased, for the epizootic begins before the epidemic as a rule.

But of all things the most difficult, as well as the most important, appears to be the recognition of early cases, and pneumonia, buboes, and sudden deaths must be regarded with the greatest suspicion.

When an epidemic begins there are two periods, as Simpson points out, at which the populace takes fright, and has to be firmly handled: one at the beginning, and the second when the deaths begin to increase rapidly in number. Riots and assassinations of magistrates, medical officers, and inspectors may occur, and must be foreseen.

As diagnosis is so difficult at first, a house-to-house inspection by competent medical officers will be necessary to find out the number of cases, and in no instance must a body be allowed to be buried without being viewed by a medical officer. If this is not done, it will be impossible to gauge the extent of the disease.

Rats must, of course, be regularly and systematically examined, and their mortality curves constructed. The sick must be isolated, and the persons and clothing of contacts disinfected to kill the fleas. Every infected house must be disinfected by filling the adjoining houses with the gas from a Clayton apparatus, and after this the house itself. If this method is not carried out, the rats will simply pass from the infected to the non-infected houses, and spread the plague. Village houses might be burnt, which is cheaper and a fairly effective method, though, of course, measures should be taken to prevent the rats escaping. The gas in question is generated by burning sulphur at a very high temperature in a special apparatus, when SO_2 and SO_3 and some unknown gases are evolved, which are passed into the ship, house, warehouse, etc., and drawn through by an exhaust-pipe until a 3 per cent. mixture of gas and air comes out, when the exhaust is stopped, and gas passed in until 10 to 12 per cent.

is reached, at which it is allowed to remain for four hours. For the fumigation of ships it is found to be much more satisfactory if the gas is made to circulate and to penetrate better by means of electric fans and similar devices. This gas kills rats, rat-fleas, and other insects, and plague bacilli, and, if dry, will not injure food-stuffs, except fruit and some vegetables, nor will it harm merchandise or machinery. A mixture of equal parts of cyllin and petrol constitutes a reliable pulicide and bactericide.

Rats may also be killed by means of Danysz's virus, which is a bacillus easily recognized from *Bacillus pestis*, and kills the rat by a septicæmia, causing œdema of the intestinal walls, infiltration of Peyer's patches, and enlargement of the spleen, with sometimes peritonitis, and only then enlargement of the lymphatic glands. Danysz's virus is administered, by Simpson's method, on bread, and is said not to affect human beings, though recently complaints of illness of persons living in places where some sort of virus was being used has been recorded. Danysz's and similar viruses are very often inert and inefficacious in the tropics and require to be exalted by passage through animals before being used.

Bannerman has strongly advised cats as a method of rat extermination, but it must be noted that cats are not refractory to plague.

It appears to us that Black's methods of dealing with an outbreak of plague are the best. First of all, he localizes the outbreak, and begins his prophylactic measures in a circle well outside this area, and works towards the centre. This is of great importance, because beginning in the centre and working towards the periphery merely disseminates the disease. Secondly, he has recognized the fact that rats will not eat food handled by human beings, and therefore the people who handle and cut the bread into cubes prior to dipping it into poison have their hands smeared with oil of aniseed, as is also the board on which the bread is cut. The poison which he has used with great success is phosphorus paste. The phosphorus is mixed with glucose to prevent spontaneous combustion, and then a paste is made with a fatty base such as lard, but it is advisable to vary from time to time the fatty base. To our minds these little points make all the difference between failure and success. Liston advises the centralization and isolation of the stock of grain in villages, and an organization of the system of the refuse disposal, while the stabling of cattle in houses should be prohibited. He lays stress on the disinfection of the clothes of travellers coming from infected areas. Traps equivalent in number to 2 per cent. of the population should be used to catch rats.

With regard to the destruction of fleas in human habitations, washing the floors and walls with crude oil emulsion such as the one recommended by Burke will be found useful, as demonstrated by Jackson and others. Burke's formula is crude oil 80 parts, whale-oil soap 20 parts. The preparation is a jelly mixing freely with water, and a 10 per cent. solution of it will destroy fleas with certainty, as well as other insects. One gallon of the 10 per cent. solution is sufficient to disinfect a room 12 by 12 in a few minutes; the solution may be washed out afterwards with water. Tobacco and infusions of tobacco will also be found useful, as first demonstrated by Castellani and Low when studying the prophylactic measures to be taken against *Pulex penetrans* infections in Africa.

PERSONAL PROPHYLAXIS.—Ever since the middle of the eighteenth century there has been an idea that a vaccine should be obtained for the purpose of protecting the individual. Weszpremi and, later, Samoilowitz and Cerutti tried artificial inoculation, but the results were by no means satisfactory, persons dying from plague as the result of the inoculation. Recently a number of vaccines have been prepared for the purpose of personal prophylaxis, which may be classified into: (1) Vaccines composed solely of the chemical products of the bacilli; (2) vaccines composed of chemical products and dead bacilli; (3) vaccines composed of living attenuated bacilli; (4) polivaccines.

Chemical Vaccines.—In 1897 Lustig and Galeotti prepared a plague vaccine, composed of the nucleo-proteids of the bacilli obtained by shaking agar cultures with 1 per cent. caustic potash solution, and after two hours adding 0·5 per cent. acetic acid, and thus obtaining a precipitate of nucleo-proteids. It is administered by subcutaneous or intramuscular injections in doses of from 2 to 3 milligrammes. This method has been adopted in La Plata with success, and has been experimentally supported by Rowland.

Vaccines composed of Chemical Products and Dead Bacilli.—The most important is Haffkine's plague prophylactic, prepared by growing the bacillus for four to six weeks in broth, and then sterilizing at 65° to 70° C. for one hour, and then decanting into bottles, with or without the addition of a little carbolic acid. The dose for an adult man is 3 c.c., for an adult woman 2 to 2½ c.c., and children in proportion to their age (or size). The injection is made subcutaneously into the arm or loin under strict antiseptic precautions. Three or four hours after inoculation the temperature rises, and in twelve hours reaches 102° to 103° F., while tenderness and swelling may occur at the site of the inoculation, and malaise and general discomfort be felt, which disappear in one to two days, and the swelling in about a week or so. There is no doubt of the benefit of this prophylactic, which gives protection for a considerable number of weeks, and perhaps months, as shown by Haffkine and Simpson. Haffkine considers that the active principle lies in the liquid, but it appears more likely that it is in the dead bacilli. Haffkine's vaccine has been very extensively used in India and other countries since several years, and on the whole has given extremely good results.

The German Plague Commission used a growth of the bacilli on agar killed by heating to 65° C., and then suspended in normal saline, to which 0·5 per cent. carbolic acid was added.

Terni and Bandi used the sterilized exudate from the peritoneum of guinea-pigs inoculated intraperitoneally with plague bacilli, and killed some little time before they would have died naturally. The exudate is diluted with a solution of carbolic acid and sodium carbonate and chloride, and given in a dose of 1·5 to 2·5 c.c. By this method plague aggressins are produced and used.

Klein has advocated an ' organ prophylactic,' obtained by drying and powdering buboes, spleens, lungs, and livers of infected animals. The dose for an individual is from 5 to 7 milligrammes, made into an emulsion with warm, sterile, distilled water, and injected subcutaneously, but it has not yet been tried on man as far as we know.

Vaccines composed of Living Attenuated Bacilli.—Strong and Kolle have recommended the use of living virulent cultures, and Strong has practically shown that this method of vaccination can be carried out without danger. This vaccination consists of the intramuscular injection of one whole twenty-four hour agar slant of the living virulent culture in the adult, and one-quarter to one-half of such a culture in a child. The reaction is not excessive. About ten days after the inoculation Strong has observed a marked rise in the opsonic index, and that the phenomenon of complement fixation is given by the blood serum, thus proving the presence of specific antibodies.

Simpson, Strong, and Kitasato are of the opinion that Governments should unite to deal with plague by attacking it in the endemic centres by general vaccination of the population.

Polyvaccines.—During the contemporaneous epidemics of plague and cholera in Ceylon, in 1914, Castellani used with satisfactory results a mixed bivaccine plague + cholera, using the local strain of *B. pestis*. He also prepared and used a pentavaccine plague + cholera + typhoid + para A + para B, and an hexavaccine containing in addition Malta fever.

The double vaccine plague-cholera consisted of a carbolized emulsion of *B. pestis* and *V. choleræ*, containing per c.c. 1,000 million plague and 2,000 million cholera organisms. One c.c. was given by subcutaneous injection the first time, and 2 c.c. a week later. The pentavaccine consisted of a carbolized saline emulsions of *B. pestis*, *B. typhosus*, *B. paratyphosus A*, *B. paratyphosus B*, *V. choleræ* containing per c.c. 500 million plague, 2,000 million cholera, 500 million typhoid, 250 million para A, and 250 million para B; ½ c.c. was given the first time and double the dose a week later. The reaction was severe, but not more than after Haffkine's monovaccine. The inoculated persons developed immune bodies for the five diseases. The penta- and hexavaccines have recently been further investigated by Castellani and Taylor, *Journal of Tropical Medicine*, November 1, 1917.

Masks.—These used to be worn in the Middle Ages as a prophylactic measure, the use of which has been demonstrated by Strong and Teague, and by Barber and Teague, in epidemics of plague pneumonia. The best mask is a hood of heavy Canton flannel-cloth covering the entire head and tied round the neck, and provided with a window in front composed of sheet celloidin.

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CHAPTER LV

UNDULANT FEVER

Synonyms—Definition—History—Climatology—Etiology—Pathology—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—Para-undulant fever—References.

Synonyms.—Mediterranean fever, Malta fever, Melitensis septicæmia, Melitococcæmia, Bruce's septicæmia, Goat fever, Mountain fever, Slow fever (Texas), Gibraltar fever, Neapolitan fever, Cyprus fever, Munhinyo (Uganda). *Latin:* Febris Undulans, Febris Sudoralis, Septicæmia Melitensis. *French:* Melitococcie, Fièvre Caprine, Fièvre Cipriense. *Italian:* Febbre Mediterranea, Febbre Maltese. *German:* Malta Fieber.

Definition. Undulant fever is a chronic, rarely an acute, febrile disorder, with many undulatory relapses, caused by *Micrococcus melitensis* Bruce, 1893, and probably other closely allied germs, and usually spread by the agency of goat's milk.

Remarks.—It seems certain that, like enteric, the term 'undulant fever' may cover in reality a group of infections due to very closely allied germs. Nègre and Raynaud have described a *Micrococcus paramelitensis*, and previously to them Sergent and Zammit a *M. pseudomelitensis*. These germs have been proved to differ biologically from the common type of *M. melitensis* by means of agglutination and absorption tests.

History.—Undulant fever has probably existed in the neighbourhood of the Mediterranean for centuries, and passages are cited from Hippocrates recounting cases of long-drawn-out fevers, with short apyrexial intervals lasting as long as 120 days, which may perhaps refer to the disease.

In the eighteenth and the early part of the nineteenth centuries references were made to protracted fevers occurring in Malta by various observers—*e.g.*, Howard in 1786, Hennen in 1816-25, Davy in 1842-62—but it is difficult to be certain what disease is referred to. During the Crimean War there appears to have been a very large temporary increase of the fever incidence in Malta, much of which was undoubtedly enteric, but some of it was not. The change in the type of fever appears to have been so marked that some people thought that a new disease had been imported from the Crimea by the returning troops.

In 1859 Marston, who personally suffered from the fever, first gave an accurate account of its clinical history and post-mortem appearances under the term 'Mediterranean remittent' or 'gastric remittent fever,' distinguishing it clearly from enteric and what he called 'Maltese fever.'

From this date there seems to have been much confusion, for it was often diagnosed as some form of rheumatism, but the disease appears to have been clearly recognized by Boileau, Chartres, Thomas, and others. In 1879 Veale gave an account of it as seen in invalids at Netley, as did Fazio in Naples, who not merely described the disease, but suggested that it might be found to be of bacterial origin.

In 1886 it was proved to be a separate pathological entity by Bruce, who discovered a micrococcus in the spleen. In 1887 he found the organism several times, and was able to cultivate it on agar-agar, and to reproduce the disease by inoculation in monkeys, from which he again obtained the organism in pure culture. In 1889 he published the first full account of the clinical symptoms, and in 1891 he grew the micrococcus from blood aspirated from the spleen during life. Thus, Bruce proved that this organism, which he called *Micrococcus melitensis*, was the true cause of the fever.

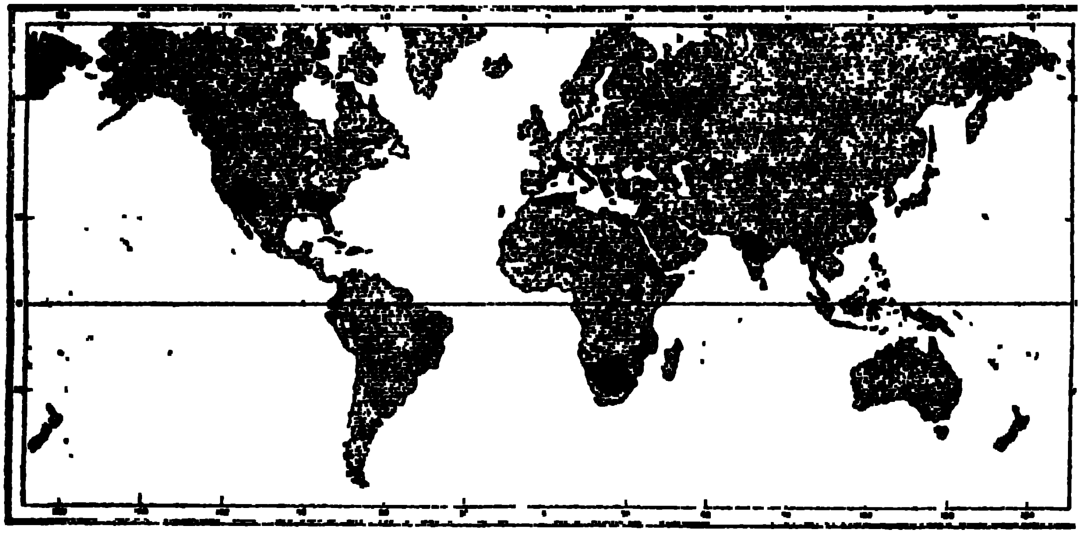

FIG. 671.—DISTRIBUTION OF UNDULANT FEVER.
(After Bassett-Smith.)

In 1897 Wright and Semple showed that the disease could be diagnosed by the agglutination of the micro-organism by the serum of patients, and in the same year Hughes published a full historical and clinical account.

In 1904 a Commission was appointed by the Admiralty, the War Office, and the Civil Government of Malta to investigate the disease. This Commission (J. C. Kennedy, Zammit, Horrocks) demonstrated that the micrococcus leaves the body mainly in the urine, and is then capable of existing for a long period outside the body. Zammit discovered that the milk of many goats agglutinated *M. melitensis*, and Horrocks isolated the germ from such goats. It does not appear to affect injuriously such animals living in the blood-stream, and also occurring in the milk, by means of which the disease is conveyed to man.

Eyre has made the suggestion that undulant fever was primarily a disease of the goat, which had its origin in the Persian hills, and has been carried by these animals all over the world.

Prophylaxis on the lines indicated by the ætiology has resulted in the reduction of the disease in British troops in Malta from 643 cases in 1905 to 7 cases in 1907, and 1 case in 1910. In 1906 Lamb and Pai proved that the organism existed in India in men, while Foster did the same for goats.

In 1912 Bassett-Smith drew attention to the fact that, though the disease has been reduced by prophylactic measures in some places, it had spread to (or been diagnosed in) Spain, Portugal, and France. In the same year Nègre and Raynaud described *M. paramelitensis*, and their findings have been confirmed by Bassett-Smith, who has fully described a case of para-undulant fever contracted in the South of France.

Climatology.—The endemic areas of the disease are, undoubtedly, firstly, the coasts and islands of the Mediterranean, Italy, France, Greece, Spain, Northern Africa, the Levant, etc.; and, secondly, India, especially the Punjab, where the causative organism has been obtained in human beings and goats. We have met with cases in Ceylon. Recently it has been reported from many other parts of the world—in fact, it may be said to be cosmopolitan, and to extend into the interior of the continents. A case contracted in Northern Nigeria has been reported by Low.

It is certainly a disease of tropical, subtropical, and temperate climates, and exists, in addition to the localities mentioned, in Russia, East and South Africa, Uganda, where it is called 'munhinyo,' the Sudan, Mauretania, China, the Philippine and Fiji Islands, North and South America, and the West Indies. It occurs all through the year, but is more common in the warm weather in Malta.

Ætiology.—The cause, as has been indicated in the history, is *M. melitensis*, and some extremely closely allied bacteria, *M. paramelitensis* Nègre and Raynaud, 1912, and *M. pseudomelitensis* Sergent and Zammit, 1908, which can be differentiated by agglutination and absorption tests. *M. melitensis* is found in the spleen, liver, kidney, lymphatic and salivary glands, the blood, bile, fæces (rarely), and probably in the alimentary canal (as Eyre's researches on rabbits indicate), the urine, and the milk. It does not occur in the expired air, the sweat, the saliva, or in scrapings from the skin.

It can be inoculated, and it may be found in the stomach of mosquitoes which have fed upon patients, but neither they nor any other biting fly, such as a *Stomoxys*, or a flea, have been proved capable of spreading the disease. It is, however, very resistant, and can live for eighty days in dust, or in water, fresh or salt, for a month, but has never yet been found naturally in air, dust, soil, or water, neither have any of these in a natural way been proved capable of spreading the disease. It is, however, true that dust, infected with damp organisms from a culture, has infected monkeys, as have suspensions of the organism when applied to mucosæ of the nose or throat. It appears, however, to be best conveyed to animals in food, especially milk.

The organism has also been found by the serum reaction to be present in 50 per cent. of the goats examined in Malta, and has also been obtained from the milk of 10 per cent. of the goats investigated, and, when looked for, it has been found in the blood of goats and other animals. The milk of such animals contains agglutinins for the germ (Zammit's lacto-reaction). Notwithstanding this infection, the animals are quite healthy, though a chronic mastitis, as observed by Neri, may occasionally be noted. It appears to be conveyed to man by infected milk, the best evidence in favour of which is the infection of a ship's crew by the milk of goats, which were being conveyed from Malta to America, 53 per cent. of which were found to be infected.

The distribution of the disease, therefore, depends upon the consumption of infected goat's milk, for people who use this milk will be more liable to infection than others—hence its occurrence in Malta and the Mediterranean districts, in South Africa and India. This is also the reason why the richer classes are more affected than the poorer, and why individual institutions are picked out. It also explains why there is no age or sex incidence, why infants rarely suffer, and why occupation and surroundings have but little influence.

How the disease spreads from goat to goat is not known. Brumpt states that they drink human and animal urine if deprived of salt, and in this way the infection may be kept up. The percentage of infected goats has been found to be 3·4 per cent. in Algeria, 29 per cent. in St. Marthal, 30·7 per cent. in Tunis, 34·2 per cent. in Marseilles, and 50 per cent. in Malta.

Mules, asses, horses, oxen, cows, dogs, rabbits, and fowls, are all apparently capable of spreading the infection, while often they do not show any sign of disease.

The question of the human carrier is only just coming forward with any degree of prominence as a factor to be considered in the spread of the disease, but Shaw has drawn attention to this possibility in Malta, where many of the dock labourers showed agglutinins in their blood for *M. melitensis*, and Missiroli has obtained the micrococcus from the blood of an apparently healthy man who subsequently developed the fever typically in fifteen days.

The carriers and ambulant human cases may pass the *Micrococcus melitensis* in the urine, infecting the soil, and in this way may convey indirectly the malady to other persons.

Four modes of infection are described: (1) By the alimentary canal, which is the usual method; (2) by the respiratory system, inhaling dust contaminated by goat's urine, which is rare; (3) by the cutaneous system, which is very rare; (4) by sexual intercourse, which is possible.

A variety of *M. melitensis*, called *M. paramelitensis*, is described by Nègre and Raynaud as the cause of a variety of fever termed 'para-undulant fever' (see p. 1447).

Pathology.—The micrococcus enters the blood-stream via the mucosæ of the alimentary canal, and causes a genuine septicæmia, with enlargement and congestion of the spleen as the most marked feature; so that the disease somewhat resembles typhoid fever in many of its characters, without, however, producing such typical intestinal lesions as that disease. According to some authors (Ross, etc.), the germ can be conveyed by mosquitoes, but this has not been proved. For clinical and experimental reasons Bruce believes that one attack produces an immunity, but Manson and Bassett-Smith doubt this. The organism produces hæmolysins, while the reaction on the part of the body is shown by the formation of agglutinins, which may last from four to ten years, and a specific serum, which may be useful for immunization. There is also an immune body in the blood suitable for complement deviation, and this corresponds generally with the quantity of the agglutinins.

Morbid Anatomy.—The morbid anatomy shows an enlarged and congested spleen, some congestion of the liver, kidney, and mesenteric glands, duodenum, jejunum, large intestine, and lungs. The spleen is usually much enlarged, weighing from 10 to 44 ounces. It is dark red in colour, and may be soft and friable, and is very congested, with enlarged Malpighian bodies. The liver is congested and enlarged, and shows cloudy swelling, with a round-celled infiltration between the lobules. The kidney is congested, and may show a glomerular nephritis. The alimentary canal may not merely be congested, but the colon may also be ulcerated, particularly in cases of hæmorrhage. The lungs are congested, especially at the bases, and may show patches of consolidation.

Symptomatology—*Incubation.*—Monkeys fed with infected milk require an incubation of fifteen days, while in human beings the period, according to Johnstone, is fourteen days. The prodromata are usually malaise, chilliness, headache, muscular pains, and dyspepsia.

Onset.—The onset comes on gradually, and the patient continues his work though feeling ill, while the temperature rises in a ladder, being higher each evening, and remitting somewhat in the morning. About the fourth or fifth day of the illness a doctor is consulted for the headache, and pains in the body and limbs, which may have been thought to be rheumatic. The patient looks ill, and his temperature is found to be about 103° F., his pulse 80 to 90, and his tongue coated dorsally with a white fur, while the edges are red, and may be indented by the teeth. There is usually a slight sore throat and a tender epigastrium, with some bronchial catarrh or congestion of the lungs, and enlargement and tenderness of the spleen, which develop in the course of a week or so.

Course.—All these symptoms continue for about a couple of weeks, the temperature remaining high—103° to 105° F.—but at the end of this period the fever declines, and the temperature may become normal, while the patient feels much better. In a day or so, however, a relapse occurs with much the same symptoms as the attack. This relapse subsides, and another follows, relapses and intermissions recurring for months.

The temperature now becomes undulating, with a marked rise at night and fall in the morning, while the patient becomes more and more anæmic, weak, and wasted. The alimentary canal is irritated, as is shown by the dyspepsia and the constipation or diarrhœa. The throat may be sore, the gums spongy, and bleed on pressure; the spleen is often enlarged and painful, and the lung may show signs of bronchitis, and occasionally lobular pneumonia, while the heart is easily excited, and hæmic murmurs are heard. The patient shows signs of prostration and headache, and pains all over the body are felt. Insomnia and hysterical emotions are not uncommon, but actual delirium is not usual, and the memory may be impaired, while neuritis—*e.g.*, sciatica—may occur. The skin is pale but damp, due to local or general perspiration, which is very common, and occurs with each remission of the temperature, the sweat being of a peculiar disagreeable odour. Sudamina is not uncommon after the third week. Desquamation may occur, as well as prickly heat, boils, bedsores, subcutaneous abscesses, or hæmorrhages.

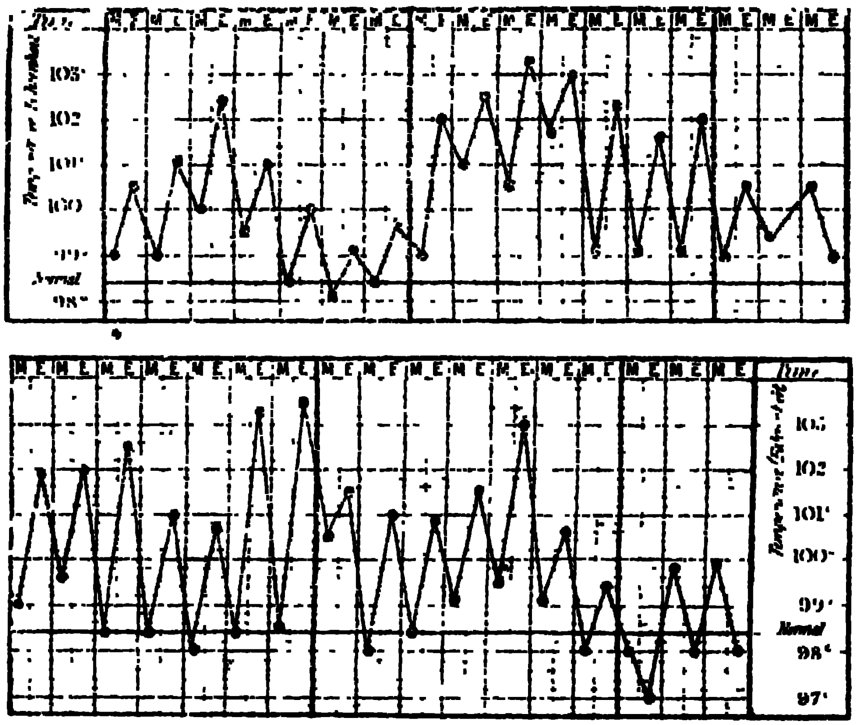

FIG. 672.—TEMPERATURE CHART OF UNDULANT FEVER.

The joints may become swollen and very painful, but the skin over them is seldom reddened. Of all the joints the hip, shoulder, ankle, and knee appear most commonly affected. Inflammation or neuralgia of the testes may occur, and at times the parotid also becomes inflamed.

The blood has been more particularly studied by Bassett-Smith and Gabbi, who find a secondary anæmia with a loss of 20 to 40 per cent. of the corpuscles, with some poikilocytosis and an even greater reduction of the hæmoglobin. The leucocytic count is normal, but there is a decrease in the polymorphonuclears, and an increase in the mononuclears up to as much as 80 per cent. in some cases. Phagocytosis is said to be diminished, as is also the bactericidal power of the blood.

The urine is passed in fair quantity, and has a slightly acid reaction, with a deposit of urates and phosphates, but there is very seldom any albumen, though bile may be present in severe cases, and the specific germ can be found in the urine even two years after an attack. Albuminuria and nephritis may occur, and very rarely hæmaturia.

The patient is now anæmic, and prostrated by the repeated attacks of fever, when gradually the symptoms begin to improve, the intermissions lengthen, the attacks lessen in length and severity, the temperature becomes normal or subnormal in the morning, rising a little at night. Gradually the evening rise diminishes until it stops, the tongue clears, the symptoms abate, and convalescence begins after an illness of from 20 to 300 days, with an average of 90 days.

Varieties.—Two varieties distinct from the typical description given above are recognized by Hughes viz., a malignant and an intermittent—to which a third or ambulatory variety may be added.

The Malignant Variety.—Suddenly, without warning, the patient is attacked with high fever, the temperature rising to 104° or 105° F., with severe pains all over the body, flushed face, and all the other symptoms already mentioned, but in an aggravated form, and often associated with basal pneumonia, and diarrhœa with offensive stools.

After a little the symptoms abate somewhat, but instead of improving, the pulse becomes intermittent, the breathing is laboured, and vomiting becomes serious, and the patient gradually passes into the typhoid state, when hyperpyrexia sets in, and death takes place from the fifth to the twenty-first day of the illness.

The Intermittent Variety.—The onset in this variety is very gradual. When the attack is fully developed, the temperature is about normal in the morning, but rises in the afternoon to 99° or much higher, up to 105° F., this rise being accompanied by malaise, irritability, and chilliness. During the night sweating occurs, and the temperature falls to nearly normal. This fever continues usually for about six weeks, but may be prolonged for about six months, and is usually unassociated with any serious symptoms—in fact, so mild may the attack be that it is not discovered until the patient's general health begins to be unsatisfactory, and he seeks medical advice.

The Ambulatory Variety.—Apparently at times the organism may produce such little effect that the infected person may be unaware that he is suffering from any complaint, and may pursue his daily vocation. Thus, out of 525 dock-hands examined by Shaw at Malta for the serum reaction, 79 gave positive results; and of 22 tested, 9 contained the organism either in the blood or urine, or both.

Complications.—Ulcers may, though rarely, occur in the small and large intestine, and give rise to hæmorrhage, while persistent vomiting, diarrhœa, hyperpyrexia, pneumonia, pleuritis, effusion, and cardiac failure all form serious complications. Orchitis is common. As shown by Frotta, the micrococcus may occasionally acquire a pyogenic action, and cases of suppurative localized periostitis have been recorded similar to those seen in enteric infections.

Sequelæ.—Paralysis, neuritis, common in Cairo, wasting of muscles, loss of memory, tremulousness, and neurasthenia are possible sequelæ.

Diagnosis.—The principal clinical signs on which to base a diagnosis are the prolonged undulant character of the fever, the profuse sweatings, and the articular symptoms.

Bacteriological methods of diagnosis should be always resorted to whenever possible. The agglutination reaction, if the blood is sufficiently diluted (at least 1 in 80), the test properly performed and carried out, using a known and reliable strain of the germ, is, in our experience, sufficiently certain. The agglutination test must be performed in a dilution of at least 1 in 80, otherwise errors in diagnosis will result. Bassett-Smith recommends a high dilution (1 in 1,000), but in our experience 1 in 80 is generally sufficient, with a time-limit of thirty minutes. This reaction is said to last for a very long time *i.e.*, two to seven years. Birt and Lamb have made this serum reaction the basis of prognosis, which is considered to be unfavourable if continuously low, or rapidly altering from a high to a low figure. Agglutinins are present also in the saliva (saliva-reaction of Polacci and others). Whenever possible the agglutination test should be carried out in various dilutions, to avoid results caused by a paradoxical reaction— viz., the possibility of the serum agglutinating in high dilutions and not in low or medium dilutions. In any doubtful case the blood should be investigated for the presence of *M. melitensis*, using nutrose media or Castellani's dilution method, as in enteric infections (see p. 1390). In case of a negative result, the examination should be repeated at least three times at different periods of the disease.

Nicolle and Conor consider that many of the errors are due, firstly, to leaving the serum in contact with the clot, and state that either the blood should be used at once or the serum separated from the clot; and, secondly, in order to prevent obtaining positive reactions with non-undulant fever serum, that sera, to be tested, should be heated to 56° C. for half an hour in order to destroy the non-specific agglutinins, as first recommended by Nègre and Raynaud.

symptom. The physical examination of the patient will reveal nothing abnormal, apart from, occasionally, signs of slight anæmia. The liver and spleen are not enlarged. In a few cases some superficial lymphatic glands may be slightly enlarged. In some cases the red blood cells are decreased. An interesting feature in most cases is the distinct increase in the number of eosinophile leucocytes, even when no evidence of intestinal worms can be found in the motions. The course of the fever is very long. We have seen cases lasting six months.

Diagnosis.—This fever may be diagnosed from *Malaria* by the absence of Laveran's parasites, and by the fact that the spleen is not enlarged; from *Malta fever,* a type of which it closely resembles clinically, by the absence of the *Micrococcus melitensis* in the blood, and the constant negative result of Wright's reaction: from trypanosomiasis by the absence of trypanosomes; from low fever of tubercular origin by the negative cutireaction.

Prognosis.—This is good—*quoad vitam*—but the patient feels weak, tired, nervous, and unfit to do his work properly for months.

Treatment.—A change of climate is always beneficial, and often quickly stops the fever. A long course of injections of quinine cacodylate is useful in many cases. The ordinary preparations of quinine by the mouth or by injection do not influence the fever in the least.

HIGH INTERMITTENT NON-MALARIAL FEVER.

Remarks. This fever has been described by Castellani in 1909 in children in Ceylon.

Symptomatology. Apart, perhaps, from slight anæmia, the child does not show any symptoms except the fever. He takes his food well, runs about and plays, and seems apparently in his usual health. The fever begins in the late morning, and lasts several hours every day, reaching 103° to 104° F. and more. There is no shivering fit at the onset, nor perspiration when the temperature falls to normal. The blood does not show anything abnormal, except, occasionally, a slight degree of anæmia. The course of the fever is very long, lasting at times several months.

Treatment.—Quinine does not influence it in the least. As a rule, a change of climate stops the fever almost immediately.

MOSSMAN FEVER.

Synonym.—Endemic glandular fever.

In 1910 Smithson described a fever, which he called Mossman fever, and which was characterized by an irregular remittent fever of three to twenty-one days' duration, accompanied by painless enlargement of the posterior or subscapular group of axillary glands, which were tender. The symptoms were mild, accompanied by a macular or vesicular rash. It almost exclusively affects sugar-cane cutters. The blood is normal and the death-rate is low, but it may end fatally, apparently from a form of septicæmia. It affects white and black people in the endemic area. The incubation period is six to ten days, and the onset is sudden or gradual.

The mortality is less than 1 per cent., and an attack confers a slight immunity. It is thought that it may be due to some insect on the cane. The dermatitis often found in cane cutters is described in Chapter XCIV. on p. 2163.

In 1913 Clarke described this disease more fully, and in 1914 Breinl, Priestley, and Fielding gave a longer account.

NASHA FEVER.

Synonyms.—Nakra fever, Nakhra Jawhur.

Remarks.- Under the above terms Fernandez, in 1894, described a fever characterized by swelling of the nasal mucosa as occurring in Bengal.

Climatology.—It is found mostly in the months of April to August, and is rare in the cold weather.

Ætiology.—The causation is unknown.

Symptomatology.—The illness is ushered in by a chill associated with high fever and hyperæmia, with swelling of the mucosa of the nose, and pains in the head, neck, shoulders, and small of the back. The face is flushed, the pupils contracted, and there is an eruption of small papules, often accompanied by bronchial symptoms.

The fever, which is usually remittent in character, disappears in three to five days, when the nasal swelling also subsides.

Relapses may occur in one to four weeks, and sometimes a severe relapse may end in delirium, coma, and death.

Treatment.—A saline purgative and a mild diaphoretic are first administered, and then the nose is sprayed with iced water two to three times a day, or the congestion is relieved by pricking the mucous membrane. Tannin and 10 per cent. cocaine solution may also be applied to the nasal mucosa.

TIENTSIN FEVER.

A somewhat similar fever has been reported by A. C. Fox from Tientsin, but in his cases the fever lasted from ten to fourteen days. He thinks it may have been a paratyphoid infection.

It is characterized by sudden onset, remittent fever for ten to fourteen days, frontal headache, constipation, slow pulse. The constitutional symptoms are slight, relapses are rare, and the mortality is nil, while convalescence is rapid. It occurs in persons inoculated against typhoid and having no malaria. It may be enteroidea.

WHITMORE'S FEVER.

Synonym.—Morphine injector's septicæmia.

Whitmore, in 1915, has described several cases of a glanders-like disease in Rangoon, characterized by intermittent fever, bronchopneumonic symptoms, and often multiple abscesses in various parts of the body. The bacillus isolated seems to be very similar to *B. mallei*.

In 1915 Knapp came to the conclusion that this fever might exist in other parts of India, and showed that the disease is due to the contamination of the hypodermic syringe.

WOOLLEY'S FEVER WITH JAUNDICE.

This fever was described by Woolley as occurring in the Andaman Islands. He thinks that it is separate from malaria.

Jaundice appears on the third to fourth day, and in bad cases there are hæmorrhages, delirium, and a rapid pulse, while 40 per cent. of the cases die.

It seems to us that it must be *Febris castrensis gravis*—*i.e.*, Weil's disease.

THE MACULAR FEVER OF TUNISIA.

Synonym.—La fièvre boutonneuse de Tunisie.

Definition.—An acute febrile disorder of unknown causation, characterized by a peculiar macular eruption on the abdomen, palms of the hands, and soles of the feet, which often persists for several days after the temperature has fallen to normal.

Remarks.—This fever was described by Conor, Bruch, and Havat in 1910 in Tunisia, and by other persons more recently.

Ætiology.—The causation is unknown, and inoculations into monkeys were negative.

Symptomatology.—The onset is sudden and accompanied by rigors, fever, pains in the joints, injection of the conjunctiva, nausea, vomiting constipation, and insomnia. The rash appears on the second to fourth day in the form of rose-red or dark red spots about the size of a lentil, which disappear on pressure. The blood shows a lymphocytosis of about 35 per cent. These spots appear upon the abdomen and the palms of the hands and feet. After lasting about two weeks the temperature falls to normal, and after a few days the rash dies away without any desquamation.

Diagnosis.—The characteristic feature of this fever is the distribution of the eruption and the fact that it frequently persists for several days after a normal temperature has been reached. It most nearly resembles Brill's disease—that is to say, a mild form of typhus fever—which, indeed, it may well be.

Prognosis.—This is good.

Treatment.—The treatment is purely symptomatic.

TACAMOCHO FEVER.

In 1918 Henao gave an account of five cases of a fever at Tacamocho, on the Antioquia Railway, Colombia. It was characterized by high fever, vomiting, intense headache, and diarrhœa. The vomit might have blood in it or might be bilious. The liver was not enlarged. There was temporary suppression of urine, followed by albuminuria in the cases which recovered. Two cases died. Microscopical findings did not confirm the idea that it was a form of yellow fever.

KYOTO FEVER.

A fever lasting for seven days in Kyoto, Japan, and described by Masuda in 1918. Ineda found a spirochæte in the blood. The peculiar feature was that adult males of the farmer class were the principal sufferers, and that it produced a cloudiness in the vitreous humour of the eye.

BAN BACH.

Synonym. *La miliaire cristalline fébrile.*

This fever was first described by Montel in 1912, and in 1916 by Saralhé in Cochin China. It is characterized by an insidious onset, followed by six to eight weeks' fever, terminating by lysis, and attended by pulmonary catarrh and a very abundant vesicular eruption, which is difficult to see unless looked for, and which comes out in crops. The skin is dry, conjunctiva yellow, and there is constipation, lassitude, and enlargement of the spleen and liver, with rapid compressible pulse and sometimes delirium. Convalescence is prolonged, and there is a complete loss of hair. Blood tests show no parasites, and are negative for the enteric fevers. It is thought to be infectious. This resembles in many particulars the cases described by Smith and Loughnan at Aden in 1914, but they do not mention the vesicular rash or the loss of hair. Both fevers probably belong to the enteroidea, and should be examined bacteriologically as to the blood and the fæces.

FEBRIS PALUSTRIS REMITTENS.

Described by Ludwig in 1917 as being characterized by an incubation of twenty-one days and a fever of seven to ten days, of a remittent type, with headache, pains in the muscles, weakness, jaundice, and nephritis. It sounds like *enteroidea.*

REITER'S DISEASE.

This was also described in 1917, and resembles the above, but there were pains in the joints, conjunctivitis, iritis, and cystitis, with enlargement of the spleen and fever lasting about seventeen days.

OVOPLASMOSIS.

A fatal fever described by de Raadt in an Annamese aged forty-four years, with enlargement of the spleen, but not of the liver, and with a temperature somewhat resembling subtertian malaria, without malarial parasites in the blood, but with pigment in the mononuclear leucocytes and resisting quinine therapy. The temperature rose very high, and the patient died. Small intraglobular rings were seen staining blue with Giemsa's mixture, and without any trace of chromatin. These were also seen in the mononuclear leucocytes, and were called *Ovoplasma anucleatum* de Raadt, 1913. This sounds like subtertian malaria.

HÆMOCYSTOZOON FEVER.

Hæmocystozoon brasiliense Franchini, 1913, is a flagellate which encysts in the peripheral blood, and was judged to be the fatal cause of a quotidian fever in an Italian physician coming from Brazil.

The fever came on after the removal of a tumefaction in the neck. Spleen and liver were enlarged, and there was great anæmia and emaciation. Brumpt considers that the organism is a *herpetomonas*, and compares the non-flagellate forms to *Schizotrypanum cruzi*, while the flagellate, he thinks, are contaminations, but Franchini does not agree.

He reports that he has found in smears from the liver--

(1) Oval and lanceolate forms 3-6 and 1-2·5 microns, without blepharoplast or flagella. (2) Oval or lanceolate forms, sometimes dividing, 16×3 microns. (3) Flagellate forms, with a flagellum arising near the blepharoplast. (4) Non-flagellate forms with a large nucleus. (5) Encysted forms with chromatinic masses.

The patient had enjoyed good health until three years previously, when he began to feel ill and lost his appetite, while his weight declined. One year later a hard indolent tumefaction appeared on the right side of the neck. This was removed, but the wound did not heal and discharged a white non purulent secretion. He now began to suffer from irregular quotidian fever, preceded by shivering and followed by sweating. The spleen became somewhat enlarged, but the liver gradually extended to the umbilicus, and a cyst formed in the right lobe, puncture of which gave a reddish fluid. The patient now became very anæmic and emaciated. The lymphatic glands were normal, the urine showed traces of albumen, the blood showed signs of acute anæmia, with leucopenia, no eosinophilia, and a few parasites. Puncture of the liver showed more parasites.

No malarial parasites, leishman bodies, spores, or fungi could be found by examination or by cultures. Wassermann's reaction was negative. Sections of the tumefaction showed granulomatous tissue and some parasites.

SEPTIC BILIOUS FEVERS.

A febrile complaint described by Gartan, in 1918, as occurring mostly in women, associated with enlargement and tenderness of the liver, and lasting five to thirty days. One death is recorded.

BUNGPAGGA.

This appears to us to be myositis purulenta tropica (*vide* p. 1975)

ROBB'S HEAT FEVER.

This is described as non-infective cerebro-spinal fever, occurring in East Africa.

NON-MALARIAL QUARTAN FEVER.

This fever, described by Castellani, is characterized by having a quartan periodicity and no malarial parasites in the blood, and quinine given in massive doses does not influence the course, which is prolonged, lasting several months.

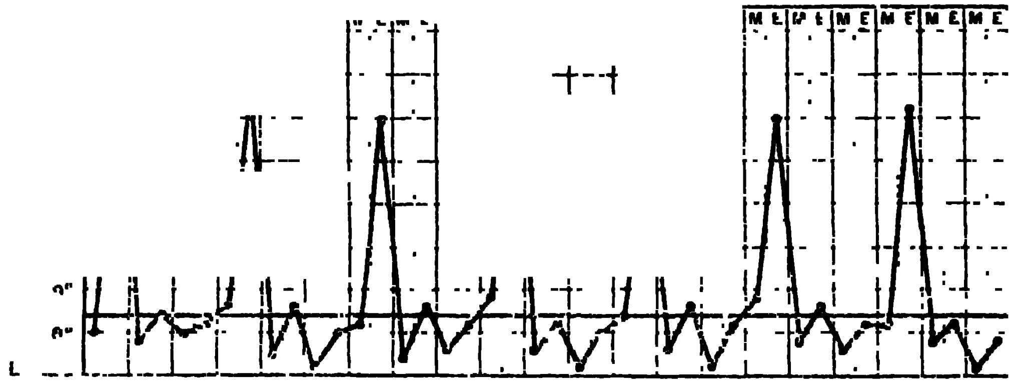

FIG. 677.—TEMPERATURE CHART OF NON-MALARIAL QUARTAN FEVER.

ANÆMIC LOW FEVER.

In young European and native women aged sixteen to twenty-two years there is a persistent low fever lasting for several months, reaching above 99·4° F. in the afternoon and associated with a certain degree of anæmia, which is met with at times. The patient may become extremely nervous and hysterical. This temperature may be due to the degree of chloranæmia, and has nothing to do with hysterical fever of certain authors, as it disappears on the anæmia being treated.

VESICULAR FEVER.

Definition.—A febrile disorder associated with acute pain in some region of the body, followed by the appearance of a vesicular eruption which becomes general.

Remarks.—This is a fever which at its commencement resembles an attack of chicken-pox, and when it is fully developed closely resembles modified smallpox. We have seen several such cases in Ceylon during the last ten years.

Ætiology.—The causation is unknown.

Symptomatology.—At no stage of the illness is the patient severely ill, but the commencement is ushered in with sometimes pain in some part of the body, followed in a day by a rise of temperature to about 101° F. and a quick pulse. The eruption may appear at first in the region of the pain, or may be general from the commencement, which, however, is not relieved, and may, on the contrary, have extended to other regions of the body. The pain gradually disappears, a scattered general eruption of vesicles appears, and the temperature becomes normal, while the patient feels better. The vesicles are discrete, dome-like, or flattened; later, a few may become umbilicated. The size is generally much less than those of chicken-pox, and a few may become umbilicated. There is little or no inflammation of the base. The contents are at first clear and then purulent. Superficial scabbing may occur, and, as a rule, no scars are left, though rarely some scars may be found.

Diagnosis.—The diagnosis is based upon the characters of the eruption, there being no true pustulation, with scabbing and scars, as in smallpox, and by the fact that during convalescence Jenner's vaccination is generally successful.

In chicken-pox the vesicles are generally larger, and often leave thick crusts.

In alastrim the eruption is often confluent, pustular, and clinically almost identical with smallpox.

Prognosis.—This is good.

Treatment.—The treatment is purely symptomatic.

PAPULAR FEVER.

Definition.—A slight febrile disorder, described by Castellani, of unknown causation, characterized by a maculo-papular eruption and rheumatoid pains.

Remarks.—We have seen an epidemic of this peculiar fever in Ceylon: it resembled measles in the appearance of the rash, but was without any catarrhal symptoms.

Ætiology.—This is quite unknown.

Symptomatology.—The disease begins with a prodromal period, during which the patient suffers from malaise, depression, and rheumatoid pains, especially in the back, which are associated with chilliness. After three or four days the rash comes out suddenly all over the body, but most marked on the arms, trunk, and legs, the face being least affected. The eruption is morbilliform, being composed of bright red pin head papules and red maculæ. It is, as already stated, visible on the arms, legs, and chest: while there may be a few maculæ on the palms of the hands and soles of the feet. The face is not much affected, and there the eruption is rather more macular than papular. Filatow's papules in the mouth are absent. There is generally slight fever lasting for a day or two. There are no catarrhal symptoms of the eyes, nose, or throat, no enlargement of the lymphatic glands. The eruption generally lasts between two to five days, and then fades without any desquamation and without leaving any marks. In most cases the eruption is associated with itching, especially on the arms, and in a few cases there is no fever.

Diagnosis.—It is to be distinguished from measles by the absence of the catarrhal symptoms, absence of Filatow's and Koplik's signs, from German measles by its longer duration and the diffuse type of the eruption, from toxic rashes of intestinal origin by the absence of any intestinal symptoms, and from dengue by the rash being frankly papular.

Prognosis.—This is good.

Treatment.—The treatment is symptomatic, small doses of aspirin or pyramidon being given to relieve the pains, and calamine lotion to alleviate the rash.

HÆMORRHAGIC FEBRILE GASTRO-ENTERITIS OF CHILDREN.

Synonym.—Fièvre à Vomissements noirs des Enfants.

Definition.—An endemic fever limited to 'Grande terre' in Guadeloupe, and characterized by black vomit and by occurring only in children.

Remarks.—This disease, which closely resembles yellow fever was first described by Dr. Guesde in 1891.

Climatology.—It is only known in 'Grande terre' in Guadeloupe.

Symptomatology.—The disease begins suddenly with an attack of vomiting, and is followed by an attack of febrile bilious vomiting. The child then becomes very ill, with remittent fever, slight icterus, obstinate constipation, and later black vomit. After lasting from two to five days the symptoms may improve, sleep returns, the fever disappears, and the child gradually recovers; on the other hand, the symptoms may become worse, and the child die. Convalescence is prolonged.

Diagnosis.—The disease seems to us to be indistinguishable from yellow fever.

Prognosis.—The prognosis is always grave.

Treatment.—This is symptomatic.

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CHAPTER LVIII

COSMOPOLITAN FEVERS

General—Epidemic cerebro-spinal meningitis—The exanthemata—Vaccination—Alastrim—Vaccinia in natives—Vaccine rashes—Influenza—References.

GENERAL.

At the present time many so-called tropical diseases have become cosmopolitan, *e.g.*, amoebic dysentery, while others, such as malaria, probably have always been world-wide in their distribution. There are, however, some few fevers which, though they really belong to cool climates, nowadays are of importance in the tropics—for example, the exanthemata and influenza. We think it advisable to give a brief account of these.

EPIDEMIC CEREBRO-SPINAL MENINGITIS.

Synonyms.—Spotted fever. *French*, Méningite cérébro-spin épidémique. *Italian*, Meningite cerebro spinale, *German*, Epidemi Genickstarre.

Definition. An acute specific fever caused by sseria intracellularis Weichselbaum, 1887 (*Diplococcus intracellularis*), and d organisms, spread from man to man by aerial carriage, and characteriz a brief septicaemia, leading to a cerebro-spinal meningitis, and occasion y a more prolonged and dangerous septicaemia associated with a petechial eruption.

History.—The disease may have been known to the ancients, but to our minds the *phrenitis* of Hippocrates and of Celsus has nothing in common with cerebro-spinal meningitis. We have been unable to refer to the works of Aretaeus or of Paul of Ægina, and, therefore, are unable to state whether the disease which they are said by Kutscher to have described in Italy resembled cerebro-spinal meningitis or not, and the same remarks hold good with regard to the epidemic described by Aldere de Lucien.

On the other hand, we have carefully read Sydenham's 'Rise of a New Fever,' which Arnell considers to be identical with the disease which he saw in Connecticut in 1807; and which, he also says, is the same as Cullen's 'Typhus Petechialis' and the disease described in *Medicin. Novissimus*, published at the beginning of the eighteenth century. When superficially considered, Sydenham's new fever does, at the first glance, read like cerebro-spinal meningitis, but when the symptoms are carefully analyzed they will be observed to resemble those of the enteroidea group of fevers, and therefore we are convinced that Sydenham's new fever is not cerebro-spinal meningitis.

We have been unable to peruse Vieusseux's original account of the outbreak in 1805 at and around Geneva, but North's translation in 1811 of the article in the *Journal de Médecine de Paris* makes it quite clear that this was undoubtedly the disease in question, and the same author's verbatim account of Danielson and Mann's article published in the *Medical and Agricultural Register* of Boston, with its careful clinic and post mortem histories, leaves no doubt that these two authors were dealing with an epidemic of cerebro-spinal meningitis at Medfield in March, 1806. North's valuable little book containing all the early histories of the disease appeared in New York.

From this date onwards till about 1884 the whole ground of the history has been reviewed by Hirsch in the third volume of his classical 'Handbook of Geographical and Historical Pathology,' in which he divides the epidemics of cerebro-spinal meningitis in Europe and America into four cycles, viz.:—

(1) 1805-1830, Europe and North America.
(2) 1837-1850, Europe, North America, and Algiers.
(3) 1854-1875, Europe, North America, Africa (parts), Western Asia, and South America.
(4) 1876-1884, small epidemics in former areas, to which may be added:—
(5) 1885 to present time. Recognition of the disease in the tropics, West Indies, Fiji, Anglo-Egyptian Sudan, West Africa, Western Australia, Mexico. Severe epidemics in America and Europe—*i.e.*, this is the period of the first pandemic.

It will thus be seen that the area in which the disease is recognized has gradually extended, and that this has been quicker of late years, probably due to increased facilities for travel which has introduced it by the agency of carriers into lands in which it probably did not previously exist, as, for example, Fiji, the result being that at the present time it appears to be diffused all over the world and to occur as localized epidemics in different places in different years.

In the study of these epidemics certain important features were brought out—viz., the influences of over-exertion, starvation, overcrowding, and bad ventilation, which account for the prevalence of the disease among soldiers and poor people and for its increase in different countries in periods of bad weather—*e.g.*, during the winter and spring in cold climates and during the Haboub seasons of the hot Anglo-Egyptian Sudan, or to a less extent the cold weather of the Sudan, when the people huddle together into crowded, ill-ventilated huts and houses.

The historical portions with which we are mainly interested are those concerned first with its occurrence in the tropics, and secondly with its ætiology.

Occurrence in the Tropics.—The first record we have been able to find of the disease in a subtropical land is the occurrence of an epidemic in 1840-1847 in Algiers, in which country it has, from time to time, been reported. It is also said to have occurred in 1840 in Brazil and in Monte Video in South America.

In 1872 it was reported in Asia from Smyrna and in 1874-75 in Persia, according to Bruce Low in his paper on epidemic cerebro-spinal meningitis published in 1899.

It is believed to have been present in Central America and in the West Indies prior to 1884, but without trustworthy information.

Corney has given an excellent account of the invasion of Fiji by the disease. It would appear that the first cases were noted in 1876 in an immigrant labourer's depot at Levuka, and from that time onwards it was probably diagnosed as tetanus, sunstroke, or meningitis, until it assumed epidemic form in 1885, which he believed was due to the contagion being spread from man to man—a very advanced idea at that time.

Cerebro-spinal meningitis was reported from the West Coast of Africa by the Williams in 1900, and from then onwards from time to time. In 1905 there was a severe epidemic in Northern Nigeria, which was reported upon by Twomey and Davidson, and in 1906-08 in the northern territories of the Gold Coast, where it was ably investigated by Horn. In Northern Nigeria it was said that cattle were attacked, and in the Lorha district of the northern territories of the Gold Coast the natives are said to have noted a great mortality among fowls prior to the epidemic of the disease. According to Bargy and Horn, the disease was marked at this time in French West Africa to the west of the Black Volta.

In 1909 it was reported as being present in 1907 in the northern districts of Togoland by Jaffé, when it was known to cause 300 deaths. Jaffé obtained the true diplococcus of Weichselbaum from his cases.

Epidemic cerebro-spinal meningitis has been recorded in British East Africa since 1906, when Haran noted five cases, and has been ably described by Shircore and Ross in 1913.

In 1915 Butler drew attention to *a curious feature* of the disease, in that there are places in East and Central Africa where it has always been endemic and seldom epidemic, and he quotes Uganda in general, whilst in the highlands of British East Africa the endemic form is seldom seen, but epidemics of greater or less virulence are known. He says that in one tribe alone between 20,000 and 40,000 deaths are attributed to this disease, a mortality which sleeping sickness can hardly be said to rival.

In India it appears to have been first reported by Vandyke Carter as occurring in July, 1878, in Bombay, where he says that he is not aware that it had been previously recognized. He does not appear to have published this observation until 1882, and then only in his work 'Spirillum Fever,' p. 436, when he gives not merely a clinical but a post-mortem account of one case and clinical histories of three others. As he has been said not to have recognized the disease, it may be well to note that he heads the paragraphs in question *cerebro spinal meningitis*.

In 1884 Dimmock gave a full account of an outbreak in the preceding year in the Shikarpur Jail. Since then some cases have generally been reported year by year, and the whole subject of epidemic cerebro-spinal meningitis in India was ably reviewed by Robertson-Milne in 1906.

In 1905 Castellani described two cases which occurred in Singhalese natives in Ceylon.

In 1910 Chalmers and O'Farrell published a series of investigations upon the disease as seen in the Anglo Egyptian Sudan.

History of the Organism. In 1875 Klebs was the first to see cocci in the cerebro spinal fluid of cases of meningitis, and to assign to them a causal function. He was followed by Eberth in 1881, in which year Gaucher was the first to see micrococci in the blood and urine in a patient during life and in the exudate from the spinal canal after death; and in connection with these findings in the blood one may invite attention to the observation of Cole in 1915, who obtained films of the peripheral blood in which ten out of 2,000 leucocytes showed the organism, and also to Osler's statement that Gwyn in 1899 was the first to isolate the organism from the blood in pure culture. In 1883 Ughetti also found micrococci in the exudate and in the blood, and in 1884 Marchiafava and Celli wrote a short work on the occurrence of micro-organisms, and especially diplococci, in cerebro spinal meningitis. They were also seen in meningeal exudates by von Leyden in 1883, and by Leichstenstern in 1885, and the last mentioned observer noted that they resembled the gonococcus by being found in the leucocyte.

In 1886 Senger also noted them in the cerebro-spinal exudate, while Fränkel with Weichselbaum, Foà with Bordoni, Uffreduzzi, and Lemoine described the pneumococcus as the causal organism of a series of cases of cerebro-spinal meningitis unassociated with pneumonia.

In 1887 Weichselbaum published his paper 'Ueber die Ætiologie der akuten Meningitis Cerebro-spinalis,' in which he described eight cases of meningitis without pneumonia, two of which were due to the pneumococcus and six were caused by an organism which differed therefrom by being generally a diplococcus, more rarely arranged as tetrads, and resembling the gonococcus, being often contained in leucocytes and being Gram negative. He, however, distinguished this organism from the gonococcus by the fact that it produces in subcultures on agar agar slopes a flat viscous growth which is greyish when seen by reflected and greyish-white when examined by transmitted light. It only grew at incubator temperatures, and had but a slight vitality. This organism he called *Diplococcus intracellularis meningitidis*, and looked upon its action as being toxic in nature, while he hesitated to regard it as the causal agent of the disease.

Although Weichselbaum's observations were confirmed by Goldschmidt in 1887, and by Edler and himself in 1888, they produced comparatively little influence, and were almost unnoticed until a polemic was started in 1890, which raged till 1893, as to the identity of Bonomé's streptococcus of epidemic cerebro-spinal meningitis first reported in 1890, and Foà's meningococcus and the *Diplococcus pneumoniæ*, in which it was decided that Bonomé's organism was the pneumococcus, but the confusion was increased by Bordoni, Uffreduzzi regarding *D. intracellularis* as a variety of *D. pneumoniæ*.

This unhappy condition was accentuated in 1895, when Jaeger, while studying a regimental epidemic of fourteen cases occurring in Stuttgart, found the pneumococcus in two cases, a streptococcus in one case, and in eleven cases an intracellular Gram-positive diplococcus morphologically resembling the gonococcus, producing turbidity in broth, and forming short or even at times long chains, while it retained its Gram-positive character in cultures. It grew well on gelatine at the temperature of the laboratory, and preserved its vitality during fourteen days or more on artificial media. He concluded that this organism was Weichselbaum's *D. intracellularis*, and in this unfortunate conclusion he remained unopposed for years, and was supported by Heubner in Berlin in 1896, who not merely was the first to obtain a coccus from the cerebro-spinal fluid during life, but who produced a fatal meningitis in goats with this germ, which at the time was considered to be an important experiment, as an epizoötic meningitis was present in horses and horned cattle in Germany; further, he proposed the name meningococcus for this organism, notwithstanding the fact that Bonomé had already used it for the pneumococcus mentioned above.

This meningitis cerebro-spinalis enzootica, or epizoötic cerebro-spinal meningitis, is often called the *Borna disease*, because of the attention paid to a malignant outbreak in horses at Borna in 1894.

It is obvious that it must be of the greatest importance to definitely settle the question as to whether (as is generally believed) the two diseases are quite separate, or whether there is some relationship between the human and some undefined fraction of the animal complaint.

Thus we see that confusion has arisen not only between a disease seen in animals, but also between two human organisms.

Jaeger and Heubner's results were more or less confirmed by Holdheim, Petersen, Urban (1897), Rameny (1898), Vanzetti (1901), and many others, while Kiefer, Kister, Kischensky, and Berdach and Fioz supported Weichselbaum, and so great a confusion arose between the Gram-negative *Diplococcus intracellularis* Weichselbaum 1887, and the Gram-positive coccus of Jaeger and Heubner, which is also known as *D. crassus* von Lingelsheim, 1906, that every coccus found in connection with the meninges was considered to be a true meningococcus.

In 1898 Still showed that posterior basic meningitis was associated with an organism like *D. intracellularis*, and Councilman, Mallory, and Wright obtained Weichselbaum's coccus from thirty-one cases of the disease, while Faber in 1900 found the same organism in an epidemic in Copenhagen, and Canuet in the same year showed that it was an obligatory aerobe.

Pfaundler in 1899 recognized both the Weichselbaum type and the Jaeger-Heubner type, and in this he was supported by Hunter and Nuttall and by Lazarus-Barlow in 1901, in which year Albrecht and Ghon, reporting upon the 1898 epidemic at Trefail in Steiermark, not merely confirmed Weichselbaum's researches, but were the first to obtain the organism by cultural methods from the naso-pharynx of cases of the disease, an observation which is now of almost daily occurrence, although we are still uncertain as to the proportion of cases which become permanent carriers. They also obtained Gram-negative cocci in the throats of fifteen healthy persons who were contacts with cases, and in one such person the meningococcus was identified by cultural tests.

In 1902-03 Bettencourt and França, in Portugal, found the meningococcus to be present 271 times in 274 cases of cerebro-spinal meningitis, and Lepierre in 1903 described a meningococcus which, although originally Gram-negative, became Gram-positive, and the same year saw the *Meningococcal polemic* between Jaeger, as representing the German school, and Weichselbaum, Albrecht, and Ghon on behalf of the Austrian schools, as a result of which Weichselbaum's organism became firmly established.

In 1905 Kob and Weyl wrote on the subject of Gram-negative and Gram-positive diplococci, and in the same year Castellani described Weichselbaum's organism in cases in Ceylon, and Dunn and Gordon reported upon an epidemic simulating influenza in Hertford in which they obtained *Micrococcus catarrhalis* and forms resembling the meningococcus. It was during this investigation that Gordon brought forward the carbohydrate tests as differential agents for the meningococcus, a point which he further elaborated in 1907, in which year Buchanan introduced a modification of Loeffler's blood serum by adding neutral red in a proportion of 1 in 10,000.

The outbreaks of cerebro-spinal meningitis in 1905 in Prussia and New York produced excellent work, in the former by von Langelsheim and by Kolle and Wassermann with reference to the organism, which, together with the labours of other collaborators, was published in one volume in 1906. In this epidemic von Langelsheim found the meningococci to be present in 23·12 per cent. of the cases, but, as many of the samples came from a long distance, it is interesting to note that he obtained 70·0 per cent positive results from examinations in the hospital near the laboratory and taken during the first day of illness, and 60·0 per cent. in those taken from first to fifth day of the illness, while he obtained 24·5 per cent. from sixth to tenth day, 11·29 per cent. from eleventh to twentieth day, and only 4·39 per cent. after the twenty-first day. Thus in three weeks 90 per cent. of the cases were free from meningococci, but he found that 15 per cent. of the contacts became carriers. He also gave an account of *D. crassus* and, with Leuchs, of experiments on animals with the meningococcus.

The American epidemic was investigated by Elser, Durham, Goodwin, and Sholly, and produced results similar to those of von Langelsheim, and in the same year Robertson Milne reported upon cerebro-spinal meningitis as seen in India.

In this year Kutscher described a coccus in the naso-pharynx of carriers which agreed morphologically and culturally with the meningococcus, but which could be differentiated by Castellani's absorption test, and Westenhoeffer stated that the primary focus of the disease was in the pharyngeal tonsils, post-nasal region, and the nasal sinuses, in which in the early days of the disease he reported that it caused an inflammation. In 1907 Taylor investigated the opsonic index with a view to diagnosis. In 1909 Elser and Huntoon named Kutscher's organism the *Pseudo-meningococcus*. At first it was thought that organism was rare and had nothing to do with the disease, but, when Gordon and Murray's researches mentioned below are considered, it is obvious that it would agree with such of their groups as do not agglutinate with and absorb intracellularis serum; at the present it is only differentiated from the strains with which Kutscher and Elser and Huntoon were working, and may or may not be the same as Dopter's parameningococcus, which is mentioned below.

In 1908 von Langelsheim gave the following differentiation of the organisms found by him in the naso-pharynx of the contacts. —

(1) *Micrococcus catarrhalis*.- Frequent, colonies, dry crumbling; when seen under microscope granulated, generally with irregular borders. Attacks neither grape sugar, nor maltose, nor levulose.

(2) *Diplococcus flavus I.*- Colonies on ascitic agar very similar to those of meningococcus. Twenty-four hours' culture exhibits clear yellow pigment in thick layer.

(3) *Diplococcus flavus II.*- Colonies polymorphic, sometimes moist and glistening, sometimes dry and wrinkled. Twenty-four hours' culture exhibits yellow pigment in thick layer.

(4) *Diplococcus flavus III.* -At commencement difficult to cultivate, and therefore rarely coming under observation. All three species of *flavus* form acids in the presence of grape-sugar, maltose, and levulose; whilst the meningococcus ferments only grape-sugar and maltose, the latter regularly.

(5) *Diplococcus mucosus.*- Colonies more prolific and juicy than those of meningococcus. Grows also on gelatine at room temperature. According to many authors, markedly pathogenic for mice.

(6) *Micrococcus cinereus.*—Coarse, uneven granular. Colonies and cultures

delicate, reminding one of *D. crassus*. Does not attack grape-sugar, levulose, and maltose.

He also considered the possibility of the spread of the disease by insects, by dwellings, and by clothing, food, and water, and concluded that none of these were effective agents in the propagation of the disease.

In 1909 there appeared a most important work by Elser and Huntoon in which they described most carefully the cultural, biochemical, and serum reactions of the meningococcus and its allies, as well as its viability, and especially its selective affinity for the cerebro-spinal fluid, a point little considered by the majority of investigators. They also considered the subject of mixed infections, which was dealt with by Specht in the following year.

In the same year Dopter described his *Parameningococcus*, which was not agglutinated by meningococcus serum (a fact confirmed by Gordon and Murray in 1915), but showed complement fixation. Two years later he described seven cases of cerebro-spinal meningitis as being due to this organism, and in 1912 used Castellani's saturation test to differentiate it from the meningo-

The agglutination reactions of the meningococcus are unsatisfactory, as may be gathered by a study of Elser and Huntoon's careful work, as well as by the discordant results obtained by numerous observers. In 1915 Hine instituted a rapid method of preparation of a high titre agglutinating serum in rabbits, and Gordon and Murray investigated genuine strains of meningococci obtained from the cerebro-spinal fluid of cases, and found that by agglutination tests and by Castellani's absorption method they could split up thirty two strains into the following groups:—

(I.) With serum from No. 1, 19 strains.
(II.) With serum from No. 20, 8 strains.
(III.) With serum from No. 28, 4 strains.
(IV.) With serum from No. 32, 1 strain.

They also distinguished by these sera Dopter's paramenigococcus from all the other groups, and they noted that one strain absorbed the specific agglutinins from two groups, while out of ten carriers one belonged to Group (I.) and five to Group (II.), while the others were not classified.

In the same year Crowe attempted to meet the difficulties met with in the agglutination tests by devising a simpler method.

We have now given a rough sketch of the history of Weichselbaum's organism, and we might well pause, as Crowe has done, and ask where do we stand as regards its recognition.

It is admitted on all sides that there is a close resemblance between the gonococcus and the meningococcus, except as regards the human diseases which they produce, and, indeed, many years ago it was suggested that the latter might be the former adapted to the cerebro-spinal nervous system and the naso-pharynx, but to-day it is admitted on all sides that they are separate, mainly because of an experiment in which the meningococcus was found not to cause gonorrhœa when injected into the human urethra.'

As regards the meningococcus, we can aptly quote Crowe, who, writing in 1915, says:—

'The present state of our knowledge so far as it bears on the carrier may be summed up:—

'No Gram-negative organism isolated from the naso-pharynx can be proved to be a meningococcus.

'No Gram-negative organism which resembles even faintly a meningococcus can be regarded with certainty as incapable of producing meningitis.'

Hence we have not improved our position since the days of the meningococcal controversy, but are actually in a position of greater uncertainty as to the differentiation of Weichselbaum's *Diplococcus intracellularis*, and, this being so, we will now briefly review our position as to the causal relationship between this organism and epidemic cerebro-spinal meningitis.

Indeed, this is exceedingly necessary at the present time, because, firstly, a certain amount has been written with regard to the so-called pleomorphism of the meningococcus—*e.g.*, the papers in 1915 by Lundie, Thomas, and Fleming, and by Donaldson in the same year, while in 1915 and 1916 Hort, Lakin, and Benians have doubted the causal action of the meningococcus, and in the last publication Hort has stated:—

'In order to discover the true infective agent, whether biologically related to the meningococcus or not, further research is imperative, attention being particularly directed to filtrable organisms in the naso pharnyx and cerebro-spinal fluid of acute cases.'

With regard to the question of filtrable organisms, Chalmers and O'Farrell have performed an experiment of this nature with a fresh cerebro spinal fluid, but the result was negative.

With regard to the meningococcus being the causative factor in epidemic cerebro-spinal meningitis, the above observations make it sufficiently clear that it has been regularly found in the cerebro spinal fluid of persons suffering from the disease, and that it has been found in the blodd and also in the urine when looked for at the correct time or in suitable infections. It is also generally present in the naso pharynx of the cases, and was found by Sophian, Westenhöffer, and others in such complications as arthritis, pyelitis, pneumonia, endo carditis, and in purulent conjunctivitis from a virulent [illegible] ie disease.

Epidemiological studies easily convince anyone associated with the disease that some contagion can at times pass from the sick to the healthy, causing an attack of the disease, and, moreover, as we have pointed out above, many of the contacts show the meningococcus. It is true that, as a rule, but few attendants on cases acquire the disease, [illegible] here are marked exceptions.

It is also true that the accidental infec[illegible] Sicler of his own nose with a culture from the laboratory pro[illegible] a severe rhinitis, but he did not develop meningitis, and one of us accidentally infected his thumb from some cultures, with the result that hæmorrhagic granulation tissue formed from which the germ was recovered, cultivated, and tested biochemically, and agreed with the meningococcus in these details. Although the lymphatic glands enlarged and a mild chronic fever lasting for months ensued, with almost constant and sometimes very severe headache, no meningitic symptoms developed, although the opsonic index varied from 0·8 to 1·3, until meningococcal vaccine therapy cured the condition.

In the first case it is possible that the coccus never got into the system, and in the second that it never entered the blood-stream, and hence the lack of meningeal infection.

Turning now from man to experiments upon animals, von Lingelsheim and Leuchs, followed by Flexner in 1906, reported successful inoculations of monkeys subdurally. They were followed in 1908 by M'Donald, but neither he nor Davis in 1905, nor any of the above experimenters, were able to infect animals by injections into the blood-stream, although M'Donald produced an acute toxæmia by this method, nor were Kolle and Wassermann or Davis able to reproduce the disease in the same animals via the nose. Elser and Huntoon consider that the value of these experiments is questionable when the *peculiar affinity* of the meningococcus for the leptomeninges is taken into account. They point out that other organisms injected subdurally will cause a meningitis, but no other common pathogenic organism shows a similar *selective action* for the meninges of man.

Further, it is to be remarked that Bettencourt and França and Kolle and Wassermann were unable to infect monkeys even by means of subdural injections, and this has happened to us both with fresh cerebro-spinal fluid from which growths were subsequently obtained and with cultures, although we have also had successes.

Only Councilman, Mallory, and Wright have succeeded in infecting a goat when dealing with the true meningococcus, and Vansteenberghe and Grysez produced meningitis in rabbits and guinea-pigs, but it seems to us to be doubtful whether they worked with a true meningococcus.

We have been unable to peruse Flexner's original papers, but according to Batten the general circulation became infected in his monkeys.

We shall give below reasons why carriers do not become infected, and it is possible that monkeys may be resistant except when damaged by an operation like trephining or otherwise below par; moreover, the meningococcus is often damaged in the drawn fluid and degenerated on cultivation, for we have seen it fail to infect a monkey after five generations of growth of the same organism which was infective during the second generation.

We now turn to inquire in what way the human body reacts to the organism. Davis showed in 1907 that at the end of the first week agglutination up to 1 in 50 could be obtained, and in the eighth week up to 1 in 200, and pointed out that the agglutinins were thermostable, resisting a temperature of 65° C. for an hour, while they appear to be practically absent from the cerebro-spinal fluid, but many observers, including ourselves, have found this test uncertain.

Davis in 1905 showed that the coccus multiplied in two normal defibrinated bloods, but in four other bloods it was killed, as it was by the blood from patients after the tenth day. He noted that the meningococcidal power of the blood serum of patients which seemed to be greater than that of normal blood serum was diminished by heating to 60° C. for thirty minutes. He found that the phagocytic index was 13 for normal human serum, 0 for serum heated to 60° C. for thirty minutes, while in meningitic serum from cases between the second and seventh week of convalescence it was 11·1. Normal cerebro-spinal fluid did not contain opsonins.

Houston and Rankin in 1907 found that opsonins were exceedingly low in normal serum, and lower still in cerebro spinal fluid, while in cases from the sixth day onwards they rose remarkably, except in two fatal cases, while in one relapse the rise was postponed till the eleventh day.

MacGregor observed that the highest indices occur in the second and third week of the disease, but that the degree of immunity after recovery, as measured by the opsonic index, was variable, and concluded that a high opsonic index was a sign of forcible reaction to a fairly severe infection.

Meakers and Dopter have shown the presence of immune bodies in the blood of meningitic patients by means of complement-fixation, and McKenzie and Martin have also demonstrated the presence of these bodies by injecting the serum of recovered cases intraspinally into other acute cases with fair results. It would therefore appear that immune bodies are formed in patients' systems, which is in support of the causal action of the meningococcus.

We now turn to see whether specific serum treatment and vaccine therapy will help the problem.

With regard to the serum treatment, Jochmann in 1905 experimented with a specific immune serum which was afterwards manufactured by Merck. He tested his serum by the opsonic test, the bactericidal test, and by agglutination.

Kolle and Wassermann also made an immune serum upon which they reported in 1907.

In 1906 Flexner wrote upon a specific serum which protected monkeys and small animals. Later this serum was made from immunized horses, and has been extensively used.

With regard to vaccine treatment, Davis in 1907 was the first to inject killed meningococci into normal persons and into patients suffering from the disease, and Collis in 1913 tried specific serum treatment together with vaccine therapy. In the same year Sophian reported on his experimental inoculation of eleven medical students, and eleven months after these inoculations Merck re-tested eight of them, comparing the results with those of a normal person and a recently recovered case, and concluded that a person *so vaccinated may consider himself to be immune for at least one year.*

In October, 1915, Surgeon-General Rolleston reported upon sixteen cases of vaccine treatment with four deaths and twelve recoveries; the vaccine, however, was never used alone, but combined with serum treatment in some form or with soamin. In his report lumbar puncture alone in thirteen cases resulted in four deaths and nine recoveries, serum intrathecally alone forty-three deaths and nineteen recoveries, or alone and combined with vaccine, soamin, or hexamine, sixty-four deaths and forty-one recoveries, while symptomatic treatment gave ten deaths and four recoveries.

In 1916 Chalmers and O'Farrell, studying an outbreak of cerebro-spinal meningitis in the Anglo-Egyptian Sudan, came to the following conclusions:—

1. The important causal agent is *Neisseria intracellularis* (Weichselbaum, 1887), and only once has *Diplococcus crassus* von Lingelsheim, 1906, been found acting in this capacity, and so far no other organism.

2. Only *man* has been found to be the host of *Neisseria intracellularis*, and he acts in this capacity as *the true carrier* of the germ, and as such does not acquire the disease because of an *immunity* conferred by autovaccination.

3. In order to acquire the disease, two factors at least are required, viz.:—

(*a*) Infection with *Neisseria intracellularis*.

(*b*) Lack of capability on the part of the body to produce the necessary *immunity*.

The infection takes place from the nose of a carrier or a case to the nose of an uninfected person, and is favoured by overcrowding and bad ventilation. The lack of power to produce the necessary immunity is favoured by poor and insufficient food, bad hygienic conditions, and over-exertion.

4. In susceptible persons the germ passes into the mucous membrane of the nose and of its connected cells, and multiplies therein, and then entering the blood-stream forms in the early days of the disease a bacteriæmia. Normally, however, it does not long remain in the blood-stream, and therefore normally does not produce a prolonged septicæmia, which, when present, should be considered as a complication. Apparently the organism is strongly attracted to the cerebro-spinal fluid, into which it quickly passes via the choroid plexus of the lateral ventricle, and perhaps other vascular structures of the brain and spinal cord, and so causes the disease.

The reason why the cocci as a rule do not pass in relays day after day from the mucous membrane of the nose into the blood is because the patient is either dead or the resistance is raised in a short time, but if this resistance again becomes lowered it is possible that relays may again pass from the nose, and in this way a relapse or recurrent attack ensues.

5. There are various strains of *Neisseria intracellularis*, and to be successful in treatment a *polyvalent serum and a polyvalent vaccine made from local strains* are necessary. Vaccine alone will cure many cases, but requires time to act, which may not be available, and hence the value of the serum in such cases, especially when followed by subsequent vaccine therapy.

6. Prophylaxis depends upon

(*a*) The search for, isolation of, and treatment of cases and carriers, and here vaccine therapy is of use in helping to cleanse cases and carriers.

(*b*) The increase of the immunity of the general population, which can probably be done by prophylactic vaccination in doses of 5, 50, and 100 millions, but further experience is required of this when given on a large scale. There is little doubt that a negative phase is produced, at all events at times, in the first stages of the vaccination, and this may possibly be aggravated by fear, poor or insufficient food, and bad hygiene. It also appeared to them that vaccine prophylaxis ought to be tried on a large scale, as it causes no general or local symptoms if the germs are killed at 50° C., and the vaccine is aseptic and isotonic with the fluids of the body, and if the site of injection is the subcutaneous tissue just below the angle of the scapula, which in their opinion is the best place for prophylactic and other subcutaneous injections.

7. There are a great many questions with regard to epidemic cerebro-spinal meningitis which are at present unsolved, and one of the most important appears to be the question as to whether any animal or animals act as host of the germ.

In 1917 the Medical Research Committee of the National Health Insurance issued a report on bacteriological studies, and in 1918 upon serum treatment in connection with the disease.

Ætiology. The causal agent in the large proportion of cases is *Neisseria intracellularis* (common name: meningococcus) or one of its immediate allies.

It lives in the naso-pharynx of healthy people whose opsonic index for the germ is abnormally high, and it passes from these carriers to healthy people, who may, according to their resistance, become carriers, temporary or permanent, of the germ, or victims to the disease.

Its ætiological relationship depends upon.—

1. Its presence in all cases of the true epidemic disease.
2. Its pure culture from these cases, and the reproduction of the disease in monkeys by inoculation of cultures.
3. The sera of persons suffering from the disease can agglutinate and give positive complement-fixation with meningococci obtained from other patients.
4. It produces a protective mechanism in carriers which is lacking in susceptible persons.

Pathology.—The meningococcus appears to enter the blood via the mucosa of the nose and air sinuses, but it quickly leaves this fluid and enters the cerebro-spinal fluid via the choroid plexuses, and perhaps by other routes. Arrived in the cerebro-spinal fluid, it causes a cerebro-spinal meningitis.

Morbid Anatomy.—In fulminating infections meningitis is absent, and little is to be seen beyond hæmorrhages in various parts, while the cerebral vessels are intensely congested and the perivascular subarachnoid spaces show scattered patches of pus.

In ordinary fatal cases there is considerable amount of purulent exudate in the subarachnoid, the most intense being over the uppermost part of the vertex.

In chronic cases there may be but little sign of pus and no vascular congestion, but the ventricles are distended by a quantity of fluid, the pressure of which causes flattening of the convolutions.

Symptomatology—*General Remarks.*—As seen in the tropics the disease is of sudden onset, with or without a rigor, but with marked headache, vomiting, and fever. The next day there is often some remission in the symptoms, but with stiffness in the muscles of the neck and sometimes Kernig's sign. On the third day vomiting returns, with headache and a condition of *resistant stupor*, retraction of the head and Kernig's sign, and from this time onwards the symptoms in fatal cases go from bad to worse and the patient dies within four to six days of the commencement of the attack. If the case is to recover, the symptoms begin to abate about the seventh to eighth day, the temperature falls to normal, and convalescence begins.

Slightly fuller details of this usual type may be given.

Incubation Period. Judging by persons who have left an uninfected area, visited an infected and returned to the uninfected area, the incubation period is short, varying from two to five days, and more usually about four days, but there are obvious fallacies in this calculation, and it may perhaps be better to admit that the length of time of the incubation period is only approximately known.

Attack. The onset is sudden and may begin with a rigor in an adult or convulsions in a child, but these may be absent. The patient feels very ill and exhibits three so-called cardinal symptoms, viz., fever rising to 102° to 104° F., vomiting, marked headache, which may be associated with severe giddiness. As the first day progresses there may be pain and stiffness in the neck and some retraction of the head. If the blood be examined at this early stage of the disease, only a moderate amount of leucocytosis, amounting to about 10,000 cells per cubic millimetre, will be found, while the differential count will show an enormous preponderance of polymorphonuclear leucocytes, amounting to over 90 per cent. in some cases.

Blood cultures are usually very successful at this early stage of the disease, but not later in uncomplicated cases. By direct examination of blood films Gram-negative diplococci can be seen in about 1 per cent. of the polymorphonuclear leucocytes examined, while a very few similar organisms may be found outside the cells. Even at this early stage of the disease the cerebro-spinal fluid is usually more or less turbid, and shows a variable number of white cells, which may amount to 20,000-30,000 per cubic millimetre, and of which some 98 per cent. are polymorphonuclear leucocytes, while the remaining 2 per cent. are generally mononuclears. As the day goes on there may be pains in the limbs and some slight catarrhal symptoms in the nose and throat.

Slight Remission.—On the second day there is often, but not always, a slight remission of the symptoms, which may be assigned to the treatment, but which is really part of the disease.

Course.—On the third day, if there has been some slight remission the symptoms all return, as violent as before, the temperature continues to be high, but the pulse varies—it may be quick or it may be slow—the respirations are irregular, vomiting returns, and there is an intolerance of light and noise, while the stiffness of the neck, the retraction of the head, and Kernig's sign, become well marked, and headache, insomnia, restlessness, and delirium may be present, or the patient may be huddled up in a state of *resistant stupor*, from which he can be temporarily roused.

This is about the time at which a rash should appear, but this must be extremely rare in the tropics, as we have never yet met with it in this ordinary acute type of the illness. Flushing may be present and herpes of the lips may develop, but the petechial rash is extremely rare. The leucocytosis is now more marked.

Terminations.—During the fourth and fifth days death is not uncommon, but the symptoms may persist and death occur later on, somewhere about the sixth to eighth day or later, the temperature may decline, the symptoms abate, and the patient become convalescent.

Varieties.—Such is the common course of the disease, but there are other types—*e.g.*, the fulminating type, spotted fever type, chronic type, abortive type, infantile type.

The Fulminating or Septicæmic Type is associated with a sudden attack, rapid development of coma, and death in a few hours. It is often associated with a purpuric rash, with petechial or large hæmorrhages. The cerebrospinal fluid may be quite clear when first examined, but it contains a number of meningococci, and in a few hours has a typical appearance and shows polymorphonuclear leucocytes.

Usually by the time death has taken place there is sufficient evidence of pus at the vertex of the brain to support the diagnosis, even without microscopical examination. There are, however, cases which die before this pus is formed, and then the brain and meninges are congested, but the pia mater at the base shows patches of cloudiness due to pus cells.

Spotted Fever Type.—Somewhere between the first and the fifth day generalized petechial eruption may appear, which is most marked on the inner side of the knee, but it may also be found wherever there is pressure—*e.g.*, the great trochanter, the points of the shoulder, etc. It is a sign of severe toxæmia, and when exaggerated becomes the purpuric rash. *Other rashes* are:—A macular rash appears at times after the second day. It comes out in one crop, and is seen on the lower part of the abdomen and the thighs, but may occur on the forearms, legs, hands, or feet.

A fugitive erythema or blush has already been mentioned.

Chronic Type.—The acute symptoms of an attack pass away, the temperature may become normal, but the patient does not improve, and fever of an irregular type may or may not return, while opisthotonus may occur, wasting set in, and the patient slowly die of exhaustion, the amount of cerebro-spinal fluid obtained by puncture becoming less and less and thicker and thicker as time passes on.

Abortive Type.—These are cases which, though beginning with the ordinary symptoms, undergo the remission on the second day, are much better on the third day, and convalescent on the fourth day or thereabouts.

Infantile Type.—This is the so-called cervical opisthotonus of infants, a symptom which is *en evidence* by the fourth day, while as a rule there is little or no fever, but considerable and progressive wasting and marked vomiting. It is chronic and has a high mortality, death commonly ensuing in four to six weeks after the onset.

Mimicry.—At times the disease imitates enteric fever, broncho-pneumonia, gastro-enteritis, or rheumatic fever.

Relapses.—These are not uncommon, and are usually mild in type.

Sequelæ.—There is usually some permanent damage to the nervous system in cases which recover.

Diagnosis.—The cardinal early signs are:—(1) The sudden onset; (2) the headache and sense of general illness; (3) the vomiting; (4) the fever; (5) stiffness in the neck muscles; (6) the presence of the meningococcus in the cerebrospinal fluid as obtained by lumbar puncture.

The *Differential Diagnosis* has to be made from malaria, relapsing fever, typhus, enteric, influenza, and pneumonia.

From ***malaria*** it can be recognized by the absence of the leucopenia, the presence of the leucocytosis, and the absence of malarial parasites from the blood, as well as the absence of a large spleen. It may, however, occur in a malarial subject, but the leucocytosis will be present.

From ***relapsing fever*** it can be separated in the early stages by a blood examination revealing the absence of spirochaetes.

From *typhus* it can be distinguished by the vomiting, by the stiffness in the neck, and Kernig's sign.

From *enteric* it may be diagnosed by the headache and delirium occurring together, by the rigidity of the neck, Kernig's sign, and lumbar puncture.

From *influenza* it may be differentiated by Kernig's sign and by lumbar puncture, which may relieve some of the symptoms of a cerebral influenza.

From *pneumonia* by the irregular pulse-rate, the presence of Kernig's sign, and the absence of those of consolidation of the lungs.

Prognosis.—This is always serious—firstly, *quoad vitam;* secondly, with regard to after-effects.

Treatment.—Systematic daily lumbar puncture, with the withdrawal of a few cubic centimetres of cerebro-spinal fluid and the intrathecal injection of anti-meningococcal serum, in quantity to be judged by the amount of cerebrospinal fluid withdrawn at the time and by the blood-pressure and pulse-rate.

In cases where the pus is very thick an attempt to wash the spinal canal by intrathecal injections of warm sterile saline, followed by serum injections, may be tried.

In chronic cases or relapses vaccine therapy may be attempted.

Symptomatic treatment and careful nursing are also required.

Prophylaxis.—The proper method in prophylaxis is to avoid overcrowding, bad hygiene, and to provide ample space, good ventilation, and ample and good food for a community. When an attack has begun the sick and their attendants should be isolated, or the attendants should be constantly examined bacteriologically and have systematic naso-pharyngeal disinfection.

Contacts should be isolated and examined bacteriologically on three separate occasions, and have the naso-pharynx disinfected.

A search for carriers should be made in the immediate neighbourhood of the patient, and these carriers should be isolated and treated.

The nose and fauces should be sprayed with a solution of 1 per cent. iodine, 2 per cent. menthol in parolin, or if this is too expensive with ½ per cent. watery solution of formalin, which may be snuffed into the nose if an instrument is too expensive. This solution of formalin is especially useful for natives; it is rather too strong for Europeans.

If this fails and the carriers be isolated and placed under improved sanitary and dietetic conditions, vaccine treatment is beneficial, and may succeed when under other conditions the natural vaccination of contained organisms will fail. General vaccination of the population may be tried, but it is not certain as yet whether it will be successful or not, as the application so far has been limited.

THE EXANTHEMATA.

Scarlet fever has often been introduced into the tropics, but it does not spread. Thus we have seen cases introduced into Colombo from the steamers, but there has never been an epidemic of scarlet fever in that town to our

knowledge, nor have we seen an indigenous case. The tropical practitioner should be careful not to mistake for true scarlet fever, cases of scarlet fever-like eruptions such as *erythema scarlatiniforme*.

Measles is endemic in most tropical countries, but differs in no important details as a rule from the same disease in the Temperate Zone, except that when first introduced into Fiji it gave rise to a severe epidemic, and is still severe in Oceania.

FIG. [illegible] CHICKEN-POX: [illegible] DAY OF THE ERUP

Chicken-pox in the tropics is very often a disease of the adult, being most common in India in February to March. The majority of the cases are mild, but some are severe, and there may be great difficulty in diagnosing chicken-pox from smallpox. Varicella cannot be transmitted to man very readily by inoculation. Rabbits' cornea can be inoculated, and fine granulations have been described by several observers in the epithelial cells, which may be early stages of a cytoryctes arrested in its development, which would support the people who believe the two diseases to be closely allied.

VARIOLA.

Synonyms.—Smallpox. *French*, La petite vérole; *Italian*, Vajuolo; *German*, Blattern; *Spanish*, Viruelas; *Arabic*, Jadari.

Definition.—Variola is an acute specific fever of unknown causation spread by various agencies, but especially by air, and characterized by a more or less general eruption passing through the stages of papule, vesicle, pustule, crust, and often scar.

History.—There can be no doubt of the great antiquity of the occurrence of smallpox in India and Africa, but whether it arose *de novo* in these two centres we cannot say, but there is a suspicion that there are two varieties of the disease—viz., the ordinary smallpox, which may have had its origin in India and spread to Europe, and so to America, and later to the islands of Oceania; and an African variety variously known as South African Amaas, or milk-pox, which may have been imported by the negro slaves into the West Indies, where it is called West Indian modified smallpox. Apart, however, from conjectures of this nature, there are the facts that in India there was a special worship defined in the Atharvaveda, and there were special prayers to be said by the Brahmins when performing the operation of inoculation of smallpox virus. References in the Charaka-Saṁhitī and the Susruta-Saṁhitī make it almost certain that the disease was well known when they were written. It would appear that the disease was introduced into China perhaps from India, in the course of the third century B.C.

Equally ancient is the evidence of the existence of smallpox in Africa, for Ruffer and Ferguson have found an eruption on the skin of a mummy belonging to the period of the twenty-eighth dynasty (1200-1100 B.C.), which they believe to be suggestive of smallpox, and it is quite possible that there has existed from time immemorable an endemic focus in Africa, perhaps in Central Africa.

From these two foci in Asia and Africa it would appear probable that the disease has spread all over the world. With its introduction and spread in Europe we are not concerned, but with that into America a few remarks must be made, as it is very interesting. It would appear not to have been known in America until after the advent of the Spaniards, it is first recorded as occurring in the West Indies in the year 1507, when it was introduced from Europe, as has happened on many occasions since—e.g., into Chili in 1554—also by the agency of the Spaniards.

More interesting than this is the fact that it is recorded that importations of slaves from Africa were often followed by the appearance of the disease—as, for example, in Brazil, where, according to Piso, it appeared in 1560, being introduced in this manner.

With regard to Oceania, it has been introduced from Asia or America at various times—as, for example, Australia in 1838, from China to Sydney, the Hawaiian Islands in 1853, from San Francisco to Honolulu; while New Caledonia became infected in 1859, and Marquesas in 1863.

To-day the disease is widespread all over the world, but is especially common in the tropics, where institutes for the preparation of calf-lymph are urgently required in order that efficient vaccination, the only method of keeping the disease in check, may be successfully carried out.

Climatology.—It is believed that smallpox is perhaps most active at the present time in Central Africa, but if this is true certainly some portions of tropical Asia must come very nearly equal in endemicity, and briefly the disease, though world-wide in its distribution, is of the utmost importance in the tropics. When first introduced among peoples previously unaffected with the disease, it was most virulent—as, for example, its incidence on the Mexicans and the North American Indians.

Ætiology.—The causation is unknown, but various protozoal bodies have been described, of which the most important is *Cytoryctes variolæ* Guarnieri, 1892, minute spherical homogeneous bodies, to 4 μ in diameter, and staining well with Romanowsky, when it takes on a chromatin coloration, while Councilman and his colleagues have described a complicated life-history (p. 535).

Whatever the virus may be, it is usually spread by the air, and enters the body by means of the respiratory passages. Cases are on record of the infection being probably carried by cotton from Egypt to England, and there starting sporadic outbreaks, and this is possible if the cotton was handled by an infected person. Hence the request for the vaccination and revaccination of cotton-workers.

Symptomatology.—This is described in all books on general medicine, and need be only very briefly repeated here.

Briefly, a typical attack of discrete smallpox, after an incubation of nine to fifteen days, begins with a chill in an adult and a convulsion in a child, and continues with high fever, severe headache, lumbar pains, and vomiting, with or without a scarlatiniform or morbilliform rash on the second day, which may be general or local; or hæmorrhagic rashes, which are either petechial or petechio-erythematous, which appear from the first to the third day. If these latter rashes are associated with hæmorrhages from the internal organs, they indicate the onset of hæmorrhagic smallpox. Generally the initial stage of the disease lasts two days, but it may be shorter and milder than that recorded above, or more severe. The peculiar odour of a smallpox case may be noted in these early stages.

The typical rash appears on the second, third, or fourth day as papules on the face, arms, back of the wrists and hands, and, later, on the trunk and limbs; and at the same time on the mucosa of the mouth, nose, and throat, and more rarely on the vulva, vagina, and rectum. Generally it is more marked on the extensor surfaces of the limbs than on the flexor surfaces, and is often most marked in areas where there has been pressure. The papules are bright red in colour, but this may not be very evident in the dark skin, 2 to 3 millimetres in diameter, and have a hard, shotty feeling. As the rash comes out the temperature falls, and the initial symptoms improve. On the fifth to sixth day the papules become umbilicated vesicles, which turn into pustules when the umbilication disappears, and a surrounding areola of injection appears. During the maturation of the pustules the secondary fever appears, and the eyelids become swollen and closed. In the discrete form the fever disappears by the tenth to eleventh day, and convalescence sets in.

The confluent type of smallpox is more severe than in the above, and presents much less difficulty in its recognition, and need not be described.

Varieties.—There are, however, two varieties which are of importance in the tropics—viz., variola hæmorrhagica and varioloid—and these must be mentioned at greater length.

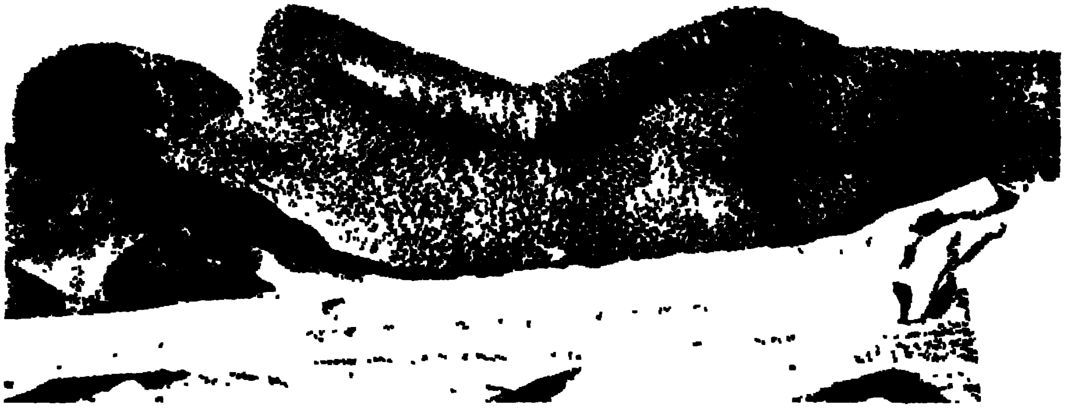

FIG. 679.—SMALLPOX.

(From a photograph by Balfour.)

VARIOLA HÆMORRHAGICA. Hæmorrhagic smallpox is, or was, by no means rare in Africa, and is met with in Asia, though by no means so frequently.

There are two varieties: *Purpura variolosa* and *Variola hæmorrhagica pustulosa*.

Purpura Variolosa. This variety commences with the same symptoms as ordinary smallpox, but they are much more severe. The fever is not considerable, and may be below 100° F., but the pains in the body, especially the backache, is very severe, and the vomiting may be very persistent and associated with severe epigastric pain. The pulse and the respirations are both much increased in frequency. At the end of the second or the beginning of the third day an erythematous rash appears in some part of the body, very often in the groins and flexure of the joints, but it may be absent, or it may extend and become general. At the same time and in the same places appear red and purple petechiæ, and about the same time subconjunctival hæmorrhages in one or both eyes, while purple spots appear on the forehead, eyelids, and face, and ecchymotic areas in various parts of the skin, and also on the tongue and pharynx. The patient now becomes pale and anæmic, except where the blotches are situate, and bleeding occurs from the mucous membranes and internal organs, of which the most common are oozing from the gums and hæmaturia, but epistaxis, hæmatemesis, hæmoptysis, melæna, and metrorrhagia, may one or all be present. Even retinal hæmorrhages may occur.

The temperature is now below normal, the patient is restless, with often a sensation of weight in the præcordium. The pulse is now soft and compressible. Sordes form on the gums, and the patient dies on the third to sixth day, with a clear mind and often without any sign of the typical smallpox eruption.

Purpura variolosa fulminans.—Very rarely the disease is more severe, with a temperature of 105° F. or more, associated with delirium, coma, and collapse, and followed by death in a few hours without any signs of external hæmorrhage.

Variola hæmorrhagica pustulosa.—In this variety the initial symptoms are severe, and delirium sets in early. Hæmorrhages appear from and under the mucous membranes and under the skin, and at the same time the typical smallpox eruption appears, into which blood also passes. The symptoms resemble those of confluent smallpox, with the addition of hæmorrhages.

A milder form is when the hæmorrhage occurs only into the eruption, and may or may not be associated with hæmaturia and some bleeding from the mouth.

Varioloid - Repeated vaccination is an excellent protective against smallpox, but if the disease does appear in a person who has been several times vaccinated, it is remarkably modified and is most difficult to recognize. Epidemics have been known to show such a mild type that the disease was mistaken for a length of time for chicken-pox, and have also been considered to be due to a new form of disease, to which such names as 'Cuban itch' and 'Philippine itch' have been given. Indeed, such epidemics have in some cases not been recognized until a fatal case has occurred, and Osler and McCrae have recorded a small outbreak in one of their wards for coloured patients in which the disease was at first mistaken for chicken-pox.

The varieties of 'Varioloid' are numerous. In the first place, there may be no eruption, and the usual initial symptoms may be slight, or they may be severe and accompanied by an erythema, but all symptoms disappear by the third or fourth day.

In other cases the disease begins with the usual symptoms, but at the end of the first day a few maculæ appear, which become vesicles in another twenty-four hours, when the constitutional symptoms begin to abate, and are full grown in about three to four days, when they are seen to be conical vesicles, often without any depression, surrounded by a very faint red line. On the third to fourth day they become somewhat opaque, and then shrink and desiccate forming small dry prominences on the skin, which finally desquamate, and the patient is convalescent. In other cases a few vesicles may become pustules by the sixth day of the eruption, which dry up and cast off their crusts in about a week.

Diagnosis. -The headache, the severe backache, the epigastric pain, the vomiting, the high temperature, and the rapid pulse, associated with an erythematous or petechial eruption on the abdomino-crural region, are important factors. The erythema, however, is apt to be irregularly distributed in blotches, but it does not affect the face. The petechial eruption is usually found about the flexures of the joints as small bright red petechiæ. Any acute febrile disorder associated with purpura should be suspected as being probably variola.

The typical eruption comes out on the second or third day of the illness as hard shotty papules on the forehead, face, arms, and legs, which have become papulo-vesicles and pustular, presenting umbilication, and *not* flattening on pricking.

From Varicella.—The first point in the differential diagnosis between smallpox and chicken-pox is to remember that it is very difficult, and that the most distinguished physicians have owned to not one mistake, but a series. No one point of absolute diagnostic value can be given, but the following table will indicate some of the points —

Sign or Symptom.	*Chicken-pox.*	*Smallpox.*
Initial symptoms ..	Absent as a rule, but may resemble smallpox.	Usually well marked, but may be absent.
Temperature ..	Does not fall with the appearance of the rash.	Falls with the appearance of the rash.
Situation of rash ..	Most marked on the trunk.	Most marked on the face and limbs.
Vesicles	Develop in twelve to twenty-four hours; are rarely umbilicated, collapse on pricking, all stages, papules, vesicles, and flattened scabbing, puckered pocks, appear together.	Papules hard and shotty; are slow in developing; vesico-pustules are more commonly umbilicated; eruption more uniform, and the scabbing margin is not puckered.

From Measles.—The diagnosis from measles may be made as follows.—

Sign or Symptom	*Measles*	*Smallpox.*
Catarrhal symptoms	Lachrymation, coryza, cough present from the beginning and marked	Usually absent, but there may be some conjunctival effusion.
Filatow or Koplik's spots	Usually present	Absent.
Eruption	Appears on the third to fourth day as minute pink papules behind the ears, on the forehead, chin, cheeks, neck, limbs, and chest. Papules not hard or shotty	Initial measly eruption on the first or second day on face, trunk, and limbs simultaneously. If partial, appears in the abdomino-crural area. Papules hard and shotty
Temperature ..	Reaches its height with the appearance of the rash.	Falls with the appearance of the rash.

From Influenza, etc.—In German measles the initial severe symptoms are absent, and in the fourth disease the face is free, while in influenza the typical eruption fails to appear.

From Typhus.—The diagnostic features are —

Sign or Symptom.	*Typhus.*	*Smallpox.*
Erythema	Appears on the third to fourth day of the illness.	Appears on the first or second day of the illness.
Typical eruption ..	Petechial. Appears on the fourth or fifth day, and is rarely seen on the face.	Papulo pustular. Appears on the third or fourth day, and is common on the face.

From Hæmorrhagic Diseases.—Any case of high fever of an acute nature associated with purpura may be smallpox. It is extremely difficult to separate hæmorrhagic measles and scarlet fever from hæmorrhagic smallpox, but in the former diseases there is not so much bleeding from the mucous membranes. The isolation for sixteen days and vaccination of all contacts, and the isolation of the sick are the most important.

Prophylaxis.—As smallpox is endemic in nearly all tropical countries, it is important that the natives should be taught concerning it, and the fact that vaccination is an excellent prophylactic measure, and this should be done by verbal instruction and by vernacular pamphlets, if possible illustrated; in this way the native prejudices, which are usually not strong, must be overcome. Secondly, vaccination should be made compulsory by law; and, thirdly, a vaccine service should be established. This vaccine service should consist of an institute for the preparation of lymph, with a reliable man to make the lymph, an inspector of vaccination, or more, according to the needs of the country, and a series of native vaccinators.

ALASTRIM.

Synonyms.—*African*, Varioloid varicella, Amaas, Kaffir milk pox, *American*, West Indian modified smallpox, Epidemic varioloid varicella; *perhaps* Pseudo-smallpox (Kersten), Sanaga smallpox (Plehn).

Definition.—An acute specific fever resembling in all its symptoms and pathological appearances a mild form of variola.

History.—As already stated in the history of smallpox, there is a possibility that there were originally two distinct endemic foci of variola—viz., Asia and Africa—and therefore, bearing in mind the different varieties of relapsing fever, it is hardly surprising that there should be at least two varieties of smallpox, even though the clinical symptoms are similar, and Guarnieri's bodies are found in both. Moreover, the disease is known in Africa and America, and there is no reason why it should not occur also in Asia when the considerable intercommunication between India, Ceylon, and China, with Africa, is considered. One of the earliest descriptions is by Anderson, in 1806, of an epidemic in 1805 in Jamaica, and there was another epidemic described by Dickson and Lasselle in 1903, while Korte gave an account of amaas, or Kaffir milk pox, in 1904. In 1905 Welch and Schamberg gave an account of it in their work on 'Acute Contagious Diseases' in 1908; Scheult described it as seen in Trinidad from 1902 to 1904; while Grant, in 1910 described 'amaas' as seen in South Africa, and in the same year Ribas describes it as seen in Brazil in 1900, and Carini as seen in the States of St. Paul, Minas, and Paranà.

Ætiology.—The causation would appear to be the same as that of ordinary smallpox, as it is generally agreed that Jenner's vaccination is protective, and Guarnieri bodies have been found, and the classical reaction in the inoculated cornea of the rabbit has been produced; after sixty hours the Guarnieri bodies have been recovered from the cornea, but it would appear to be due to an attenuated virus.

The question which has been much debated is whether it is smallpox, chicken-pox, or a new disease halfway between the two. In the first place, there are still some persons who disbelieve in the difference between variola and varicella, but their objection is usually disregarded. In the second place, alastrim differs from varicella because of—

1. Confluence of the vesicles in certain cases.
2. Its frequency among adults.
3. The partial protection by Jenner's vaccine.

It differs from variola vera by—

1. Its low mortality (1 to 2 per cent.).
2. Because it is less severe in children than in adults, and is often found among babies, in whom the vesicles are often small.

3. There is no secondary fever in children.

4. Though Jenner's vaccine is in some degree protective, the disease can occur after recent successful vaccination.

5. Jenner's vaccination can be successfully carried out shortly after an attack of alastrim.

6. According to some authorities, an attack of smallpox does give a lasting immunity to alastrim.

Provisionally we may conclude that it is probably a slightly different form of disease from true variola.

Symptomatology.—It begins with high fever, severe pains, and vomiting, with very often delirium. The rash comes out on the third day, when the temperature descends, the symptoms disappear, and the patient feels so well that he may resume his ordinary avocations. Secondary fever is usually absent, especially in children, but may occur about the eighth day. Papules become pustules and scabs, and these drop off, leaving little scarring, but only pigmentation.

FIG. [illegible] TRIM. (After Rib

Complications.—Hæmorrhagic cases are unknown.

Mortality.—The death-rate is remarkably low, about 1 to 2 per cent.

Prophylaxis.—The usual isolation, quarantine, and vaccination of contacts and cases must be adopted.

VACCINATION.

Vaccination from arm to arm is very dangerous in the tropics, as syphilis, yaws, relapsing fever, sleeping sickness, etc., may be inoculated. It should therefore only be performed when calf-lymph is not available, and only by means of children under eight years of age who are found to be healthy. These vacciniters can be sent to suitable districts if necessary; and if the amount of lymph required is considerable, two or three drops of glycerine may be placed on the vesicles, which are then punctured in several places, and the mixture used for immediate vaccination. With regard to the systematic work, *lanolated* seed-lymph can be obtained from many institutes at present, for example, from the Lister Institute in London.

Preparation of Lymph.—The vaccine institute requires an inoculating-room, a preparation-room for the lymph, an office, a store-room, a good stable for the calves—all of which should be rendered flyproof, and should have cement floors and be as cool as possible, and have a good supply of water. The special apparatus required are means for sterilization, Dornig's hand roller machine for trituration, and Entrican's machine, fitted with a small Geryk pump, for filling the tubes, as well as the ordinary glass and other materials of a laboratory.

The lymph should be obtained as lanolated seed-lymph from a reliable institute, and should be inoculated into fair-skinned heifers, not into black-skinned heifers, which should be specially fed during and after inoculation.

When tubes of calf lymph cannot be obtained, monkeys may be directly inoculated from cases of variola, and the calves may then be subinoculated from the monkeys, and if calves cannot be obtained rabbits may be used.

All animals should be carefully isolated and watched for a week before being used for inoculation. During this period the temperature should be taken and a tuberculin test applied.

When lymph first arrives in a tropical country from the temperate zone it requires to be acclimatized—that is to say, its virulence should be increased by passing it through about three calves before use, otherwise failures may occur.

The calves are vaccinated on the shaved abdomen, which has been washed with soap and sterile water, by linear incisions, about 1 inch apart, into which the lymph is gently and immediately rubbed, and a sterile cloth tied over the vaccinated area. No straw should be given for bedding, but a wooden grating should be used, and the calf's head should be secured by two tie-ropes to prevent it licking the inoculated area.

The lymph may be collected after 96 to 120 hours by first washing the area with soap and water, then with sterile water and a sterile gauze mop, and then removing the contents of the liver vesicles by means of a Volkmann's spoon.

The lymph is now weighed and mixed with an equal weight of sterile distilled water or glycerine, and after being worked into a paste is triturated until it is in an extremely fine condition, and if urgently required is treated with a stream of chloroform vapour for fifteen to thirty minutes, after which sterile air is bubbled through until no chloroform remains, and another part of sterile water and 2 parts of sterile glycerine, or 3 to 5 parts of anhydrous lanoline are added. The lymph is now filtered through a special fine sieve into test-tubes till nearly filled, and stored in cold climates for four to five weeks at a temperature of 15° to 20° C., when the number of micro-organisms is found to have decreased considerably. The chloroform method of purifying the lymph is to be preferred in the tropics, as it is much quicker. The technique is found in any modern work on the preparation of lymph.

A bacteriological examination is always necessary, especially to discover whether tetanus bacilli are present, and if these are found the lymph must be rejected. The lymph must be stored at temperatures at 5° to 10° C.; if this precaution is not used the lymph becomes inert very quickly in tropical countries.

The capillary tubes are filled in a vacuum in the Entrican filling-machine, and should be tested for vaccine activity before being issued.

Lanolated lymph, not being sterile, is more apt to contain a large number of micro-organisms. Dried lymph has been placed upon the market, and is now on trial on a large scale.

In vaccinating natives the left arm should be used about the middle, and not near the shoulder.

Vaccinia.—The only modifications in vaccinia between the Native and the European is the difference produced by the colour of the skin, and the greater risk of septic sequelæ; therefore the area of skin should be carefully cleansed before being utilized for vaccination.

The slight redness and swelling due to the scratches disappear in twenty-four hours, while the papules appear on the third to fourth day, and are succeeded by the vesicles, which become umbilicated pustules about the eighth to ninth day. These quickly begin to dry in the centre and form a scab, which falls off about the fourteenth to twenty-first day and leaves a scar.

VACCINATION RASHES.

Generalized Vaccinia.—This eruption is rare, but has been reported upon in natives by Hill and Ross in Natal, and by Chalmers and Archibald in the Anglo-Egyptian Sudan. It appears some twelve to twenty-two days after vaccination, associated with fever, in the form of a generalized papular rash, which as a rule comes out during several days. The papules form vesicles which become umbilicated, and then the case resembles closely a very mild attack of varioloid. The vesicles pass on to pustules, and these to scabs, which eventually leave small depressed scars.

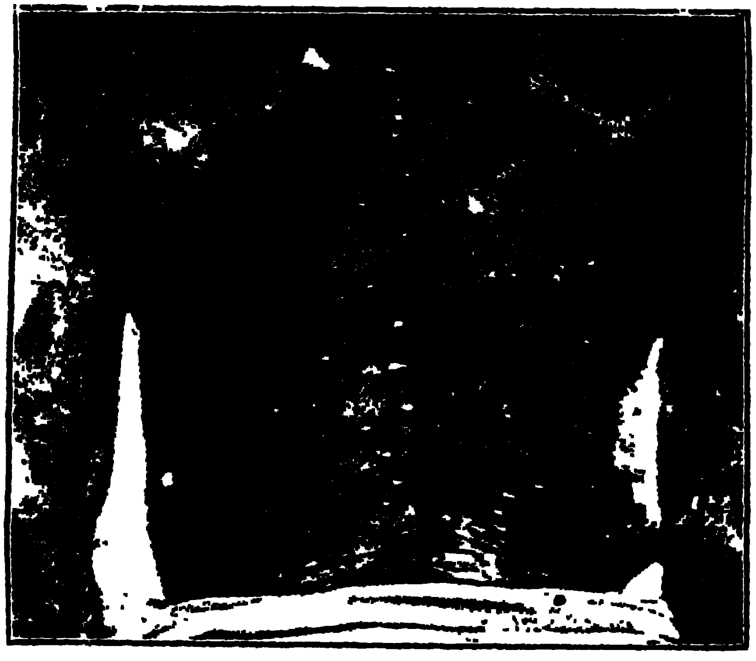

FIG. 681.—GENERALIZED VACCINIA.

In a typical case the rash appears twelve to twenty-two days after vaccination, requires some six days to reach its full development, and another eight days to decline to the stage when the scabs are thrown off and the patient is convalescent.

Localized Gangrenous Vaccinia.—Fortunately this is a very rare disease, but has been met in the tropics by Chalmers and Archibald. It occurs in cases in which no reasonable precaution has been omitted to guard against septicity in the performance of the vaccination, and, indeed, there may be no sign of septic infection in the disease, of which the following is a typical case:—

During the first three days after vaccination there was nothing to report, but on the third day the area became red and swollen, and on the fourth there was a number of small vesicles.

On the fifth, although there was only slight fever, the patient felt ill, while some of the vesicles ruptured and discharged their contents.

On the sixth day the vaccination area was covered by a yellow crust, and surrounded by a ring of vesicles and by a congested dark red area measuring about 1 inch in diameter. The temperature on this day did not exceed 102° F.

On the seventh day the crusted area became quite black, and extended until it measured some 2 inches in diameter. It was surrounded by a ring of umbilicated vesicles and by a dark red border measuring 1 inch in width, outside of which was a light red area of about the same depth. The whole region felt somewhat brawny to the touch, and the temperature rose to between 104° and 105° F.

On the eighth day the condition of the leg may be described as follows:—

In the centre there lay a black slough some 2 inches in diameter, surrounded by a ring of collapsed vesicles and by a raised dark red border, which, in its turn, was surrounded by a purplish area of skin some 3 inches in width, while, finally, the whole area was defined by a red zone of about an inch in diameter. On this day the temperature did not exceed 103° F., and the patient felt better, though the leg looked worse.

On the ninth day there was a decided improvement, the ring of vesicles had dried and formed a circular scab, the brawny resistance was softer and was beginning to disappear at the edges. The purple hue was lighter and showed signs of becoming reddish in places. The surrounding red area had, however, extended down to the ankle and up to the knee. The temperature did not exceed 102° F

From this date onwards the signs and symptoms began to steadily improve. The temperature fell slowly, remaining about 101° F. for two days, about 100° F. for another day, and then reached 99° F. The purple area became reddish and the reddish area white.

At this stage an attack of *acute gout* set in, beginning on the thirteenth day, when the temperature, which had never reached normal, rose to 100° F. The gouty symptoms were marked in the left hip, left arm, left side of the jaw, left wrist, the back, and the right ribs. These symptoms lasted some seven days, but gradually gave way to the usual remedies, and the temperature slowly sank to normal.

During this time the slough, mentioned above, came away, and a clean, healthy-looking, healing surface was left at the bottom of a depressed ulcer with raised, but not undermined, red edges, while the surrounding skin had returned to its normal colour.

There were no enlarged lymphatic glands, and no signs of sepsis. The urine was febrile, but did not contain albumen or sugar.

The patient made a good and rapid recovery.

Ætiology.- In attempting to define the causation of the above condition it is important to clearly distinguish between *localized gangrenous vaccinia* and the condition called *dermatitis gangrænosa infantum*, as the latter is a generalized eruption probably of septic origin, following *Varicella* and other pustular eruptions in children, and often assumed to have something to do with vaccination.

Localized gangrenous vaccinia, on the other hand, is quite different. It is not septic, but vaccinal in origin, and it is not generalized, but localized to the vaccination area.

Acland, Crocker, Balzer, and Hutchinson have met with similar cases, some of which are stated to have ended fatally.

In such cases as Chalmers and Archibald have been able to find any account of, there has been some latent infection or disease in the patient. Thus, for example, in Crocker's case there was *latent scarlet fever*, and in Chalmers and Archibald's case there was *latent gout*.

It therefore seems probable that *localized gangrenous vaccinia* can be produced by perfectly pure calf-lymph and by a satisfactory technique in persons suffering from any form of *latent constitutional disturbance* of severe nature, and that the severity of the local signs is caused by the lowered resistance of the tissues due to this latent infection, which, judging from this and other cases, makes itself sufficiently evident in the course of the illness which follows the vaccination.

Treatment.—At first the area should be merely protected from septic infection by pieces of sterilized lint lightly held in position by pieces of bandage. When the inflammatory symptoms appear, antiseptic dressings in the form of 1 in 80 carbolic lotion may be applied on lint, while the whole area is covered with cotton-wool, loosely held in position by first a bandage and then a handkerchief.

Closed dressings are not indicated, and the affected area should be simply exposed to the air in an elevated position, and treated at first by dry powders, later by lead and opium lotion, and finally by *calamine lotion*.

Papulo-Vesicular Vaccinia (Synonym, *Vaccine Lichen*).—This rash, which was first described by Crocker as vaccine lichen, has been observed in a number of cases by Chalmers and Byam in the Anglo-Egyptian Sudan. Some seven or eight days after vaccination the patient suffers from a mild attack of fever, which may reach 102° F., and may be attended with a slight sensation of itching in various parts of the body. The febrile symptoms subside as the rash appears, and do not return; but during the fever some of the patients suffer from a dry cough, which becomes worse as the eruption develops, and then slowly disappears. There is no vomiting or diarrhœa or other symptom worthy of record, while the vaccination pursues a normal course.

With regard to the rash, it appears, as already stated, some seven to nine days after vaccination in the form of dark coloured maculæ, which quickly become papules or papulo-vesicles, because, although no actual vesicles can be seen by the naked eye, still they produce a hard shotty sensation on palpation, and on microscopical examination show minute vesicles in the epidermis. A fully developed papule is about the size of a large pin's head, dome-shaped, and projects above the surrounding skin, which, as a rule, is quite normal, though in some cases it may be distinctly congested and may even be swollen. They appeared firstly upon the back of the hands and forearms, then on the back of the neck, then on the face, chiefly on the forehead, and then on the chest and back, and varied considerably in number from a few dozen to several hundreds.

The blood showed no parasites, but there was a leucocytosis and a marked relative increase of mononuclear and eosinophile leucocytes.

After lasting some four or five days, the rash slowly disappears, and is followed by a well-marked desquamation.

With regard to its ætiology, it was associated with vaccination because it occurred in two quite distinct detachments of Nuers and Nubas. The first detachment of twenty-four were vaccinated on February 10, 1914, and the eruption developed in eight, while the second detachment of thirty-six was vaccinated on February 23, 1914, and three developed the rash. It is to be noted that the vaccination in all was performed with lymph from one and the same calf. In every case the vaccination took well and developed normally, and in no case was there any sign of septicity or infection. No fungi or bacteria could be found in or cultivated from the papules; on the other hand, bodies which bore a resemblance to Guarnieri bodies were found in the vesicles.

The chief diagnostic points are:—

A papular or papulo-vesicular eruption beginning about eight days after vaccination and heralded by slight or no constitutional disturbance, but with moderate itching, and usually commencing on the arms, is most probably this eruption, which may be called a *vaccine lichen*, but which would be better termed a *papulo-vesicular vaccinia*.

The diagnosis should be confirmed by attempts at vaccination of a monkey from a papule or a vesicle.

The differential diagnosis may be made from:—

Lichen acuminatus by the fact that the hair follicles are not attacked.

From *craw-craw* (in the restricted sense of the word) by the absence of the horny consistency, and by the smaller size of the vaccinal papules.

From *lichen convex* by being non-follicular and by being an acute and not a chronic eruption.

From an ordinary *generalized vaccinia* by the main lesion being a papule and by the usually small size of the vesicles.

Prognosis.—This is invariably good, as all our cases and apparently most of Crocker's cases recovered very quickly without any scarring or pigmentation. Crocker has pointed out that it may go on to vesiculo-pustular formation, and in some of these cases fresh crops may continue to appear for months, or the vesicles may enlarge and become herpetiform or bullous, but it is possible that these exceptional forms are due to secondary infections and not solely to the lymph.

Treatment.—The essential treatment is rest and quiet. On quinine by the mouth and an antiseptic ointment—*i.e.*, carbolic ointment—for the skin, rapid recovery takes place.

Prophylaxis.—There is no explanation why eleven out of sixty persons vaccinated by the same lymph and belonging to the same African tribes, living under similar conditions, and about the same age and of the same sex, should develop an eruption while others did not. Therefore it is not possible to suggest any prophylactic measures.

INFLUENZA.

Remarks.—An acute specific fever, until recently believed to be caused by *Hæmophilus influenzæ* (Pfeiffer, 1892) (usual term: *Bacillus influenzæ*), spread from man to man aerially, and typically characterized by a sudden and severe onset, pains in various parts of the body, some catarrh of the respiratory passages, which typically subside in some two or three days and are apt to be followed by a prolonged convalescence. Recent researches by Charles Nicolle and Charles Lebailly tend to show that the malady may be due to a filter-passing virus. Bradford, Bashford, and Wilson state that the virus isolated in cases of influenza consists of minute Gram-positive, roundish, coccus-like bodies, varying from 0·15 μ to 0·5 μ, capable of passing through Berkefeld N and V filters. It is an anaerobe, and is not destroyed by heating to 56° C. for thirty minutes. They have isolated this organism from the blood and sputum of a number of cases.

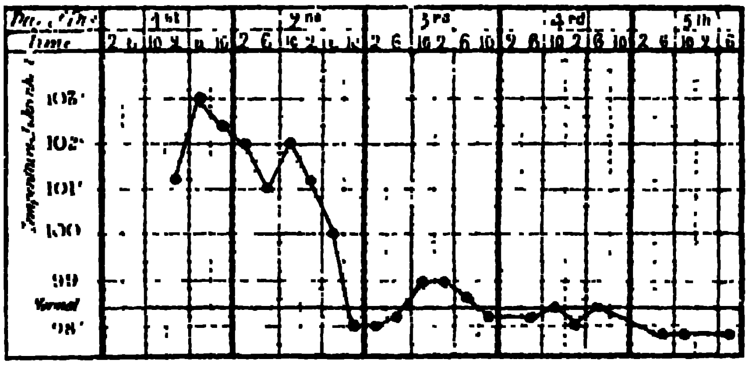

Fig. [illegible]52.—Temperature Chart of Influenza.

It is not our intent to discuss the ætiology or to enter upon a full description of influenza, which can be found in any textbook on medicine, but rather to attempt to impress upon the tropical practitioner the necessity of recognizing this complaint, which is very apt to be mistaken for pappataci and dengue fever, and *vice versa*.

Typical Attack.—Suddenly, without warning, the victim feels very ill; he may shiver, feel sick, or be giddy, but in any case he feels acute pains in various parts of the body, but especially in the lumbar region, behind the eyeballs, and in the muscles and bones, as well as a dry burning sensation in the eyes, nose, and throat, and sometimes also behind the sternum. His temperature rises quickly to 103° to 105° F., his pulse and respirations are increased, and he suffers from a troublesome cough, and herpes may occasionally appear on the lips.

After two or three days of these symptoms the temperature falls, slight catarrhal symptoms appear, the patient becomes convalescent, and may recover completely or may feel out of sorts for weeks or months.

In the *catarrhal type* there are the ordinary signs of a bronchitis, to which may be added those of a lobular pneumonia, and such cases are very dangerous. In the *gastro-intestinal type* there are the signs of gastro intestinal catarrh, which is rare, but more frequently there is a pseudo-enteric condition, with fever, lasting, however, about a week.

In the *cerebral type* the onset may be sudden or gradual, be with or without catarrhal symptoms, and is associated with pains in various parts, delirium, aphasia, hemiplegic or monoplegic symptoms, and, indeed, may at times simulate a cerebral hæmorrhage, especially in afebrile cases. These are very fatal cases, but at times recovery takes place, often with permanent mental disturbance.

Blood.—The blood practically shows no change. The total leucocytes vary from 8,000-12,000, while the differential count is within normal limits.

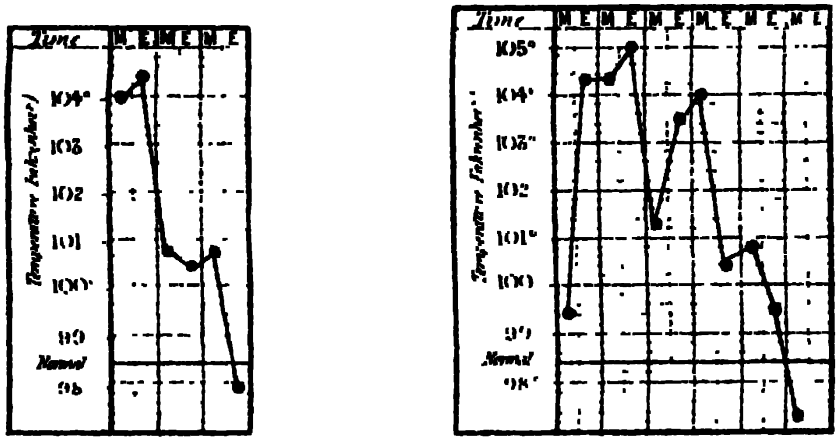

Fig 683 Fig. 684

FIGS 683 AND 684.—TEMPERATURE CHARTS OF INFLUENZA

Complications and Sequelæ.—These are numerous and frequent, but for them an ordinary textbook of medicine must be consulted.

Diagnosis.—The cardinal features of a typical attack of influenza are:—(1) The sudden and violent onset, (2) the high fever and quick pulse, (3) the violent pains in the muscles and bones; (4) the catarrhal symptoms, (5) the absence of any typical rash; (6) the presence of Pfeiffer's organism, whether it is the true specific agent or a nosoparasite; (7) the absence of a marked leucocytosis.

In the tropics the most important points in the *differential diagnosis* are the separation of the malady from malaria, dengue and pappataci fevers, and from plague. From malaria it can be recognized by the absence of the parasites in the blood, the absence of the mononucleosis and of the enlarged and tender spleen, and by the presence of catarrhal symptoms.

From *dengue* it can be separated by the absence of the leucopenia and of the rash, and by the presence of catarrhal symptoms.

From *pappataci fever* it can be diagnosed by the absence of the leucopenia, the quickness of the pulse, and as a rule the presence of the catarrhal symptoms, which in pappataci fever are absent or slight.

From *plague* by the absence of plague bacilli in the sputum in the pneumonic type, or in blood as demonstrated by hæmo-cultures in the septicæmic variety.

Prognosis.—This is good *quoad vitam* in typical uncomplicated cases, and bad in the varieties mentioned above.

Treatment.—It is important that the patient should remain in bed and be carefully nursed.

Liquor ammoniæ acetatis in ½ drachm doses in a mixture combined with 3 to 5 grains of sodium salicylate, alternated with 1 drachm doses of the ammoniated tincture of quinine, well diluted, should be given every two hours until the symptoms are relieved.

Pyramidon may be administered with benefit, if desired.

The diet should be light and nutritious, and the heart and respiratory organs should be carefully watched.

Prophylaxis.—The patient should be isolated as far as possible, and on recovery his room, bedding, clothing, etc., should be disinfected. Vaccines have not been very successful.

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CHAPTER LIX

WAR ZONE FEVERS

General remarks—Trench fever—Icterus castrensis gravis—Icterus castrensis levis—References.

GENERAL REMARKS.

It may be thought that it is unnecessary to introduce the subject of the diseases of the different zones of the war into a work on tropical diseases, but many of the maladies which have affected the troops during the war in the Salonica area, in Egypt and Palestine, in Mesopotamia and East Africa, are essentially tropical diseases, as were those of Gallipoli. Most of the fevers from which the troops suffered have been described in the preceding chapters, and many of the other diseases, such as the dysenteries and skin diseases, will be dealt with in the chapters which follow; but, excluding these, there are three conditions which merit a little consideration—viz., trench fever and the severe and mild forms of infective jaundice, often called icterus castrensis gravis (or Weil's disease), and camp jaundice—because, in making a diagnosis of a fever, these conditions must be considered, and we are now preparing the way for the chapter on diagnosis.

We therefore consider that a very brief account of these three conditions is necessary for our present purpose.

TRENCH FEVER.

Synonyms.—Periodic one day fever, Salonica fever, Pyrexia of unknown origin, Five days' fever, Volhynia fever, Russian remittent fever, Meuse fever, Trench skin, Gaiter fever, Shin fever, Trench shin, Shank fever, Polish fever, Quintan fever. *French*, La Fièvre des tranchées. *German*, His-Wernersche Krankheit, Fünftagefieber, Periodische Fieber; *Latin*, Febris quintana, Febris volhynica.

Definition.—A relapsing fever of as yet unknown origin, and spread by *Pediculus corporis* de Geer, 1778, commonly by the infected faeces being rubbed into the excoriated skin. It is characterized by a sudden onset of fever associated with pains in muscles and bones, particularly in the legs, with especial tenderness of the shins, and lasting twenty-four to forty-eight hours or longer, followed by other attacks of fever of less and less severity, separated by apyrexial intervals of five days' duration (more or less), and ending in complete recovery.

History.—As Strong has pointed out, there is insufficient data to permit any of the diseases described by the ancients, or in mediæval or modern times, being connected with the disease; while McNee believes that it is unlike any disease reported in other wars, and that it may have been introduced into the British Army by Colonials. Early in 1915 Graham drew attention to the disease as seen in the British Army, in which thousands of cases occurred between April and October. In January, 1916, it was observed in Salonica by McGavin, Wylie, and Acland, of No. 1 New Zealand Stationary Hospital. In May, 1916, it was observed in Mesopotamia, and in the same month was reported by Beauchant and Boidin as being present in the French Army in France, and about this time Werner in Warsaw drew attention to its existence in the German armies, and Hurst gave a good general account of the disease. In the same year McNee, Renshaw, and Brunt showed that the disease could be transmitted to healthy men by intramuscular and intravenous injections of the blood of patients, and the Germans also were similarly successful. In the same year it was observed at Salonica that the clothes or body louse, *Pediculus corporis*, was the only possible source of infection in a certain hospital orderly who had never been in contact with patients, and in whom the incubation was eighteen days from the first time he became infected with lice from some clothing. In 1918, Strong, Swift, Opie, McNeal, Baelzer, Pappenheimer, and Peacock, in France, showed that the virus was present in the blood plasma and would not pass through a filter. They also proved that the louse was the infective agent, and that the virus was naturally conveyed by its bite. This virus is present in the plasma, sometimes in the urine, and occasionally in the sputum. Artificially the disease may be transmitted by rubbing lice fæces, human infected urine or sputum, into excoriated skin, but the incubation resembles that of the inoculation of infected plasma.

A little later, in the same year, the British Committee in London showed that lice bites did not produce the disease, which, however, could be produced in healthy men by rubbing infected louse fæces into excoriated cutaneous areas. Further, they demonstrated that the incubation period was six to eight days, and that blood taken from the infected men and injected into healthy men could reproduce the disease after an incubation of five days. Also, in 1918, Couvy and Dujarric de la Rivière claimed that a spirochæte, *S. gallica* Couvy and de la Rivière, 1918, could be found in the blood of man and infected guinea-pigs, and in the liver and kidneys of these guinea-pigs. The infected guinea-pigs were shown to suffer from a fever resembling that in man. They, however, did not retransfer the disease from the guinea-pig to man, and the general opinion at present is that the organism is not the cause of the disease. Other organisms such as a piroplasma and a hæmogregarina have been described as causal.

In 1916 Toepfer found ***Rickettsia*** bodies similar to those described in 1909 by Ricketts in Rocky Mountain spotted fever, and by

Ricketts and Wilder, in 1910, in typhus. In 1917 Da Rocha Lima called the bodies found in trench fever *Rickettsia quintana*, to distinguish them from those found in typhus (*R. prowazecki*) and those occasionally seen in normal lice (*R. pediculi*). These findings were supported in 1918 by Arkwright, Bacot, and Duncan.

In 1919 Bradford, Bashford, and Wilson described minute bodies which they had succeeded in cultivating from the blood of patients, using Noguchi's method of anaerobic cultures. These bodies are morphologically identical with Rickettsia bodies, but they are Gram-positive.

Climatology.—The disease is known to exist in England, Flanders, France, Salonica, Greece, Macedonia, Tyrol, Galicia, Poland, Russia, and Mesopotamia.

Ætiology.—The ætiology has not been completely elucidated. Toepfer first found minute bodies in the intestinal contents of lice fed on trench fever patients, which he considered to be Rickettsia bodies: these bodies were somewhat similar to those found in Rocky Mountain fever and typhus. Toepfer's work was confirmed and enlarged by Da Rocha Lima, who called the parasite *Rickettsia quintana*, and more recently by Arkwright, Bacot, and Duncan. These latter authors describe the bodies as being minute Gram-negative organisms, round, oval, or lancet-shaped diplococci, 0·3 microns in their shorter diameter by 0·3 to 0·4 in length; the first appearance in the excreta of lice being as a rule eight to ten days after the first infecting feed. They seem to be slightly smaller and less frequently lancet-shaped than those found in typhus. The size of these bodies is such that they should not pass as a rule a bacterial filter, but may occasionally pass a filter which retains such bacteria as *B. typhosus*.

Bradford, Bashford, and Wilson report that they have cultivated from the blood of patients, by using Noguchi's method, minute bodies which seem to be very similar to Rickettsia bodies, but are Gram-positive.

The trench fever virus is considered to be a resistant filterative virus by the American Commission. This Commission (composed of Strong, Swift, Opie, Macneal, Baetjer, Pappenheimer, Peacock, and Rapport) carried out a very thorough investigation in 1918, and came to the conclusion that the virus was carried from the sick to the healthy by the agency of the clothes louse, *Pediculus corporis* de Geer, 1778, and that it was usually conveyed by the bites.

The War Office Commission (composed of Byam, Carroll, Churchill, Dimond, Lloyd, Sorapure, and Wilson) came to the conclusion, after a series of important experiments, that the infection was contaminative by means of the louse fæces infecting scratches on the skin.

Pathology and Morbid Anatomy.—Unknown.

Symptomatology—*Incubation.*—Clinically the incubation period is believed to vary from fourteen to thirty days, because this is the time required to induce the disease experimentally by infected lice when permitted to bite healthy persons. Experimentally it is six to eight days from the time that infected lice fæces are rubbed into scratches, and five days after the inoculation of infected blood. During this stage there may be slight prodromata in the form of headache and pains in the limbs, but these may be absent.

Attack.—The *onset* is sudden, the patient feeling giddy, weak, and shivering. He feels so ill that he has at once to stop his work, and complains of shortness of breath, pain in the left side, in the back, legs, and behind the eyeballs, as well as of headache. The temperature quickly rises to 101° to 104° F. The conjunctivæ are injected, and nystagmus may be present if the eyes are turned completely sideways.

There are two curious types of this stage of the illness—viz., the *appendicular* and the *cerebro-spinal*. In the former, the patient suffers from abdominal pain, constipation, slight abdominal distension, tenderness, and vomiting, and in Allied and German armies the diagnosis of appendicitis has been made. At other times there may be pains and stiffness of the neck, and the case may be mistaken for cerebro-spinal meningitis.

The *Course* of the disease is that the next morning the temperature has fallen to normal or nearly normal, but it may remain high, the appetite is lost, the tongue is furred, and there may be pharyngitis and constipation. Now the patient complains of pains in the muscles and bones of the legs, and has tenderness in the shins, over which there is cutaneous hyperæsthesia, and there may be pain and tenderness in the fibula, humerus, ulna, or along the vertebral column.

Herpes labialis may appear, and fairly often a discrete roseolar rash, and very rarely a scarlatiniform or small papular rash, may be seen on the chest, back, or abdomen. The spleen and more rarely the liver may now enlarge. The blood shows a leucocytosis, with a relative mononuclear increase. The red corpuscles are not reduced in amount, but the hæmoglobin is usually reduced, and there is polychromatophilia.

First Intermission.—After twenty-four to forty-eight hours, or longer, the temperature falls to normal, the symptoms disappear, and the patient feels well, though sometimes he feels slight discomfort in the muscles and bones.

Second Attack.—Some two to ten, but more usually five, days after the cessation of the first attack the patient begins to feel ill, with headache, pains in the legs, and fever, the temperature rising to about 101° F. Next day the temperature is normal, and this attack may cease, or the fever may recur in the evening, but usually ceases next day.

Intermissions and Attacks. These now succeed one another at regular intervals of about five days' duration, but the attacks of fever become shorter and shorter and the temperature lower and lower, so that unless care is taken to register the temperature every two hours about the time of an expected attack, the fever may be missed by the day and night temperature chart. Although the patient does not feel or look ill, the pains and tenderness in the shins may become worse during each attack and may keep him from sleeping. The number of relapses is variable, and may reach six or seven.

Rash.—In a fairly large number of patients a delicate macular rash appears with each recurrence of the fever. It is generally seen on the chest and abdomen, and consists of small red macules which disappear on pressure.

Termination.—After lasting a variable time (five to six weeks), the disease gradually dies out and the recovery is complete.

Complications and Sequelæ.– Tachycardia and so-called soldier's heart may occur.

Varieties.—English observers recognize a short and a long type. In the former the fever lasts for three to four days, falls to normal, and after a few hours rises again for two to five days, when it falls to normal and the fever stops. This variety resembles dengue fever. The long type is the typical fever.

The Germans also recognized a simple paroxysmal form, but they also mention a typhoidal and a rudimentary form.

Diagnosis.—This has to be made from influenza, dengue, pappataci fever, relapsing fever, malaria, smallpox, typhus, and enteroidea.

From *influenza* it may be distinguished by the absence of catarrhal symptoms and the mononucleosis.

From *dengue* and *pappataci* by the absence of leucopenia.

From *relapsing fever* by the absence of marked enlargement of the spleen and of the spirochætes in abundance in the blood.

From *smallpox* and *typhus* by the absence of the severe constitutional symptoms.

From *malaria* by the absence of the leucopenia and of the typical parasites from the blood.

From *enteroidea* by the sudden onset and the pains in the muscles and bones, and by negative hæmoculture and serological reactions.

Prognosis.– This is good, as the mortality is nil and the recovery complete.

Treatment.—Pyramidon is strongly recommended, but constipation must be relieved, and the patient should be disinfected at once. His clothing and bedding should be disinfected in moist heat at 70° C. for half an hour.

Prophylaxis.—This is mainly louse destruction (*vide* the chapter on Typhus, p. 1338), but the urine and sputum of patients should also be disinfected. Cups should be provided for the sputum.

ICTERUS CASTRENSIS GRAVIS.

Synonyms.—Weil's disease, Epidemic jaundice, Infective jaundice, Spirochætal jaundice, Spirochætosis icterhæmorrhagica, Larrey-Weil disease. *French*, Maladie de Weil, Typhus hépatique; *German*, Infektiöser Fieberhafter Ikterus, Infektionikterus, Weilschen Krankheit; *Japanese*, Odan-eki; *Latin*, Icterus febrilis seu infectiosus, Typhus biliosus nostras, Morbus weili.

Definition.—An acute specific fever caused by *Spiroschaudinnia icterohæmorrhagiæ* (Inada, Ido, Hoki, and Keneko, 1915), and characterized by jaundice, albuminuria, enlargement of the spleen, pains in the muscles, with sometimes hæmorrhages and a high mortality.

History.—The disease was first mentioned in Minorca in 1745, and then along the coast of Italy. Larrey, in 1800, seems to have described this disease as seen in Napoleon's army in Egypt. It was also noted by Carville in 1859, and by Worms in 1865, while a number of cases occurred during the American Civil War. As the mortality from jaundice was low in the South African War, it is probable that it was absent. In the present war it has occurred in the British, French, Italian, Serbian, and German armies, though it has been confused with the milder type. In 1886 Hirsch popularized the complaint and Weil again drew attention to the disease, and in 1911 Hecker and Otto wrote a monograph on it. As regards the tropics, it was noted in India in 1849, and in subtropical countries it was seen in Smyrna and Egypt. In this history authors noted two types, a mild, resembling simple catarrhal jaundice, and a severe, which some of them called a type of bilious remittent fever, and said that some of the cases had hæmorrhages and nervous symptoms. During the last few years it has received much attention, because cases of jaundice have been frequently noted in the armies In 1915 the Japanese investigators mentioned above discovered the causal agent, and this has been confirmed by French, English, Italian, and German workers. Noguchi has found that strains of *S. icterohæmorrhagiæ* isolated from patients in Japan and Belgium, and from rats in America, are identical morphologically and serologically. He has created for the organism a new genus, *Leptospira*, which will probably be generally accepted in the near future.

Ætiology.—The causal agent is *Spiroschaudinnia icterohæmorrhagiæ* (p. 447), which is considered to be the same as the spirochæte found in the kidneys and urine of wild rats, in which it lives. It is believed that the organism escaping in the rats' urine, and to a less extent in human urine, is the source of infection, which takes place through the skin when walking barefoot on sodden ground or by entering the alimentary canal in water.

Pathology.—The jaundice is probably caused by obstruction to the smallest bile ducts, brought about by a polymorphonuclear exudate into the tissues surrounding them.

Symptomatology.—The *incubation period* varies from five to seven days, the average being six days, which agrees with an accidental infection.

The *onset* is usually abrupt, with occasional shivering and high fever, faintness, giddiness, and prostration. The patient is flushed and looks and feels very ill. The spleen and liver enlarge, and the superficial lymph glands may become palpable.

Course.—Jaundice appears two or three days after the onset. The tongue is coated with a brown fur, and sordes form on the lips and teeth. Vomiting may be present from the first, and hiccough may also be troublesome. There may be pain and tenderness in almost every part of the body. The neck may be stiff, and in these cases the cerebro-spinal fluid may be under pressure and contain an excess of polymorphonuclear cells and lymphocytes, as well as albumen and bile.

The conjunctivæ may be injected, and herpes may be present on the lips.

Jaundice usually appears two or three days after the onset of the symptoms, but may be later, though it is almost always present before the temperature drops. Pruritus is slight or absent.

The blood shows a diminution of red corpuscles and hæmoglobin, and an increase of leucocytes, while a very few spirochætes are present between the fourth and ninth day. The pulse is slow in proportion to the temperature. The urine usually contains bile, albumen, granular and hyaline casts, and sometimes a few red corpuscles, and the spirochæte can be found after the first week.

Hæmorrhages from the lungs, the stomach, or more rarely the bowels, may occur, while epistaxis and purpura may be seen in severe cases.

Termination.—The temperature drops by crisis or rapid lysis from the eighth to tenth day.

Relapse.—There is often a return of the fever some few days after it falls to normal, and the relapse may last from a few days to ten or even fifteen days, but there is no increase in the symptoms.

Convalescence.—This is often prolonged.

Diagnosis.—The cardinal diagnostic points are:—

1. The presence of the spirochæte in the blood between the fourth and ninth day (it is difficult to see), and in the urine. Blood may be inoculated into the peritoneal cavity of guinea-pigs, in which illness supervenes after inoculation of not less than six days.

In order to discover the spirochæte in the urine, it is necessary to adopt Castellani's method of centrifuging 20 c.c. and pouring off the supernatant fluid, then adding another 20 c.c. and again centrifuging, and so on until about 200 c.c. of urine has been centrifuged, after which the deposit may be examined.

2. The severity of the symptoms and the sudden onset, the severe pains, the jaundice, the enlargement of the liver and spleen, the albumen in the urine, with casts and a few red blood corpuscles.

3. The pulse is slow in proportion to the temperature.

The differential diagnosis has to be made from camp jaundice, enteric jaundice, septic jaundice, malarial jaundice, acute yellow atrophy of the liver, typhus, blackwater fever, pneumonia with jaundice, yellow fever, and relapsing fever.

From *camp jaundice* (*icterus castrensis levis*) it can be diagnosed by the sudden onset, the severity of the symptoms, and the shortness of the illness.

From *enteric jaundice*, which is rare, it may be recognized by the presence of the polymorphonuclear leucocytosis and the absence of leucopenia, and the usual signs of enteric fever, while blood cultures fail to demonstrate the typhoid bacillus and its allies.

From *septic jaundice* it can be separated because the jaundice appears at an early and not at a late stage in the disease, and by the absence of septic infections clinically and by hæmoculture.

From *malarial jaundice*, and especially the Weil's disease-like type, by the absence of the malarial parasites in numbers and by the presence of the slight leucocytosis.

From *acute yellow atrophy* by the absence of the diminution of urea and uric acid, by the absence of leucine and tyrosin in the urine, and by the increase in size of the liver.

From *typhus* by the absence of the peculiar facies, of the subcuticular mottling and the typical rash, and by the presence of jaundice, which is only occasionally seen in that disease.

From *blackwater fever* by the absence of hæmoglobin from the urine.

From *pneumonia with jaundice* by the absence of right-sided lobar pneumonia.

From *yellow fever* by the pulse being rapid from the first and falling as the temperature falls.

From *relapsing fever* by the absence of abundant ordinary spirochætes from the blood, and by the peculiar characters of the typical spirochætes of Weil's disease when present in blood, in which it is found only in small numbers.

Prognosis.—This is serious, the death-rate being some 30 per cent., and convalescence being prolonged.

Treatment.—The repeated subcutaneous or intravenous injection of 20 to 60 c.c. of the serum prepared by Inada, Ido, Hoki, Ito and Wani or of Martin and Pettit's immunized horse serum is recommended. Salvarsan and its allies are useless. Symptomatic treatment for constipation by salines and aperients is also to be remembered.

Prophylaxis.—Disinfect the urine of patients for some nine weeks from the onset of the attack. Catch and kill rats. Disinfect the ground of the endemic area or remove the persons from this area.

ICTERUS CASTRENSIS LEVIS.

Synonym.—Camp jaundice.

Definition.—A slightly febrile disorder, characterized by mild febrile symptoms, followed by a mild attack of jaundice lasting some two to eight weeks, after which there is a very prolonged convalescence.

Remarks.—We have already noticed that older writers have divided Weil's disease into two types, one mild and the other severe. Camp jaundice represents the mild form, and clinically is practically indistinguishable from catarrhal jaundice. It was very common in Eastern war zones, and its symptomatology may be divided into the pre-jaundice period and the jaundice period.

Climatology.—It was common in Gallipoli, the Balkans, Italy, and France.

Ætiology.—This is at present unknown. Certain authors consider it to be of paratyphoid origin, but this is not so. Spirochætes have been described in the urine by several observers, including one of us. These organisms are often not pathogenic to guinea-pigs, and have not yet been demonstrated to be the cause of the disease.

Pathology.—It would appear as though the jaundice was due to obstruction to the common bile duct, either by swelling of the duodenal mucosa or to mucus in the duct.

Symptomatology.—The *onset* is gradual. The patient feels tired, complains of aches in various joints and muscles for weeks, the skin may appear to be normal, and the temperature is either normal or not very high (99° to 100° F.). The patient has often the sensation of suffering from very high fever, while on taking his temperature he may find it normal or subnormal. During this stage very often the urine is darker than usual and contains biliary pigments. We have come across patients feeling fairly well, but complaining of what they called rheumatism for months before the jaundice appeared: others had remarked the staining of their shirts by the urine. This stage may last for several weeks; in one of our cases it lasted three months before the jaundice appeared.

The Jaundice Stage.—First the sclerotics, then the skin, slowly become icteric. The degree of jaundice is seldom so marked as in cases of true obstructive jaundice. The patient generally feels absolutely done up, often with pains and aches all over the body; as a rule there is very little or no pruritus, in contrast to so many other types of jaundice. He has no appetite, and may feel inclined to vomit. The temperature is normal or subnormal, pulse usually slow, but may be of normal frequency; the spleen generally is not palpable, nor is the liver in most cases, there may be pain on pressure in the region of the gall-bladder, but this is not a constant symptom. There is often constipation, and the stools may be whitish or of the usual brownish colour; at times there are periods of diarrhœa, alternating with periods of constipation. The urine is scarce and very dark-coloured; it may contain a trace of albumen and casts. The *jaundice stage lasts between two and eight weeks.* Recovery is slow, and for weeks and months after the jaundice is over the patient may feel very weak.

Diagnosis.—The characteristic features of the disease are:—(1) Its epidemicity; (2) its slow onset; (3) its long course divided into a pre-icteric and an icteric period.

With regard to the *differential diagnosis*, it can be separated from *catarrhal jaundice* only by its epidemicity.

From *icterus castrensis gravis* (Weil's disease) it can be differentiated by the mildness of the symptoms, by the slowness of the onset, and by the slightness or absence of the febrile symptoms and the absence of hæmorrhages.

From *enteric jaundice* it can be separated by the absence of enteric organisms, as shown by hæmocultures, and by the absence of the enteric serum reactions in the later stages.

From *malarial jaundice* it can be diagnosed by the absence of malarial parasites in the blood and also by the absence of serious symptoms.

Prognosis.—This is favourable *quoad vitam*, but the course of the disease may be prolonged, and for weeks and months the patient may be very depressed and weak.

Treatment.—There is no specific therapy, and hence treatment must be symptomatic, with rest in bed, milk diet, and urotropin in 10-grain doses three times a day.

Prophylaxis.—The urine and fæces should be disinfected.

Nanukayami.

A seven-day fever resembling a typical Weil's disease has been reported from several Japanese observers from the province of Fukuoka. Ido, Ito and Wani have found that the causative agent is a spirochæte—*S. hebdomadis*—which is serologically distinct from *S. icterohæmorrhagiæ*. The normal host of the spirochæte seems to be the field-mouse, *Microtus montebelli*.

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CHAPTER LX

THE DIAGNOSIS OF A TROPICAL FEVER

Preliminary—Thermometric pseudo-fever—Acute fevers—Fevers of less than eight days' duration—Fevers of more than eight days' duration—Chronic fevers—Summary.

PRELIMINARY.

THE method of diagnosis contained in the present chapter is not intended to be comprehensive, and the reader who expects to find every possible situation dealt with will be disappointed, because this is not our intent, and, indeed, would be a practical impossibility.

We are endeavouring to place before him such information as we have found necessary to use in some twenty-odd years of tropical life, and we may perhaps be pardoned if we mention some plain facts before starting on our subject.

Firstly, we trust that our reader will realize that it is one thing to draw up a nice-looking scheme of diagnosis upon paper, and it is quite a different thing to give a system which will be applicable at the bedside; but no one knows better than we do how difficult it is to write a system so applicable.

Secondly, we trust that our reader has not forgotten that there is such a thing as clinical medicine—that is to say, a system of diagnosis based upon the bedside examination of the patient. In our opinion, every patient should be most carefully examined, from the crown of his head to the soles of his feet, by ordinary clinical methods before any attempt is made to utilize the resources of the laboratory.

A systematic clinical examination of every patient is most essential. It is the sum total of the various symptoms, none alone pathognomonic, which establishes the diagnosis in conjunction with which the results from the laboratory must be considered. A practitioner who is unable to come to some sort of a diagnosis without the aid of a laboratory should, in our opinion, utilize his earliest spare moments in a course of post-graduate instruction with regard to clinical methods.

Thirdly, we are of the opinion that the laboratory work should never be omitted as a check to confirm or to adjust this clinical diagnosis. Specimens sent for diagnosis to a laboratory should always be carefully collected. This collection should at least be supervised by the practitioner, and not left to subordinates entirely.

otherwise mistakes will be possible. The specimens should always be collected and forwarded in the most aseptic method possible, and should be accompanied by a statement recording the nature of the specimen, the date and time of its collection, the nature of the examination desired (which should not be vague—*e.g.*, not 'urine for examination,' but clearly stated, 'urine to be examined *quantitatively* for sugar'), and a brief statement of the salient features of the case and the suspected clinical diagnosis, because it is the duty of the practitioner to help the laboratory in its work.

Finally, we desire most earnestly to impress upon the reader that the essential feature in the diagnosis of a tropical fever is a combination of clinical examination with laboratory work.

THERMOMETRICAL PSEUDO-FEVER.

The practitioner working in high air temperatures should remember that the clinical thermometer, being of the maximum type, will rise quickly to some temperature corresponding to that of the air, and will remain thereat. Mistakes have been made, such as recording a number of cases of fever in an institution. In high air temperatures the thermometer should be taken out of cool water, placed in the patient's mouth, left there long enough to record the actual temperature, and then quickly replaced into cool water, in which it is examined.

The practitioner knows well the precautions *re* hot liquids or solids having been placed in the mouth before the thermometer, thus giving high readings, and the effect of draughts falling on the cheeks preventing the rise of the mercury: or, in other words, of the possible thermometrical fallacies of which these are examples.

ACUTE FEVERS.

The acute fevers may, for purposes of diagnosis, be divided into those which have lasted less than eight days, and those which have been in progress eight or more days when seen by the practitioner.

FEVERS OF LESS THAN EIGHT DAYS' DURATION.

These fevers may be divided into:—

I. Those exhibiting some striking physical sign.
II. Those not exhibiting any striking physical sign.

I. WITH SOME STRIKING PHYSICAL SIGN.

The physical signs to which we refer may be classified into:—

A. Traumatisms.
B. Skin eruptions.
C. Derangement of some bodily system.
D. Localized derangement of some organ.

A. TRAUMATISM.

The presence of a traumatism suggests that an acute fever may be *septic* in nature, but in the tropics no one should forget the possibility of the fever being caused by the reawakening of *old malarial infections*, or even being associated with a new malarial infection, acquired, perhaps, at the same time as the traumatism.

If the fever is intermittent, recurring every third or fourth day, it is malaria. If it is quotidian, pay attention to the following points: If the spleen is hard it is probably malaria—make a blood film; if Laveran's parasites are present or marked mononucleosis, it is probably malaria: if polymorphonuclear leucocytosis is present, it is probably septic fever.

If the evidence is in favour of sepsis, or if malaria has been excluded, bacteriological examination of the blood and of the local discharge should be made, and should include search for aerobic and, if necessary, anaerobic organisms.

B. SKIN ERUPTIONS.

These may be considered under the following headings:—

1. Erythematous eruptions.
2. Papular eruptions
3. Urticarial eruptions.
4. Purpuric eruptions.
5. Vesicular eruptions.
6. Bullous eruptions.
7. Pustular eruptions.
8. Pigmentation.

1. ERYTHEMATOUS ERUPTIONS.

(A) ERYTHEMATOUS RASH GENERALIZED.

I. *The rash is more or less typical of scarlet fever* :—

- (*a*) Onset of eruption less than forty-eight hours after the appearance of the sore throat —*Scarlet fever.*
- (*b*) Onset of eruption more than forty-eight hours after the appearance of the sore throat—*Erythema or dermatitis scarlatiniformis.*
- (*c*) Throat symptoms mild or absent :—
  - (A) Examine blood for malarial parasites:—
    1. If present —*Malaria.*
    2. If absent inquire into drugs, especially quinine—*Anaphylactic drug eruptions.*

II. *The rash has some maculo-papular elements* :—

- (*a*) Coryza and Koplik's spots have been or are still present—*Measles.*
- (*b*) Coryza and Koplik's spots absent :—
  With enlargement of the occipital, cervical, and other lymphatic glands—*German measles.*

III. *The rash has the characters of a blush, with or without œdema :—*

(*a*) The rash, though general, is more marked in one area:—

1. Evidence of a bite or sting—*Bite or sting of a venomous animal.*
2. No such evidence, special region pits on pressure:— Examine night and day blood for microfilariæ—*Filariasis.*
3. Macules on wrist and ankles only becoming general on third day; severe symptoms; yellow tinge in conjunctivæ. Occurs in Rocky Mountains—*Spotted fever of the Rocky Mountains.*

(*b*) The rash is not specially marked in one area:— Examine blood for eosinophilia and the fæces, after a purge, for the eggs of intestinal worms—*Helminth infections.*

IV. *Erythema fugitive, faint, annular, most marked on trunk :—* History of residence in Tropical Africa. Glands in posterior triangle of neck enlarged. Examine gland juice and blood for trypanosomes—*Sleeping sickness.*

V. *Erythema with marked cerebral symptoms, vomiting, retraction of head—Kernig's sign.*

1. Examine the blood for malarial parasites, if present—*Malaria.*
2. If absent, perform lumbar puncture and examine for meningococci *Epidemic cerebro-spinal meningitis.*

VI. *Erythema mild, amounting to very severe blushing, and most marked on the face :—* Eyes injected, severe pain at back of eyes, high fever. Occurs in locality where phlebotomus is endemic—*Pappataci fever.*

VII. *Erythema with little or no fever, but with marked gastro-intestinal symptoms :—* With or without signs of collapse—*Ptomaine poisoning.*

(B) ERYTHEMATOUS RASH LOCALIZED.

I. *Rash distributed on parts exposed to light :—* On face, neck, and hands, often feet; associated with gastro-intestinal and nervous symptoms. Fever is not a marked feature of simple pellagra, and when this occurs it is due to a complication, generally with one of the enterica group of fevers—*So-called typho-pellagra.*

II. *Rash not specially confined to parts normally exposed to light :—*

(*a*) Associated with œdema in some part:—

1. Œdematous and erythematous areas coincide. (*a*) Area defined by sharp edges. Sometimes vesicles present and leucocytosis—*Erysipelas.* (*b*) Lymphatics inflamed, microfilariæ in blood. —*Filarial lymphangitis.*

2. Œdema of face and eyelids and gastro-intestinal disturbance, eosinophilia, and leucocytosis—*Trichinosis.*
3. No œdema of the face and eyelids. Very rare—*Polymyositis.*
4. Swollen area affected with leprotic eruption. Signs of leprosy in various parts of the body—*Leprotic fever.*

(*b*) Not associated with œdema:—

1. Severe constitutional symptoms and marked backache; signs of vaccination absent, poor, or old. Case of smallpox known to exist in neighbourhood—*Suspect smallpox.*
2. There is a recent wound due to a rat-bite, or a history of a rat-bite seven to twenty-one days previously, of which the wound may have healed. Site of bite red and swollen, becomes ulcerated. Enlarged lymphatic glands. Erythematous eruption with purple spots—*Rat-bite fever.*
3. History of a cat-bite some ten to twenty-one days before illness; maculæ around site of bite and then on limbs; infiltration of skin, enlarged lymphatic glands. Pains in muscles and joints. Splenic enlargement. Fever relapsing in type—*Cat-bite fever.*
4. Pains and aches all over the body, but constitutional symptoms not very severe. Rash appears with the fall of the temperature on the third day. No malarial parasites in the blood. Stegomyia (or Culex) mosquitoes abundant. Endemicity of dengue-like fevers known—*Dengue.*

2. PAPULAR ERUPTIONS.

These eruptions often form part of the evanescent early symptoms of some fever, and are therefore difficult to arrange in a satisfactory manner. The practitioner will remember that drugs like iodides and the bromides may give rise to papular eruptions.

I. *Catarrhal symptoms present*:—

Maculo-papular eruption tending to form blotches. Koplik's spots present—*Measles.*

II. *Catarrhal symptoms slight or absent*:—

(*a*) *Constitutional symptoms severe*:—

1. Markedly severe headache and backache. Papules bright red and shotty, appearing between the third and fourth day, first on the forehead—*Smallpox.*
2. In a child which has been ill for three days with pain all over the body and often delirium or convulsions. Papules about the size of a pin's head on chest, back, and abdomen—*Dengue* (Van der Scheer's fever).

3. Pale dusky red papules or macules, fading into the normal skin, but slightly elevated, disappearing on pressure, at the margins of the axillæ, wrists, flanks, chest, back, shoulders, arms, and legs, with subcuticular mottling. Exclude malaria by blood examination—*Typhus fever.*
4. Large red papules on face on the fifth to seventh day of illness, spreading over body as macules, after a visit to Akitaken and Nugataken, of the Island of Nippon, Japan. Enlarged lymphatic glands in some area of the body, and a few vesicles on area drained by lymphatics going to these glands, are indicative of bites by *Microtrombidium akamushi—Tsutsugamushi fever.*

(*b*) *Constitutional symptoms not severe and not following recent vaccination*:—

1. Rash of maculo-papules, circular, discrete; not as bright or as elevated as measles. No Koplik spots. Occipital and other lymphatic glands enlarged. Pink eye present—*German measles.*
2. Fever slight or, at times of epidemic, absent in some cases. Rash general, composed of bright pinhead papules or red macules (*i.e.*, morbilliform), associated with itching and with a few macules on the palms and soles—*Papular fever* (Castellani and Chalmers).

(*c*) *Constitutional symptoms not severe, following recent vaccination*:—

Rash composed of papules and papulo-vesicles, of large pinhead size, appearing some seven to nine days after vaccination—*Vaccine lichen.*

3. URTICARIAL ERUPTIONS.

(*a*) Fever slight, after ingestion of certain foods—*Febrile urticaria.*

(*b*) Worms present—*Helminthic febrile urticaria.*

4. PURPURIC ERUPTIONS.

Purpuric puncta may be caused by flea-bites and pediculi, and have nothing to do with the fever. Many drugs, ptomaine poisoning, and snake-bite produce purpuric spots or patches. Very rarely serum injections produce purpuric eruptions about seven to nine days after the injection. The leukæmias, chronic alcoholism, Bright's disease, and jaundice, may be associated with purpuric rashes. In fevers as a rule it points to septicæmia, and is more of a prognostic than of a diagnostic value, even in epidemic cerebrospinal meningitis, in which, in our tropical experience, it is rare. Peliosis rheumatica, with its associated tonsillitis and pains in the joints, is very rare. It will be remembered that in scurvy there is no fever. With these provisos we make the following suggestions:—

Clear signs of the disease causing the purpuric eruption:—

(*a*) Yellow tinge in skin or eyes:—

1. Urine black from hæmoglobin—*Blackwater fever.*
2. Urine without hæmoglobin:—
   - (A) *Bile in the urine:*—
     - (i.) Examine blood and urine for the peculiar spirochæte with its central minute waves—*Icterus castrensis gravis* (*Weil's disease*).
     - (ii.) Spirochætes of doubtful pathogenicity may be present or they may be absent: little or no fever—*Non-febrile jaundice* (*camp jaundice*).
   - (B) *Bile not in urine:*—
     Severe fever; examine blood for malarial parasites—*Malarial fever.*
   - (C) *Albumen in urine:*—
     Epigastric tenderness. Faget's sign—*Yellow fever.*

(*b*) Without yellow tinge in the skin or eyes:—

1. Retraction of head. Kernig's sign present. Lumbar puncture reveals meningococci—*Epidemic cerebro spinal meningitis.*
2. With developed disease—*e.g.*, typhoid, diphtheria, scarlet fever, smallpox, measles (hæmorrhagic conditions known in the tropics)—*Septicæmic condition.*
3. With buboes or marked pneumonic symptoms. Examine blood culturally, sputum and fluid from enlarged lymphatic glands microscopically, for plague bacilli—*Plague.*
4. Without marked signs of any disease. Blood culture—*Septicæmia.*

5. VESICULAR ERUPTIONS.

The practitioner will be on his guard to exclude vesicles which are the result of bites of insects, such as sand-flies and mosquitoes, as well as those due to the ingestion of drugs, such as bromides and iodides. Also the pyoses, which are without fever. Among these, pyosis corletti causes bullæ.

I. *Onset with severe constitutional disturbance:*—

Rash on third to fourth day; shotty papules becoming vesicles fifth to sixth day. Vesicles circular, tense, umbilicated, and multilocular—*Smallpox.*

II. ***Onset with mild constitutional symptoms, but with severe local pain, generally along a nerve, but in any case confined to one region:—***

Rash a couple of days or more after commencement of the pain. Usually confined at first to painful region, and then becomes general, but may be general from first. Vesicles dome-like or flattened, become umbilicated; no inflammatory areola; leave scars—*Vesicular fever* (Castellani and Chalmers).

III. *Onset mild and without severe local pain, without history of recent vaccination*:—

Rash on first to third day. Often first sign of illness. Appears on back, chest, and abdomen. First in form of pale red macules, often with raised centre, quickly developing into superficial unilocular vesicles, some of which may become umbilicated—*Chicken pox.*

IV. *Onset mild, history of vaccination twelve to twenty-two days or more before eruption*:—

Generalized vesicular eruption, not umbilicated at first, and preceded by a papular rash. Vesicles become umbilicated—*Generalized vaccinia.*

6. BULLOUS ERUPTIONS.

Bullous eruptions may be caused by plants and drugs. In newly-born children bullæ on the hands and feet suggest congenital syphilis.

I. There is a well-defined raised erythematous area upon which the bullæ are present. Bullæ to be examined for streptococci—*Erysipelas.*

II. No such area present, but wounds, enlarged lymphatic glands, with severe constitutional symptoms, common in the tropics. Examine blood and bullæ for organisms—*Septic pemphigus.*

III. In recently-born children examine bullæ for streptococci and other pyogenic organisms—*Pemphigus neonatorum.*

7. PUSTULAR ERUPTIONS.

It will be remembered that there are pustular syphilides unattended by fever, and pustular tuberculides of which fever is not a marked sign.

I. *Clear history of recent vaccination with Jennerian vaccine*:—

Small dark-coloured or black centre in the vaccine area, surrounded by dark reddish swollen area, on which are the vaccinial vesicles and pustules. Around this a bluish area, the whole surrounded by a wide erythematous blush—*Gangrenous vaccinia.*

II. *No history of recent vaccination:—*

(*a*) Localized red swelling, with several points of suppuration. Examine bacteriologically for cocci—*Carbuncle.*

Localized red solid swelling, with black centre, and round it pustules often mixed with vesicles and bullæ. Examine bacteriologically for *Bacillus anthracis*—*Malignant pustule.*

(*b*) Generalized pustular eruption in a patient who has been seriously ill for six days or more, with at times swelling of eyelids, lips, or eyes—*Smallpox.*

8. PIGMENTATION.

In acute fevers the important cutaneous pigmentation is the yellow tinge due to jaundice. This is rare in *malaria* and in the early stages of the *enteric fevers,* and hence need only be mentioned. For blood pigments in the skin see the *purpuric eruptions,* and for black pigmentation see the chronic fevers.

I. *Liver and spleen one or both enlarged:—*

(*a*) Abdominal tenderness. Typical spirochætes in blood—*Relapsing fevers.*

(*b*) Abdominal tenderness not marked:—

1. Peculiar spirochætes in blood and urine—*Weil's disease.*
2. No spirochætes in the blood:—
   - (A) Hæmoglobinuria—*Blackwater fever and its allies.*
   - (B) No hæmoglobinuria, severe symptoms, albuminuria, black vomit, etc.—*Yellow fever.*

II. *Liver and spleen not enlarged:—*

(*a*) Symptoms mild. Fever slight or absent. No signs or symptoms of pneumonia—*Icterus castrensis levis* (*camp jaundice*).

(*b*) Physical signs and symptoms of pneumonia. Pneumococcus in sputum—*Pneumonia.*

C. BODY SYSTEMS.

Fevers associated with some marked sign or symptom directing attention to a given system of the body may be arranged according to the system deranged as follows:—

A. Derangements of the Alimentary Canal.
B. Derangements of the Respiratory System.
C. Derangements of the Circulatory System.
D. Derangements of the Urinary System.
E. Derangements of the Generative System.
F. Derangements of the Lymphatic System.
G. Derangements of the Muscular System.
H. Derangements of the Osseous System.
I. Derangements of the Connective Tissue.
J. Derangements of the Nervous System.

A. *Symptoms pointing to the alimentary canal:—*

I. *Mouth and Throat:—*

(*a*) Pyorrhœa, marked gingivitis, or even the presence of bridges, crowned or stopped teeth, with pain, shrinking of the gums, etc.—*Septic fever.*

(*b*) Angina with whitish or greyish membrane on the fauces or tonsils:—

Examine bacteriologically:—

1. Streptococci present—*Streptococcal angina.*
2. Klebs-Loeffler bacilli present—*Diphtheria.*
3. Fusiform bacilli present—*Vincent's angina.*

II. *Stomach:—*

(*a*) Black vomit:—

Associated with jaundice, Faget's sign, and severe constitutional disturbance—*Yellow fever.*

(*b*) Vomiting, pain and tenderness in diaphragmatic region. Severe constitutional symptoms, with or without hiccough; passage of blood *per anum*—*Poisoning with viperine venom or phlegmonous inflammation of the stomach.*

III. *Intestines:—*

(*a*) Choleraic diarrhœa, or profuse diarrhœa, or dysenteric diarrhœa with fever.

Examine blood:—

1. Malarial parasites—*Pernicious malaria.*
2. Marked mononucleosis with enlargement of the spleen.—

   Splenic or hepatic puncture:—

   (A) Malarial parasites—*Pernicious malaria.*
   (B) Kala-azar bodies—*Kala-azar.*
3. Eosinophilia without enlargement of the spleen. Blood cultures—*Intestinal septicæmias or toxæmias due to worms.*

(*b*) Vague bowel symptoms or signs of intestinal schistosomiasis. Examine fæces for eggs and blood for eosinophilia—*Fevers due to intestinal worms.*

(*c*) Pain in the appendicular region—*Appendicitis.*

(*d*) Slight diarrhœa or constipation. General disturbance of health slight or moderately severe.

Examine motions for:—

1. Amœbæ—*Amœbiasis.*
2. Enteric bacilli. Confirm by blood cultures—*Enteroidea.*

B. *Symptoms pointing to the respiratory system :—*

I. Nose:—

(*a*) *Acute rhino-pharyngitis :—*

Examine secretion microscopically and culturally:—

1. Spirochætes—*Spirochætal rhino-pharyngitis.*
2. *Micrococcus catarrhalis* and similar organisms —*Common cold.*
3. Influenza bacillus or filterable virus present—*Influenza.*
4. Influenza baccillus, or filterable virus with Streptococci—*Streptococcal complications of influenza.*

(*b*) *Nose partially blocked :—*

Examine swabs microscopically and culturally for the Klebs-Loeffler bacillus —*Diphtheria.*

(*c*) *Larynx :—*

More or less stridor. Examine swabs of throat for Klebs-Loeffler bacillus—*Diphtheria.*

(*d*) *Bronchi :—*

Signs of bronchitis, with or without blood in the sputum. Examine fresh sputum microscopically, and if necessary by the dark ground illumination:—

1. Eggs—*Paragonimiasis.*
2. Spirochætes—*Bronchospirochætosis.*
3. Fungi—*Bronchomycosis.*
4. Acid-fast organisms:—
   (A) Tubercle bacilli—*Tuberculosis.*
   (B) Nocardia—*Pulmonary Nocardiasis.*

(*e*) *Lungs and pleura :—*

Physical signs of inflammation of the lungs or pleura, or both:—

1. Expectoration chocolate-coloured —*Liver abscess.*
2. Expectoration bloody or rusty. Examine microscopically for the same points as under bronchi and for the pneumococcus —*Pneumonia.*
3. Expectoration not chocolate-coloured nor bloody—*Diseases of lungs and pleura other than above.*

C. *Symptoms pointing to the circulatory system :—*

1. Marked collapse after exposure to great heat (especially associated with high atmospheric humidity) or to the sun's rays. There may or may not have been initial fever—*Heat syncope.*
2. Disturbed action of the heart, with severe constitutional symptoms and petechial eruption—*Infective endocarditis.*

D. *Symptoms pointing to the urinary system:—*

- (*a*) Urine black, due to hæmoglobin:—
    1. Following on a dose of quinine—*Quinine hæmoglobinuria.*
    2. With malarial parasites in numbers in blood—*Malarial hæmoglobinuria.*
    3. Not associated with quinine or malarial parasites in numbers in the blood—*Blackwater fever.*
    4. Associated with the administration of some drug such as chlorate of potash for a sore throat—*Toxic hæmoglobinuria.*
- (*b*) Suppression or marked diminution of the urine:—
    Differentiate by the history of the case, the region of infection, the presence or absence of Faget's sign, black vomit, etc.—*Blackwater fever or Yellow fever.*
- (*c*) Passage of large quantities of urine:—
    Examine for malarial parasites or other signs of malaria—*e.g.*, enlarged and tender spleen—*Pernicious malaria.*
- (*d*) Bile in the urine:—
    1. Associated with hæmoglobin—*Blackwater fever.*
    2. Not associated with hæmoglobin:—
        - (A) In epidemic form:
            Examine blood and urine for spirochætes.
            - (i.) Mild cases—*Icterus castrensis levis.*
            - (ii.) Severe case with hæmorrhages—*Icterus castrensis gravis* (*Weil's disease*).
        - (B) Not in epidemic form:—
            No spirochætes. During or after an attack of typhoid or paratyphoid fever—*Bacillary jaundice* (*Enteric jaundice*).

E. *Symptoms pointing to the reproductive system:—*

- (*a*) Chill, sudden pain and swelling along the spermatic cord, with often severe fever, but no erysipelatous appearance of the skin—*Endemic funiculitis.*
- (*b*) Fever after childbirth. Examine the aseptically collected uterine discharge for streptococci and other organisms—*Puerperal fever.*

F. *Symptoms pointing to the lymphatic system:—*

- (*a*) Cervical glands enlarged:—
    1. Most marked on the left side, associated with obstinate constipation and mild symptoms. Puncture of glands reveals no organisms—*Pfeiffer's glandular fever.*

2. Most marked in the posterior triangles of both sides of the neck. History of residence in sleeping sickness areas. Glandular fluid obtained by puncture shows trypanosomes—*Trypanosomiasis.*
3. Enlarged glands in neck and other parts. Œdema of face with characteristic crepitation. Fugitive œdemas in various parts. Enlarged and tender spleen. Enlarged liver. Increase in size of the thyroid gland. Residence in Tropical South America—*Chagas' disease.*

(*b*) *Lymph glands anywhere enlarged :—*

4. Pain in some lymph glands: tender, enlarged, freely movable under skin. Search area drained by lymphatics going to gland for circular vesicle or small black or brownish necrotic area indicative of a bite. Puncture of glands shows no bipolar plague bacilli. History of residence in the Akitaken and Nugataken of the Island of Nippon, Japan—*Tsutsugamushi disease.*

(*c*) *Inguinal or axillary glands enlarged :—*

5. Acute onset, high fever, great prostration. Puncture of glands reveals plague bacilli—*Plague.*
6. Gradual onset, slight fever. Very mild symptoms, malaise, pain on walking. Inguinal or crural glands enlarged, hard, very painful on pressure. Puncture shows sterile fluid—*Climatic bubo.*
7. Glands enlarged, inflamed, or suppurating, with chancre on penis, septic wound, or ulcer or *gonorrhœal* infection—*Septic infections.*
8. Occurring in the course of one of the enteroidea fevers—*Intestinal infections.*
9. High fever, lymphangitis, associated with an erysipelatous condition of the skin. Blood examination during night (or during the day in certain cases) reveals microfilaria—*Filarial lymphadenitis.*

G. *Symptoms pointing to the muscular system :—*

(*a*) Remittent or intermittent fever, with rheumatoid pains and abscesses in various parts of the body—*Myositis purulenta tropica.*

(*b*) Remittent fever, with rheumatoid pains, but no abscess formation. Œdematous patches often present, marked eosinophilia—*Trichinosis.*

H. *Symptoms pointing to the osseous system :—*

(*a*) Pain and tenderness, especially near a joint—*Osteomyelitis.*

(*b*) Sudden attack of fever, with great tenderness over, and pain in, the os calcis or other tarsal bone, which begins to increase in size—*Endemic enlargement of the os calcis.*

I. *Symptoms pointing to the connective tissue:—*

Rigors with fever and aching or dragging sensation, and outline of a worm under the skin of affected area—*Dracontiasis.*

J. *Symptoms pointing to the nervous system:—*

(*a*) Almost any acute sign or symptom pointing to the nervous system, including signs of mania, melancholia, or dementia, and associated with fever, with or without enlargement of the spleen. Examine blood for malarial parasites or mononucleosis—*Malaria.*

(*b*) Signs of meningitis present—*e.g.*, Kernig's sign, retraction of the head, etc. Examine cerebro-spinal fluid:—

1. Polymorphonuclear leucocytes and cocci present—*Epidemic cerebro-spinal meningitis.*
2. Trypanosomes present; also in juice from enlarged neck glands. Residence in Tropical Africa—*Sleeping sickness.*

(*c*) Signs of acute alcoholism:—

If picked up by the police, even if there is a smell of alcohol, examine spleen and take blood films if necessary. Drunk or dying in the tropics is often a question of alcoholism or malaria. Fever may be absent in both instances—*Acute alcoholism or malaria.*

D. DERANGEMENT OF SOME ORGAN.

The signs and symptoms associated with some organ of the body may be considered under the following headings:—

1. The Spleen.
2. The Liver.
3. The Pancreas.
4. The Suprarenal Capsules.
5. The Parotid.

A. *The spleen:—*

I. *Enlargement slight:—*

Rose-coloured spots on the abdomen. Symptoms of typhoid fever. Make blood cultures and fæcal cultures —*Enteroidea fevers.*

II. ***Enlarged and tender :—***

(*a*) Examine blood films for malarial parasites and for spirochætes—***Malaria*** or ***Relapsing fevers.***

(*b*) With œdema of the face and enlargement of the thyroid and lymphatic glands and liver. Residence in South America—***Chagas' American trypanosomiasis.***

III. ***Enlargement considerable :—***

(*a*) Generally a history of illness lasting some time, of which present fever is only a recurrence. Firm enlargement. Malarial parasites in blood—***Exacerbation of chronic malaria.***

(*b*) No malarial parasites in the blood:—

Great increase in white blood cells with myelocytes—*Leukæmia.*

(*c*) No malarial parasites and no great increase of leucocytes in the blood:—

1. Splenic or hepatic puncture shows Leishman-Donovan bodies *Kala-azar.*
2. Shows no Leishman-Donovan bodies — *Febrile splenomegaly.*
3. Toxoplasma bodies present *Toxoplasmosis.*

B. ***The liver :—***

Enlarged and tender:

1. Pain in the right shoulder, rigidity of right rectus, diminution of movement of right side of the diaphragm. Examine motions for amœbic cysts and the blood for mononucleosis (present) and malarial parasites (absent) –***Amœbic liver abscess.***
2. Signs of severe septic infection, jaundice, etc. If origin of sepsis not evident, examine fæces for intestinal worms and for enteroidea micro-organisms—***Multiple septic liver abscesses.***
3. Slight yellowish tinge in the sclerotic, seldom signs of general jaundice. Patient not seriously ill. No amœbiasis—*Tropical liver.*

C. ***The pancreas :—***

I. With intense pain in the upper and left part of the abdomen, which is distended with gas; vomiting and constipation—***Acute pancreatitis.***

II. Signs and symptoms of diabetes: threatened Kussmaul's coma. Recurrent attacks of fever every other day. Examine for malarial parasites: if absent and if only polymorphonucleosis give a few doses of quinine and note action on fever—***Malaria and diabetes.***

D. *Suprarenal capsules :—*

Signs suggestive of acute peritonitis— *i.e.*, high fever, distended tympanitic abdomen, quick pulse. No effusion into abdominal cavity. Examine blood for malarial parasites and for mononucleosis. If absent, give quinine and again test blood —*Acute malaria attacking suprarenals.*

E. *Parotid glands :—*

Painful tender swelling of parotid, especially if bilateral— *Mumps.*

II. ACUTE FEVERS WITHOUT STRIKING PHYSICAL SIGN.

A *Patient is carrying on his ordinary work :—*

I. Fever is intermittent, every third or fourth day. Examine spleen for enlargement and tenderness, and examine blood for malarial parasites and mononucleosis, which may be absent. Clinical symptoms alone may be positive— *Malarial fevers.*

II. Fever is quotidian. Examine spleen for tenderness and enlargement. Examine blood for malarial parasites and mononucleosis. If none, give quinine and note action on fever – *Malaria.*

III. No malarial parasites, and quinine therapy without effect :—

(*a*) Pulse dicrotic: slow in proportion to the temperature. History of several days' indisposition. Tongue furred, constipation, or diarrhœa. Gurgling on pressure in right iliac region. Make blood and fæcal cultures, and examine for enteroidea organisms —*Enteroidea group of fevers.*

(*b*) Pulse not dicrotic; slow in proportion to the temperature. Attack sudden, with at first pain and tenderness, which later disappear in the region of the appendix. No malarial parasites in blood— *Gangrenous appendicitis.*

(*c*) Abrupt onset, catarrhal symptoms, with sensation of considerable illness and with generalized pains, often in epidemic form —*Influenza.*

(*d*) With or without signs of bronchitis, enlargement of liver and spleen, or with signs of broncho-pneumonia. Examine sputum for tubercle bacilli, or if lung symptoms absent test cuti-reaction— *Acute phthisis or tuberculosis.*

(*e*) Gradual onset, temperature increasing every night. Headache and rheumatoid pains in body and limbs. Tongue furred. Blood cultures for *M. melitensis* and *M. paramelitensis*—*Undulant fever.*

B. *Patient unable to carry on his usual duties :—*

(*a*) Liver and lymphatic glands enlarged. Spleen not enlarged. Examine blood. Signs of great destruction of red blood-corpuscles (presence of *Bartonella bacilliformis*). Residence in Peru—*Oroya fever.*

(*b*) Sudden onset, with injected conjunctivæ (pink eye), high fever, comparatively slow pulse. Severe rheumatoid pains. Liver and spleen normal. Patient irritable, with pain in head and eyes, and may be delirious. Endemic area for *Phlebotomus* flies—*Pappataci fever.*

(*c*) Sudden onset, with severe pain in some part of the body or all over the body. With or without enlargement of the lymph glands, with generally a maculo-papular eruption on the third or fourth day. Conjunctivæ injected. Fauces congested. Pulse increases proportionately with the fever. Endemic area for stegomyia (perhaps also for *Culex fatigans*)—*Dengue fever.*

(*d*) Sudden onset. Hyperæsthesia over shins. Pains in the legs. Often slight splenic enlargement. Mononucleosis in blood. May or may not be history of association with lice. Blood examination excludes malaria, relapsing fever, etc.—*Trench fever.*

(*e*) Sudden onset, with or without rigors and pains. Examine blood for malarial parasites—*Malaria.*

(*f*) Gradual onset. Signs of enteric fever. Make blood and fæcal cultures—*Enteroidea group of fevers.*

(*g*) Blood examination reveals marked polymorphonuclear increase. Examine gums, teeth, ear, nose, throat, fingers, toes, bones, and every orifice of the body, for possible source of infection; make blood cultures—*Septicæmia.*

(*h*) Blood examination. Examine night and day blood for microfilariæ—*Filariasis.*

(*i*) Examine fæces for intestinal eggs, especially after a purgative—*Toxæmias due to intestinal worms.*

(*j*) Gradual onset, with marked pains in the joints, profuse sweating, high fever, and relatively slow pulse. Furred tongue—*Undulant fever.*

(*k*) Sudden onset, with hyperpyrexia, delirium, or coma associated with high atmospheric temperatures—*Thermic fever* (*heat-stroke*).

(*l*) Sudden onset, with or without history of fever. Syncope associated with high atmospheric temperatures—*Heat syncope.*

FEVERS OF MORE THAN EIGHT DAYS' DURATION.

Fevers of more than *eight days'* and less than *six weeks'* duration may be classified as follows:—

A. *Fever of intermittent type* :—

With malarial parasites or pigment in blood or with enlarged spleen:—

I. Fever every day—*Quotidian malaria.*

II. Intermittent fever every third day—*Tertian malaria.*

III. Intermittent fever every fourth day—*Quartan malaria.*

B. *Fever of the relapsing type* :—

I. Without malarial parasites or pigment, and not reacting to quinine therapy. Intervals between attacks several days. During attack spirochætes in blood—*Relapsing fevers.*

II. With malarial parasites and no signs of spirochætes, and reacting to quinine therapy—*Malaria.*

III. Without parasites, and only one or two relapses; not reacting to quinine therapy. After a long fever presumed or proved to be enteroidea in type. Examine fæces and urine for enteroidea organisms—*Enteroidea type of fever.*

C. *Fever remittent or continuous* :—

I. Reacting to quinine therapy—*Malaria.*

II. Not reacting to quinine therapy.

A. WITH MARKED PHYSICAL SIGNS.

1. *Well-defined local pain and tenderness* :—

Examine blood films. Leucocytosis, blood cultures, urine cultures. Lastly, examine cerebro-spinal fluid (earlier if head or spine symptoms)—*Septicæmias or toxæmias due to foci of deep suppuration.*

2. *Signs of lung disease* :—

Examine sputum:—

(*a*) Tubercle bacilli—*Tuberculosis.*

(*b*) Other organisms and signs of pneumonia—*Broncho-pneumonia.*

3. *Organic cardiac murmurs* :—

With or without petechial eruptions. Signs of gonorrhœa or rheumatism—*Infective endocarditis.*

4. *Nervous symptoms* :—

Pain in the head, retraction of the head. Kernig's sign. Examine cerebro-spinal fluid—*Meningitis.*

5. *Skin eruptions* :—
   - (*a*) Rose-red spots—***Enteric fevers.***
   - (*b*) Flushing of the face, with subcuticular mottling and severe symptoms. Typical eruption on fourth day—***Typhus fever.***
   - (*c*) Purulent discharge from nose. Bullæ, nodules, and ulcers in skin, with papulo-pustular eruption. Work with horses—***Glanders.***
   - (*d*) Pustular eruption—***Glanders.***
   - (*e*) Dark or black pigmentation—***Addison's disease.***
6. Enlarged lymphatic glands—***Hodgkin's disease.***
7. Tenderness in a bone, especially near a joint. Blood cultures—***Osteomyelitis.***
8. Nodules and tenderness in muscles. Puncture the nodules and examine:—
   - (*a*) Pus—***Purulent myositis.***
   - (*b*) Filaria—***Filariasis.***
9. *Splenic enlargement* :—

   Examine blood:—
   - (*a*) Marked increase of lymphocytes or leucocytes with myelocytes—***Leukæmia.***
   - (*b*) Malarial parasites or pigment in leucocytes—***Malaria.***

   Splenic or hepatic puncture :—
   - (*a*) Malarial parasites or pigment—***Malaria.***
   - (*b*) Leishmania parasites—***Kala-azar.***
   - (*c*) Absence of Leishmania parasites—***Splenomegaly, febrile form.***
   - (*d*) Toxoplasma bodies present—***Toxoplasmosis.***

B. WITHOUT MARKED PHYSICAL SIGNS.

A. *Intermittent fevers* :—
- I. Fever every third or fourth day—***Malaria.***
- II. Fever every day. Examine blood:—
  - 1. Malarial parasites or distinct mononucleosis—***Malaria.***
  - 2. Malarial parasites absent; distinct polymorpholeucocytosis—***Septic fevers.***

B. ***Relapsing fevers*** :—

Fever for several days after period of apyrexia—***Relapsing fevers.***

C. ***Remittent and continuous fevers*** :—
- I. Benefited by quinine, with or without parasites in blood—***Malaria.***

II. Not benefited by quinine:—

(*a*) Test the serum reactions for typhoid and the paratyphoids, and the other common enteroide organisms of the period and locality. Confirm by blood cultures—large quantities, 10 c.c., of blood taken at night—or by fæcal cultures—*Enteroidea group.*

(*b*) Test for Mediterranean fever by serum reactions and blood cultures—*Undulant fever.*

(*c*) Culture of aseptically collected urine—*Pyelitis.*

(*d*) Examine motions for eggs of intestinal worms—*Intestinal toxæmias due to worms.*

(*e*) Wassermann reaction—*Syphilis.*

(*f*) Cuti reaction for tuberculosis—*Tuberculosis.*

(*g*) Other causes having been excluded. Bodily temperature 99°-101° F.: shows only slight rise once a day. Patient indisposed during the attack—*Low intermittent fever.*

(*h*) Patient residing in locality with high atmospheric temperatures. Patient not indisposed during the attack—*Low heat fever.*

(*i*) Same as in (*g*), but in children with higher temperatures, 103°-104° F., or more—*High intermittent fevers.*

CHRONIC FEVERS.

By the term 'chronic fevers' we mean those which continue longer than six weeks.

A. *Intermittent in type :*

I. Occurring every third day, with enlargement of the spleen and malarial parasites, or yielding to quinine therapy—*Tertian malaria.*

II. Occurring every fourth day, with enlargement of the spleen, and malarial parasites or pigment in the blood, or yielding to quinine therapy—*Quartan malaria.*

III. Occurring every day, with enlargement of the spleen and malarial parasites, yielding to quinine therapy—*Quotidian malaria.*

B. *Relapsing in type :—*

Attacks of fever lasting a few days, separated by intervals of several days, with severe symptoms. Examine blood for spirochætes. If necessary, inject monkeys and examine blood during an attack of fever for spirochætes—*Relapsing fevers.*

- C. *Remittent or continuous in type :—*
  - I. Benefited by quinine therapy—*Malaria.*
  - II. Apparently not benefited by quinine therapy:—
    - (*a*) Ulcers or tumours present in some part of the body. Examine thoroughly, including nose, naso-pharynx, and all apertures of body. Especially examine the teeth, particularly crowned teeth or bridges. Examine fingers and toes carefully—*Septic infection or absorption.*
    - (*b*) *Cutaneous dark pigmentation a marked feature :—*
      - 1. Examine spleen for enlargement and blood for malarial parasites or mononucleosis. Insufficient quinine administered—*Malaria.*
      - 2. Fever generally absent. No signs of malaria. Vomiting at times. Weakness, etc.—*Addison's disease.*
    - (*c*) *Splenic enlargement a marked feature :-*
      - I. Examine blood films:—
        No malarial parasites seen.
        - (A) Marked increase in white cells, lymphocytes, or with myelocytes *Leukæmia.*
        - (B) Having excluded leukæmia, *but not before*, examine blood obtained by splenic puncture:—
          - 1. Malarial pigment or parasites present—*Malaria.*
          - 2. Leishman-Donovan bodies present—*Kala-azar.*
          - 3. Leishman-Donovan bodies absent—*Febrile splenomegaly.*
          - 4. Toxoplasma-like bodies present—*Toxoplasmatic febrile splenomegaly.*
          - 5. All parasites absent—*Pseudo-kala-azar.*
    - (*d*) *Œdema a marked feature :-*
      - I. Examine blood for malarial pigment, parasites, or mononucleosis, and the spleen for enlargement—*Chronic malaria.*
      - II. No signs of malaria:—
        - (A) Examine motions for eggs of intestinal worms, especially ancylostoma ova—*Ankylostomiasis.*
        - (B) No eggs or signs of worms. In South America. Examine blood during an attack of fever for trypanosomes—*Chagas' disease.*

(*e*) *Intestinal indigestion a marked feature* :—

I. Examine motions after test-meal for muscle fibres, fat globules; extract fat. Examine urine for Cammidge's reaction. Fever not a marked symptom—*Chronic pancreatitis.*

II. Attacks of fever a marked symptom. No muscle fibres, etc., in motions. No Cammidge's urinary reaction. Examine fæces after a purge for eggs of intestinal worms, and if absent, for micro-organisms of proteus and allied groups—*Intestinal infections and toxæmias in helminthiasis.*

(*f*) *Enlarged lymphatic glands a marked feature* :—

I. Fever not a marked feature; glands very much enlarged in many parts of the body. No very great increase in the number of leucocytes—*Hodgkin's disease.*

II. Attacks of fever a marked feature. Glands only moderately enlarged, especially in the posterior triangles of the neck. Residence in Tropical Africa. Examine gland juice for trypanosomes —*Sleeping sickness.*

Summary.

This small sketch of the diagnosis of certain tropical fevers may be found useful when read in conjunction with the preceding chapters. We would, however, again emphasize the point that the only method of diagnosing fevers is by long bedside experience, associated with careful laboratory work.

SECTION B

GENERAL DISEASES

DIVISION. I: CAUSATION, ANIMAL PARASITES.

SUBDIVISION A: DUE TO PARASITIC PROTOZOA.

Framboesia Tropica.
Verruga Peruviana.
Rhinosporidiosis and Sarcosporidiosis.

SUBDIVISION B: DUE TO PARASITIC WORMS.

Paragonimiasis.
Katayama Disease.
Filariasis.

SUBDIVISION C: DUE TO PARASITIC ARTHROPODS.

Myiasis.
Porocephalosis.

DIVISION II.: CAUSATION, VEGETAL PARASITES.

Leprosy.
Histoplasmosis.

DIVISION III.: CAUSATION, CHEMICAL.

SUBDIVISION A: DUE TO CHEMICAL DEFICIENCY.

Beri-Beri and Epidemic Dropsy.

SUBDIVISION B: DUE TO POISONS.

Tropical Poisonings.

DIVISION IV.: CAUSATION, UNKNOWN.

Pellagra.

CHAPTER LXI

FRAMBŒSIA TROPICA

Synonyms—Definition—History—Geographical distribution—Ætiology—Histopathology—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—References.

Synonyms.—In the British Colonies the disease is usually called 'yaws': in the French colonies 'pian.' In Venezuela and other South American countries the name 'bubas' is much used. German and Italian authors generally use the term 'Frambœsia,' which was first used by Sauvage in 1750 on account of the raspberry-like appearance of the eruptive elements. Charlouis in 1882 suggested the term 'Polypapilloma tropicum': Noc, Stevenel, and Iman introduced the term 'Castellani's spirochætosis,' Da Matta 'Castellani's treponemosis,' and Violle the term 'cutaneous spirochætosis.' Other local names are 'gattoo' (West Coast of Africa), 'dubi' (Gold Coast), 'tramosi' (Calabar), 'ab oukine' (Gaboon), 'nkoulou,' 'tetia' (Congo Coast), 'momba' (Angola), 'parangi' (Ceylon), 'buena' (Burma), 'puru' (Borneo, Federated Malay States), 'patek' (Dutch Indies), 'tonga' (New Caledonia and Loyalty Islands), 'coco' (Fiji), 'tona' (Tonga Island), 'lupani tono' (Samoa), 'galis pateros' (some parts of the Philippine Islands), 'ki-mo' (French Indo-China).

Definition.—A tropical specific infectious and contagious disease caused by *Treponema pertenue* Castellani, and characterized by a frambœsiform granulomatous eruption.

History.—It has been suggested by Hume, Adams, and others that frambœsia was the disease which afflicted the Israelites during their emigration from Egypt, and that therefore the term 'saraat' in the thirteenth chapter of Leviticus does not mean leprosy, as usually translated. Ali Abbas and Avicenna, who wrote at the end of the tenth century, mention a disease called 'safat,' or 'sahafati,' with symptoms not unlike those of frambœsia; but most authors are of the opinion that the disease referred to by the two Arabian physicians was syphilis. The study of the disease first began to engage the attention of European physicians after the discovery of America. Oviedo y Valdez (1478-1557) describes it in his work, 'Historia General e Natural de las Indias.' Piso (1648) refers to the malady in his work, 'De Medicina Brasiliensis.' Rochefort (1656), Raymond Breton (1665), and Labat (1694), report it from the West Indies, stating that it occurs frequently among the natives (Caribs), who called it 'pyans,' or 'yaya.' Bontius, in 1718, reported that frambœsia was endemic not only in the West Indies, but also in Java, Sumatra, and other Dutch colonies of the East, where it was known by the name of 'anboyna pox,' or 'pimple.' In the days of the slave-trade, outbreaks of frambœsia frequently occurred in the crowded ships carrying African slaves to America. Special hospitals for the isolation and treatment of slaves suffering from the disease were built on all the important estates in the West Indies. Occasionally in the countries in which it is endemic the disease may increase to such an extent as to cause veritable epidemics. An example of such an epidemic occurred in Dominica in 1871, when two special segregation hospitals had to be built for frambœsia patients.

In 1769 an outbreak of a peculiar disease occurred in Scotland. It was called 'sibbens,' or 'sivvens' (*sivvi*, Celtic for raspberry), and was apparently imported by sailors belonging to a vessel coming from the West Indies, which was wrecked off Wigton in Cumberland.

The so-called 'button scurvy' of Ireland, endemic there in the eighteenth and the beginning of the nineteenth centuries; the 'radesyge,' which broke out in Sweden and Norway in 1710; and the 'mal de chicot' in Canada, have likewise been considered by some writers to be forms of frambœsia.

Several authors have endeavoured to distinguish between 'yaws,' 'pian,' 'boubas,' and 'parangi'; but those who have had the opportunity to study the disease in different countries have all come to the conclusion that 'yaws,' 'pian,' 'boubas,' and 'parangi,' are simply different names for the same disease, though of course each of these terms is often used by natives to cover several closely allied conditions. The term 'boubas,' for instance, is used by the inhabitants of Brazil for various ulcerative conditions, such as frambœsia, leishmaniasis, and blastomycosis, but most of the medical South American authorities use it as a synonym for frambœsia. Unfortunately, Breda used it to denote a form of leishmaniasis, and caused much confusion. The experimental researches of one of us in cases of frambœsia contracted in different parts of the world (tropical America, East and West Africa, etc.) show that 'yaws,' 'pian,' 'boubas,' and 'parangi,' are merely synonyms, but it is possible that there may be several varieties of the spirochæte which is the cause of the disease.

Since the time of Labat several authors have upheld the syphilitic nature of frambœsia. This theory was supported at one time by Sir J. Hutchinson. In recent times the disease has been investigated, both clinically and experimentally, by a large number of observers.

In 1882 Charlouis proved by actual experiment that syphilis and frambœsia are two different maladies. The clinical investigation of the disease by Numa Rat was also of great value. His report, published in 1891, has become classical.

Among the more recent observers who have investigated the disease in various parts of the tropics are Neisser, Daniels, Wellman, Jeanselme, Powell, Braush, Martin, Halberstadter, von Prowazek, Ashburn, J. Craig, Nichols, Strong, Flu, Noc, Stevenel, Iman, Da Matta, Spronk, Sheman, Schüffner, Maul, and many others.

Geographical Distribution.—Framboesia is essentially a tropical disease, as few, if any, genuine cases have been reported from places outside the tropical and subtropical zone, and in the tropics it is never found on the mountains and cold districts, as we remarked in the previous editions of this manual. Bahr states that cases who have contracted the disease at a higher elevation than 800 feet are very rare. At the present time a skin disease not unlike framboesia has been reported from Greece by several writers.

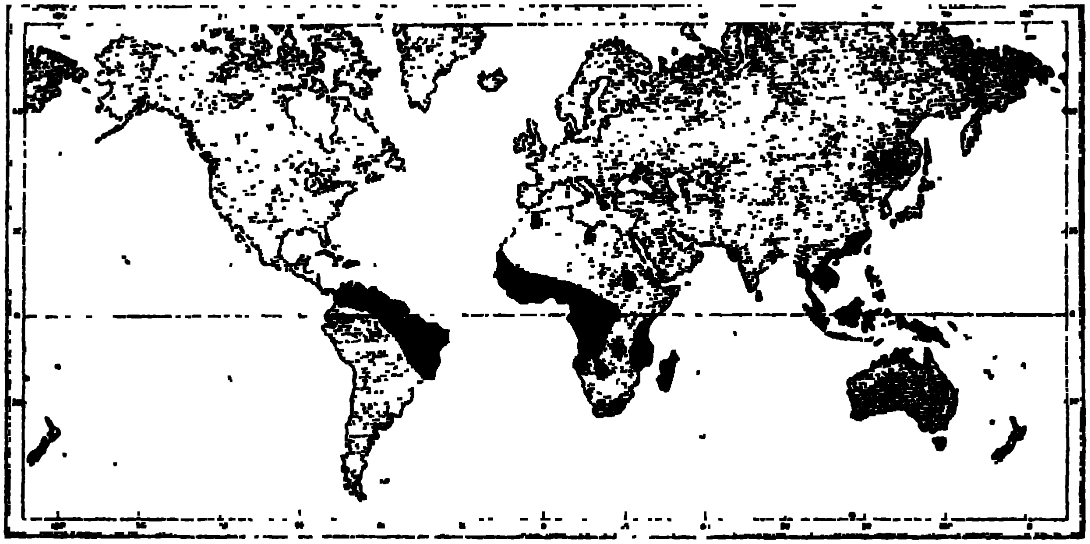


FIG. 685.—DISTRIBUTION OF FRAMBŒSIA TROPICA

Africa.—The disease till recently was said to be very rare in the northern regions of the continent, though some cases were reported from Algeria; the researches of Gabbi and Sabella have demonstrated, however, that it is common in Tripoli. It is apparently rare in Egypt, though, according to some writers, it is observed fairly frequently in the Sudan. It is very common on the West Coast, especially on the Gaboon River, in the Congo Free State, and in Angola. The disease is quite common in Nigeria. It is also found in Mozambique, in Madagascar, and the Comoro Islands. In Uganda and the region of the Great Lakes it is occasionally met with. It has been noted among the Kaffirs in South Africa, near Kimberley, by Griffith, and by many other observers in several other districts of South Africa, Rhodesia, and Nyasaland.

Asia.—The disease is very common in the Malay Peninsula, Assam, Upper Burma, Siam, Java, Batavia, and is extremely frequent in Ceylon, where the number of cases treated in the Government Hospitals during the last ten years has been on the average 3,500 per year, and it must be noted that the patients treated in hospitals represent only a small portion of all the cases.

In India it is very rare, though small outbreaks of the disease have been described by various observers. It occurs in certain parts of China, but is unknown in Japan and the central and western regions of the Asiatic continent. It is present in the Philippine Islands.

America.—It is very common in the West Indies, and occurs in British Guiana, Venezuela, Colombia, and Brazil. Cases have been reported from the southern United States, but never from the northern States nor from Canada. Recently Wood has recorded a case in a white child in North Carolina.

Australasia.—The disease is present in Northern Australia, and occurs frequently in many of the Pacific Ocean islands—Samoa, New Hebrides, New Caledonia, and Fiji. It is absent in New Zealand and Tasmania.

Ætiology.—Different kinds of bacteria have been described as causative agents of framboesia. Eijkman found some peculiar bacilli; Pariez observed numerous micrococci; Powell, in 1896, cultivated from two cases a yeast; Nicholls and Watts, in 1899, isolated a coccus which, inoculated into animals, failed to reproduce the disease. In February, 1905, Castellani observed a *Treponema*, or spirillum, as he thought it at the time. This organism, which he called *T. pertenue*, is now generally admitted to be the cause of the disease. For the description of the organism, see p. 457.

Incidence of the T. pertenue in Framboesia Lesions.—The presence of the *Treponema* is constant in the primary lesion and in the unbroken papules of the general eruption. It may be found in the spleen, lymphatic glands, and bone-marrow. In the blood it has not yet been demonstrated microscopically, though there is no doubt that the blood of the general circulation is infectious, inasmuch as monkeys inoculated with it develop typical yaws lesions in which the *Treponema* is abundantly present. The *Treponema* is absent in the cerebro-spinal fluid, and generally in the tertiary lesions.

Bacteriological Flora found in Open Sores of Framboesia.—While *T. pertenue* is the only germ found in the non-ulcerated lesions, the ulcerated lesions of framboesia are soon invaded by all kinds of germs. Apart from innumerable bacteria, various kinds of spirochætes are present. One form is rather thick, and takes up the stain easily. It is morphologically very similar to the *Spirochæta refringens* of Schaudinn. Another form is thin, delicate, with coils varying in size and number, and with blunt extremities—*S. obtusa* Castellani. A third form is likewise thin and delicate, but tapers at both ends —*S. acuminata* Castellani: *T. pertenue* is also present in many cases.

Inoculation Experiments of Framboesia in Man.—Paulet, in 1848, inoculated fourteen negroes with the secretion taken from frambœtic granulomata. All of them developed framboesia, the inoculation period varying from twelve to twenty days, when at the seat of inoculation in ten cases the first nodule appeared, soon followed by a typical general eruption. In two cases apparently the eruption did not start from the seat of inoculation.

Charlouis, in 1881, inoculated thirty-two Chinese prisoners, who had never suffered from the disease, with crusts and scrapings from a case of yaws. The disease developed in twenty-eight of them, beginning invariably at the seat of inoculation. Moreover, he inoculated a native suffering from typical yaws with syphilis. The inoculation was quite successful, a primary syphilitic sore developing, followed by all the usual types of secondary eruption. That yaws patients are not immune against syphilis is proved also by Powell and Nichols and others, who have described several cases of syphilis supervening on yaws. Syphilitic patients may contract frambœsia naturally and experimentally.

Inoculation Experiments in Monkeys and Other Animals.—Neisser, Prowazek, Halberstadter in Java, and shortly afterwards Castellani in Ceylon, have shown that monkeys are susceptible to frambœsia. According to their experiments, the inoculation period varies from a minimum of sixteen days to a maximum of ninety-two. The appearance of the lesions developing at the seat of inoculation is practically the same in all cases—viz., an infiltrated spot slowly increasing in size, and soon becoming moist, the secretion drying into a thick crust. Removal of the crust exposes a raw, granulating, red surface.

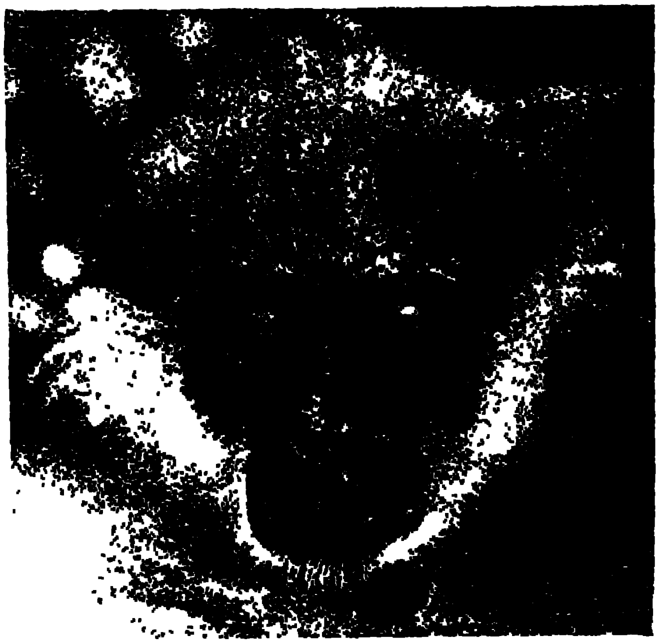


FIG. 680.—MONKEY INOCULATED WITH FRAMBŒSIA.

In the monkeys of a low class (genus *Macacus*, genus *Semnopithecus*) the eruption is, as a rule, localized to the seat of inoculation. The infection, however, is general, as is proved by the presence of *T. pertenue* in the spleen and lymphatic glands besides the local lesions. Halberstadter has obtained a general eruption in ourang-outangs. According to Castellani's experiments, splenic blood, obtained by puncturing the spleen of a patient affected with frambœsia, can reproduce the disease in monkeys. The inoculation of the blood of the general circulation also may occasionally produce the disease. The inoculation of cerebro-spinal fluid into normal monkeys has always proved negative.

Neisser, Halberstadter, von Prowazek in Java, and later Castellani in Ceylon, have proved that monkeys successfully inoculated with framboesia do not thereby become immune to syphilis, and, *vice versa*, monkeys successfully inoculated with syphilis do not thereby become immune to framboesia. According to Levaditi, monkeys immunized for yaws do not acquire any immunity for syphilis, but monkeys immunized for syphilis may acquire a partial immunity for framboesia. According to Ashburn and Craig, monkeys of the species *Cynomolgus philippinensis* are susceptible to framboesia, but not to syphilis.

The following facts are in favour of the *T. pertenue* being the specific cause of framboesia:—

1. In the non-ulcerated papules, in the spleen, in the lymphatic glands of framboesia patients, as well as in inoculated monkeys, the *T. pertenue* is the only organism present. No other germ can be demonstrated either microscopically or by cultural methods.

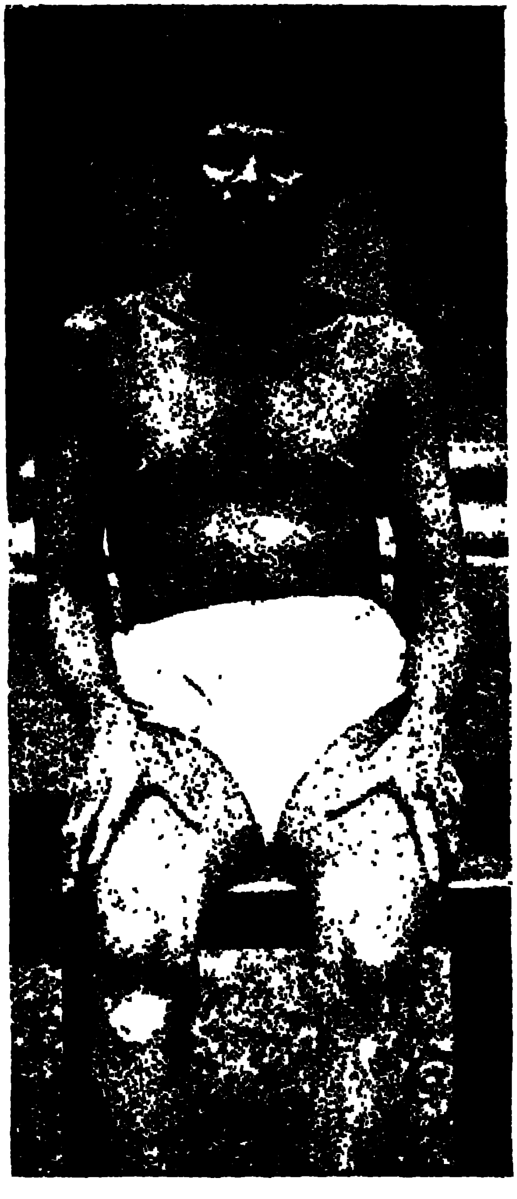
2. The extract of framboesia material containing the *T. pertenue*, but, so far as our present methods of investigation permit us to say, no other germs, is effective when inoculated into monkeys.

3. The extract of framboesia material from which the *T. pertenue*, has been removed by filtration becomes inert, and monkeys inoculated with it do not contract the disease.

PREDISPOSING CAUSES.—As is the case in other infectious diseases, dirt and other insanitary conditions favour to a certain extent the development and dissemination of the disease. The malady is rare among Europeans, and also among the better-class natives, who live amidst good sanitary surroundings, while it is very common among the villagers and low-caste natives, who live in uncleanly overcrowded huts. Sex does not exercise any influence, nor does age to any great extent, though the disease is more frequently met with in children and young people. The native practitioners of Ceylon are inclined to ascribe an important predisposing influence to certain foods. Some incriminate a kind of fish called 'balla mai,' others a cereal known as 'kurrakan.' Duprey inculpates in the West Indies the abuse of mango fruit.

Histopathology.—The histopathology of framboesia has been investigated by Unna, Macleod, Jeanselme, Plehn, and more recently by Schuffner, Marshall, Shennan, Siebert, Ashburn, Craig, and Löhe. In the frambœtic papules the surface epithelium is greatly increased in thickness, and numerous elongated down-growths are seen. The epithelial layers show many patches, in which the epithelial cells are swollen, vacuolated, and degenerating. Small, sharply circumscribed areas are also seen containing polymorphonuclear leucocytes and detritus. The layers near the corium and its processes are, however, almost normal in appearance. The connective-tissue corium forms a thin layer, from which narrow, elongated, papillary processes pass into the epithelium, some of them nearly reaching the surface. The corium is the seat of marked œdema. There is a diffuse cellular infiltration made up of polymorphonuclear leucocytes, large and small mononuclear leucocytes, eosinophiles, plasma cells, mast cells, connective-tissue cells, and some extravasated erythrocytes. In the older nodules the plasma cells are present in such enormous numbers as to dominate all the others. Macleod has shown that there is no perivascular mononuclear infiltration so characteristic of syphilis, nor any endothelial proliferation in the vessel walls. The frambœtic lesion also differs from that of syphilis in affecting the epithelium rather than the cutis, in the more considerable œdema, and in the absence, as a rule, of the giant cells.

When the frambœtic granulomata have reached a certain stage, a very well-marked hyperkeratosis is noticeable. One of us has called attention to the appearance of the films taken in the usual way from the granulomata, and stained according to Leishman's method. In such films it is interesting to note the presence of a large number of polychromatic red blood cells of very different sizes, some much larger than the normal erythrocytes, some much smaller. They are stained deep or light blue instead of pink, and sometimes have a granular appearance. The leucocytes present in the films frequently contain in their protoplasm, and sometimes in their nuclei, roundish or oval, more or less deeply blue stained bodies, which are probably polychromatic micro-erythrocytes engulfed by phagocytes. Some of these bodies present peculiar chromatin dots. In such films the Treponemata are almost constantly found. The Treponemata may be put in evidence also in sections by using the Volpino-Bertarelli or Levaditi's silver staining, as used by Spronk, Shennan, and Schüffner. The examination of sections so stained shows that the parasite is mostly found in the epithelial layers.



ig —Frambœsia: Primary Stage, showing the Primary Lesion or Frambœsoma below the Right Knee.

Symptomatology.—The course of frambœsia may be divided into three periods—a primary stage, comprising the development of the primary lesion or frambœsoma: a secondary or granulomatous stage, during which the characteristic frambœtic granulomatous eruption appears: a tertiary or late stage, in which the late manifestations of the disease develop—deep ulcerations and gummatous-like nodules. A fourth period may perhaps be added (paraframbœsial affections). This division into three or four periods is, of course, somewhat arbitrary, as symptoms considered to be characteristic of one period may make their appearance in another: tertiary symptoms, for instance, may appear during the secondary stage.

It has been stated again and again that the whole course of the disease lasts from three to six months in children, and six to twelve in adults, but according to our experience it has a much longer duration, and unless it becomes extinct after the secondary stage it may extend to many years. Indeed, we believe that in a certain number of cases, although there are periods during which the patient is apparently free from symptoms, the infection is merely latent, and sooner or later gives rise to renewed manifestations.

The Primary Stage: Frambœsoma.—After a period of incubation, varying in time between two to four weeks, characterized often by signs of malaise, rheumatoid pains, headache, irregular rise of temperature, the primary lesion or frambœsoma appears at the seat of inoculation, which is always extragenital. The primary lesion is a papule, which after about a week becomes moist, developing a yellowish secretion, which dries into a crust. Often at the place of inoculation several papules appear, become moist, and coalesce into a single element, covered by a thick crust. If after some days the crust is removed, the primary sore will appear as an ulcer, not rarely of large dimensions, with clean-cut edges and a granulating fundus. This ulcer may heal, leaving a whitish scar, which may later become pigmented; or in other cases it may develop into a granulomatous mass, not dissimilar to the granulomata of the secondary eruption, which appear later on, but frequently much larger. This large single projecting nodule is called 'mother yaw,' or 'maman pian' in French patois, 'buba madre' in Columbia of South America. Occasionally round it, before the general eruption begins, several smaller granulomata develop like satellites. The primary sore never feels indurated, and is often painful during the first stage of development. Later it may be quite painless. Occasionally there may be pruritus. The proximal lymphatic glands may become hard and enlarged, but they do not suppurate.

The seat of the primary sore is usually extragenital. The lesion may develop on an old ulceration, an itch pustule, an insect bite, a wound, or a vaccination mark. The smallest abrasion is sufficient for the entrance of the virus. Most of our female patients presented the primary sore on one of the mammæ, developing on some crack or abrasion of the nipple and areola. In several other women the primary lesion was found on the skin of the trunk, just above the hip, this being due to the custom of the Ceylon woman carrying her child astride of the hip. Any frambœtic element present on the scrotum or nates of the child, being continually rubbed against the skin of the mother, is likely to cause infection in the latter through any slight abrasion already present, or brought about by the friction. In men and children the primary lesion is frequently found on the hands, arms, and legs, but it may develop on any part of the body.

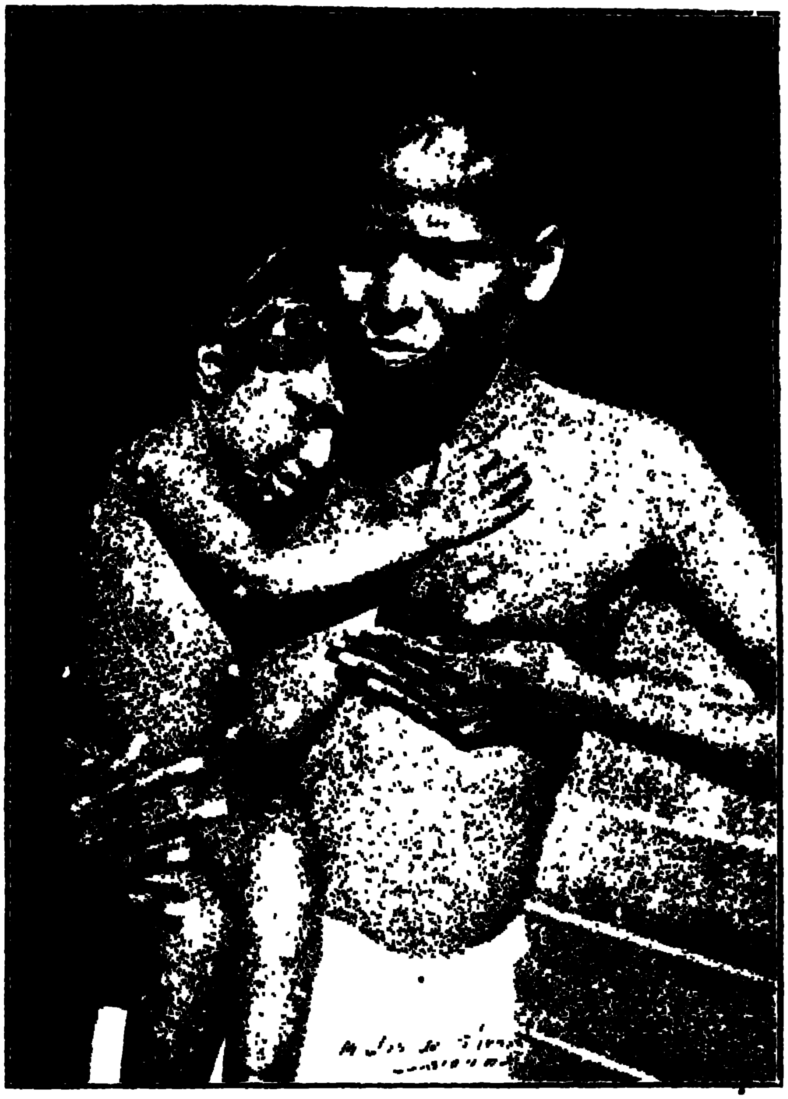


Fig. 688.—Child with General Granulomatous Eruptions, and Mother with the Primary Lesion (Frambœsoma) on the Left Mamma.

The primary lesion or frambœsoma may heal before the general eruption begins, but, as a rule, is still present when the secondary eruption appears. We observed a case in which the primary lesion was still present six months after its first appearance, and when the secondary granulomatous eruption had nearly undergone complete involution. The duration of the primary lesion, therefore, may vary between a few weeks and several months. The primary lesion leaves a whitish scar, which later on may become pigmented.

In some cases the scar is small and smooth, in others it is large and very thick. It is to be noted, however, that in Ceylon the disfiguring scar so frequently seen is partly due to the custom the natives have of cauterizing the sore deeply by very primitive methods. In other cases the large disfiguring cicatrix is due to the frambœsoma having developed on an old ulcer, which on healing leaves a coarse scar.

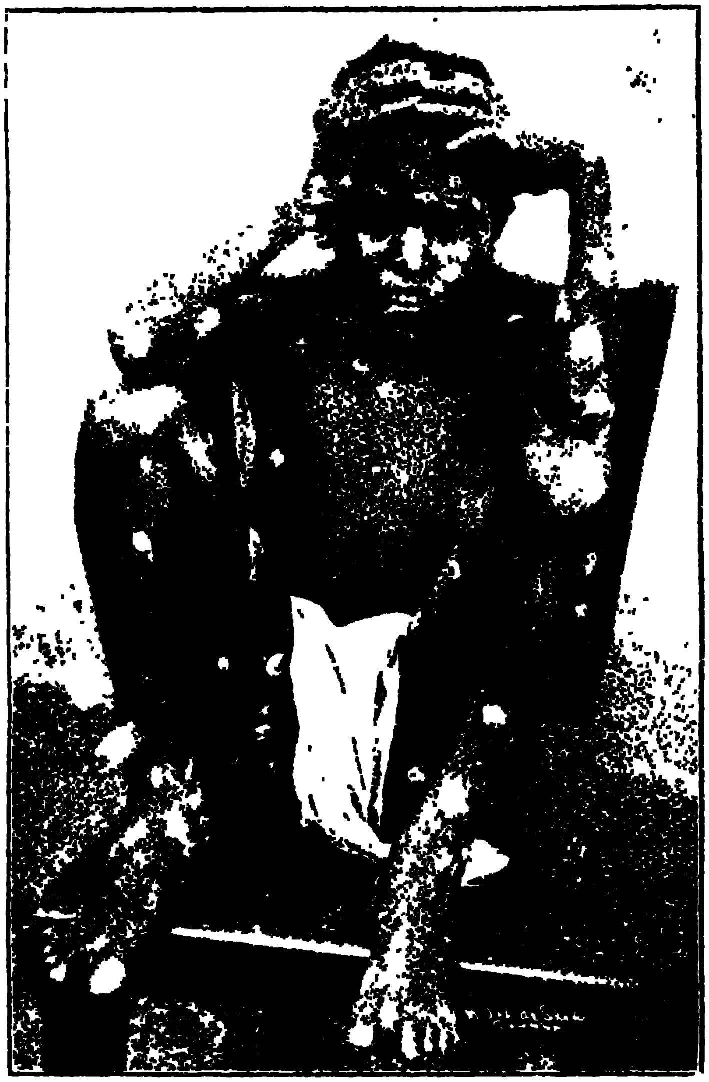
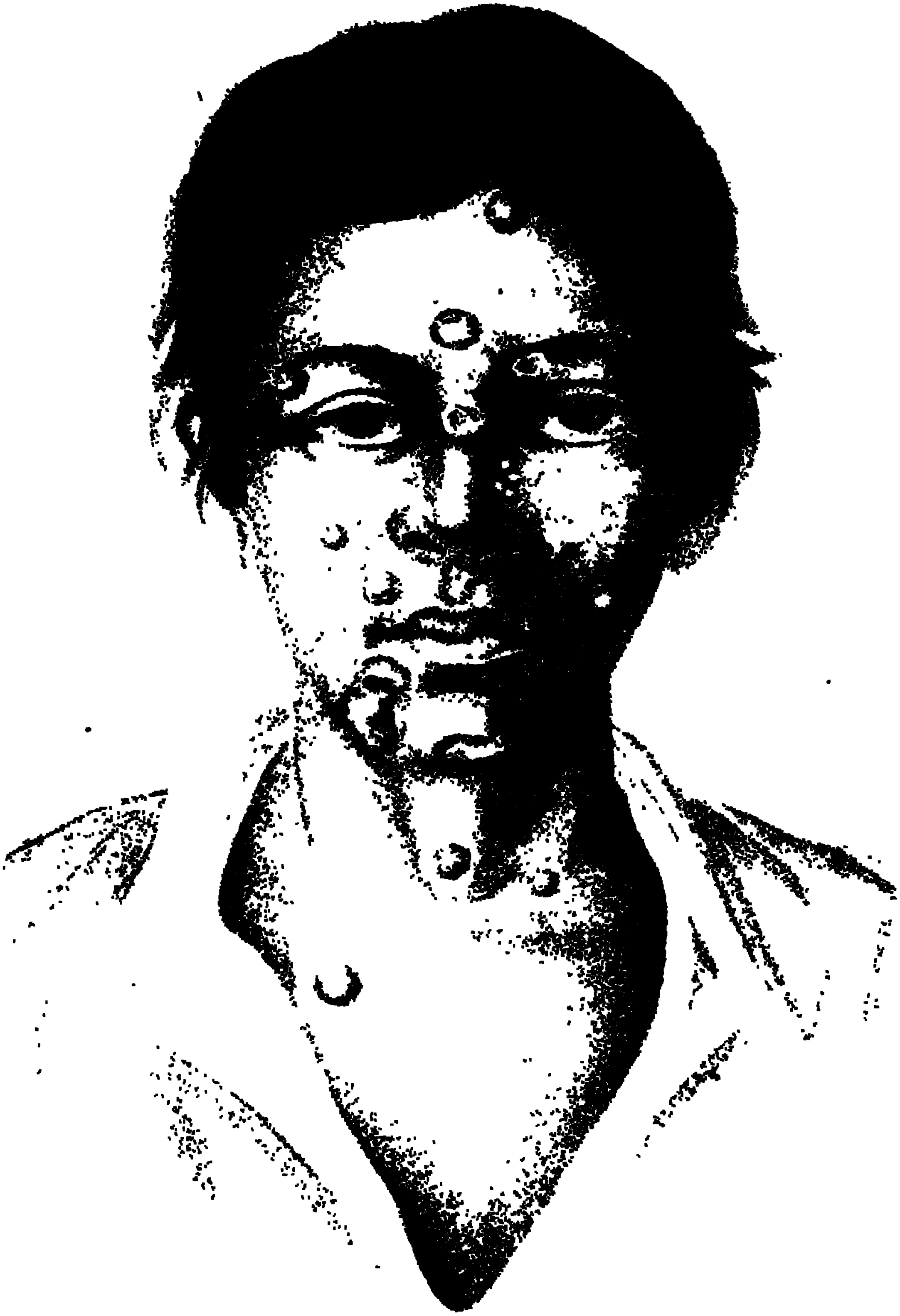


FIG. 689.—FRAMBŒSIA: GENERAL GRANULOMATOUS ERUPTION

The Secondary or Granulomatous Stage.—The general eruption usually begins between one and three months after the first appearance of the primary lesion. It is preceded by malaise, headache, severe pains in the muscles, joints, and bones. In some cases there may be fever of an intermittent type. The patient, however, is ordinarily able to attend to his work. The general eruption develops as follows: minute roundish papules, the size of pin-heads, appear on various parts of the body; some papules soon show a yellow point or minute yellow crust at their apex. Most of the papules

PLATE VI



FRAMBOESIA TROPICA.

GENERAL ERUPTION.

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remain of practically the same size for many weeks, and disappear, leaving occasionally some furfuraceous patches: others become larger, several often coalescing, and frequently acquiring a dark areola in natives, a reddish one in Europeans. Some of the larger papules increase in size, and develop into the characteristic large granulomatous nodules covered with a crust, honey-yellow or brownish, formed of desiccated secretion. If the crust covering the granulomata be removed, there will be seen a raw surface throwing up red or yellowish fungoid granulations secreting a thin, slightly purulent secretion, which soon dries into a crust. These frambœtic granulomata are of various size, from a large pea to a nut, and may be found on practically any part of the body. They are extremely common on the upper and lower limbs, and on the face. On the scalp they are very rare. They may form rings round the mouth and anus, and may enclose sound skin (so-called *yaws ringworm*). They may remain of the same size and appearance for months. Often, after a few weeks, the secretion diminishes, and a process of hyperkeratosis sets in. They then become of much harder consistency, and some of them, especially those on the dorsum of the feet and toes, may be covered with numerous small,

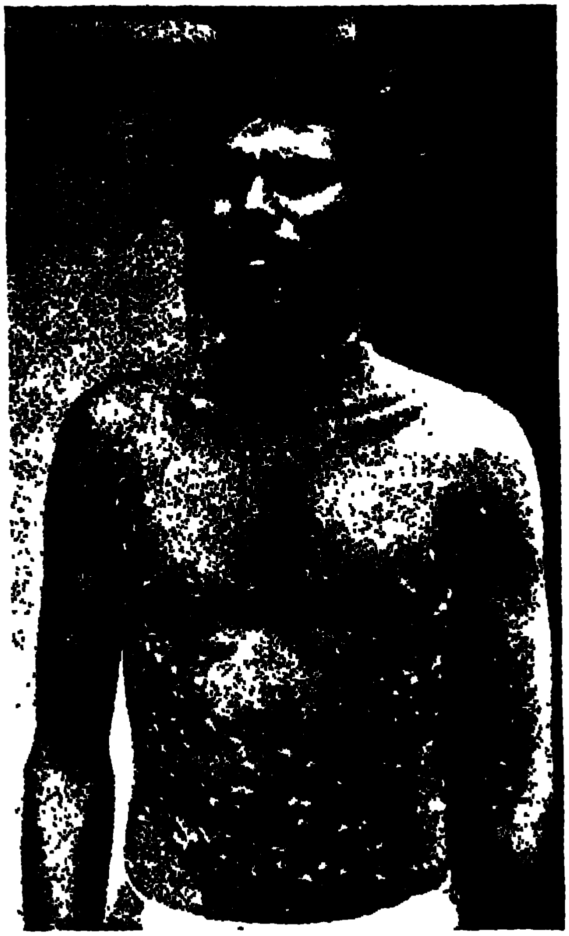

FIG. 690. FRAMBŒSIA (SECONDARY STAGE): GENERAL ERUPTION

hard, verrucose-like protuberances. In the majority of cases—within three to six months in children, and six to twelve months in adults—the granulomata dry up, shrink, and disappear, leaving dark hyperpigmented spots, or occasionally apigmented areas, on their site, which are most persistent. In some cases the granulomatous eruption may continue for several years, new crops of nodules appearing from time to time in succession. Each frambœtic granuloma generally undergoes involution within two to four months, leaving behind, as a rule, a dark area or, more rarely, a depigmented spot. Occasionally, however, the granuloma does not regress so soon. In one of our patients a single granuloma persisted for two years after all the others had disappeared.

FIG 691.—FRAMBŒSIA: GENERAL ERUPTION OF THE SECONDARY STAGE

The granulomata are seldom painful, unless they develop between the toes, on the soles of the feet, or round the nails. They very often cause itching. The patient often exhales a peculiar offensive odour, which has been variously described as sour or musty. This is probably due to the growth of various bacteria, representing secondary infections beneath the crusts of the granulomata. This offensive odour is especially noticeable when the secondary infection is due to bacilli of Vincent's fusiform type and coarse spirochætes. In such cases, if the sores are well washed with perchloride solution for two or three days, these organisms disappear, and the smell is no longer noticeable, though the granulomata do not undergo any change. Though the frambœtic granuloma is the charac-

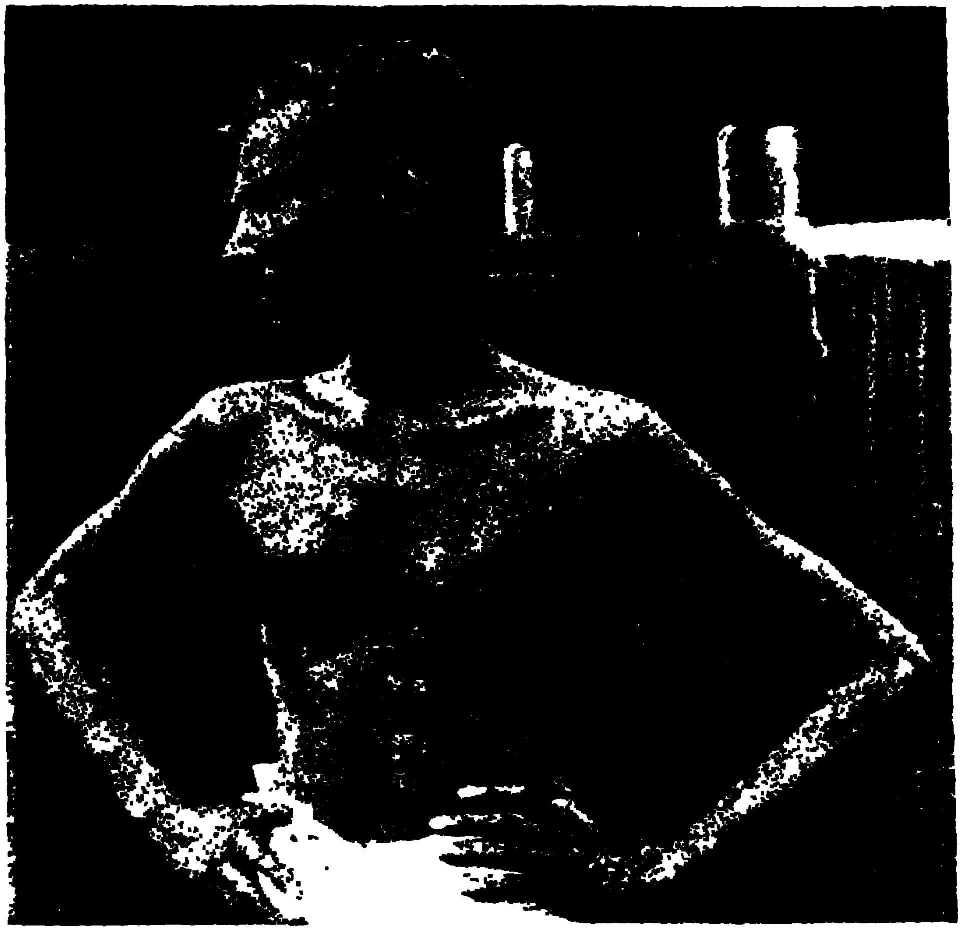

FIG. 692.—FRAMBŒSIA (SECONDARY STAGE): GENERAL ERUPTION.

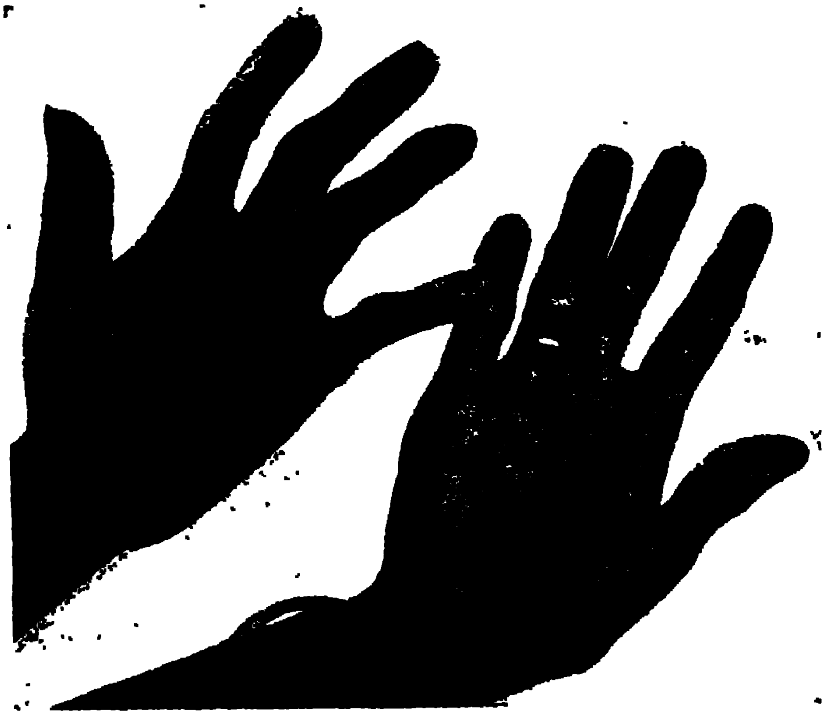

FIG. 693.—FRAMBŒSIA: ERUPTION ON THE HANDS.

teristic eruption of the secondary stage, there are during this stage other types of eruption or *frambœsides*—papular, scaly, and occasionally ulcerative. An average ordinary case will present at the

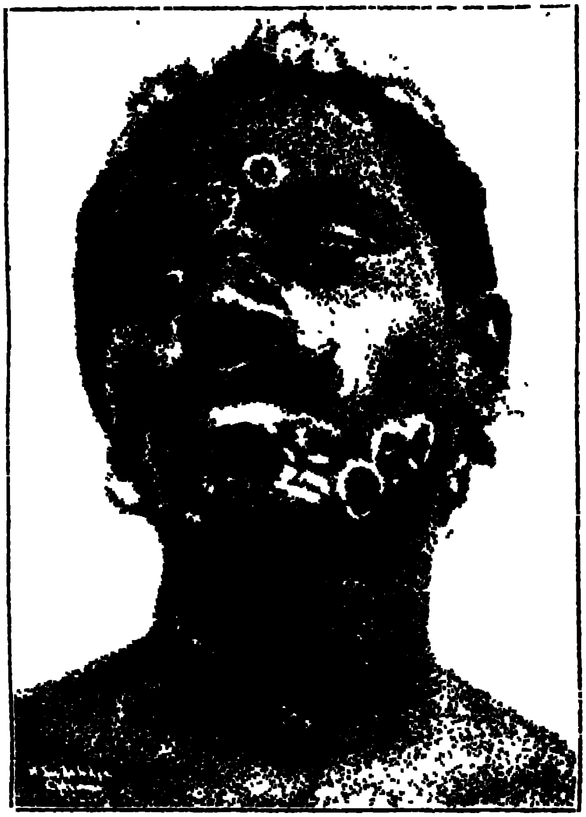

Fig. 694.—Frambœsia: Circinate Eruption

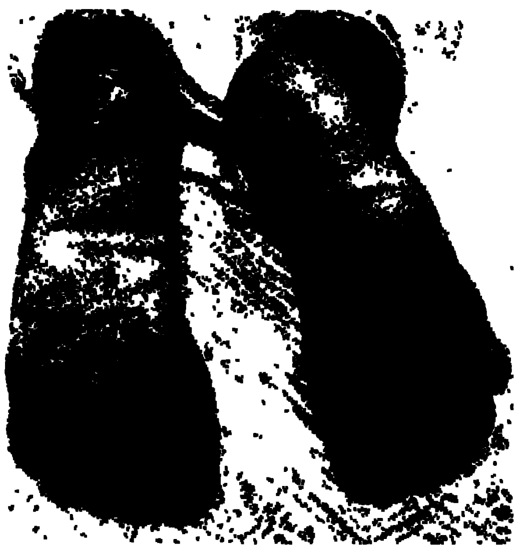

Fig. 695.—Frambœsia: Granulomata on the Heels of the Feet.

same time several typical frambœsiform granulomata, numerous small reddish papules with the epidermis intact, other papules which have become moist and are covered by a tiny yellow crust, several furfuraceous patches here and there, and spots of increased pigmentation at the place of previous granulomata. Occasionally

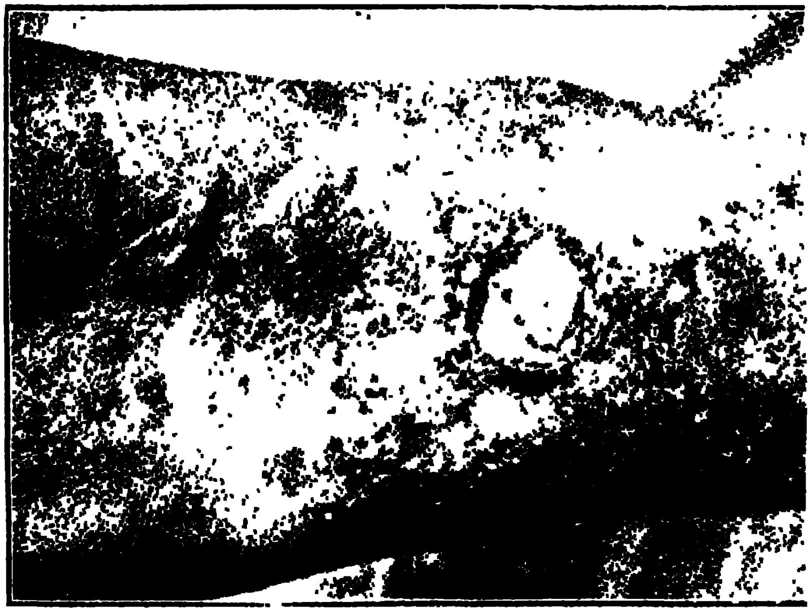

FIG. 696.—FRAMBŒSIA: LESIONS ON SOLE OF FOOT.

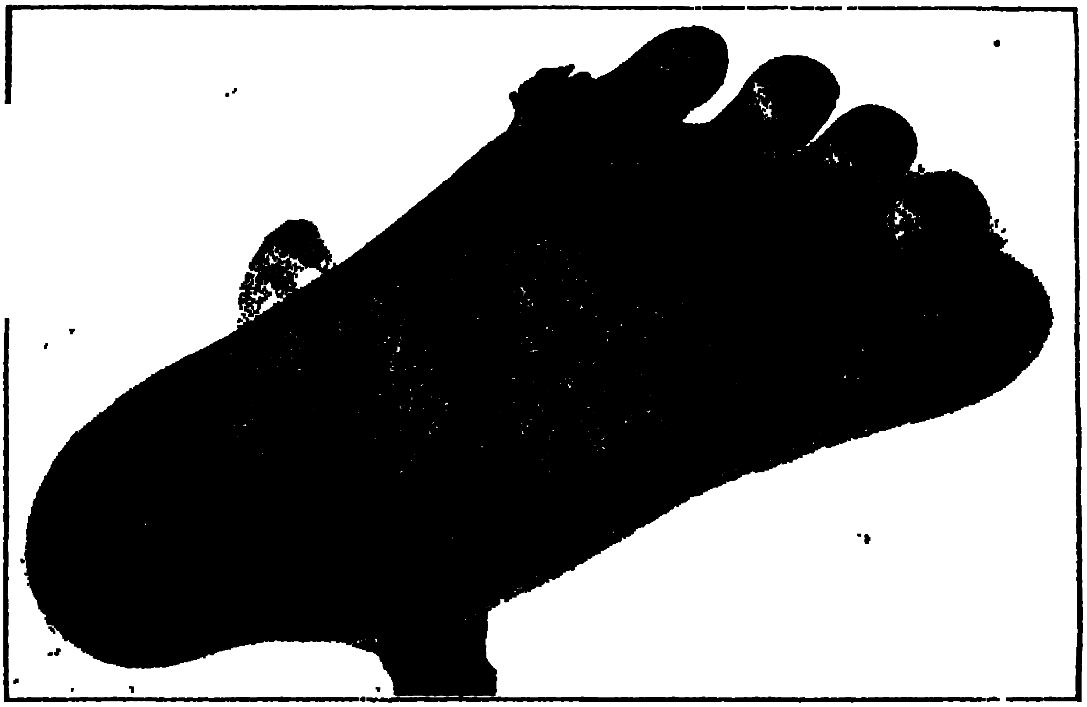

FIG. 697.—FRAMBŒSIA: LESIONS ON SOLE OF FOOT.

some granulomata break down, and large irregular ulcers form, presenting in their centre reddish papillomatous masses, which in our experience do not usually heal spontaneously. At times in the latter period of the secondary stage peculiar roundish or irregularly outlined whitish patches are present, especially on the back and arms, with a nutmeg-grater-like surface. On closer observation these patches are seen to consist of numerous hard, conical papules, containing in their centre an epidermic plug, which is easily removed, leaving a depression in the papules. Sometimes the plugs are spiny, and in this case the eruption closely resembles lichen spinulosus.

ERUPTIONS ON THE PALMS AND SOLES.—The granulomatous eruption very frequently attacks the soles of the feet. At first dark brownish or intensely livid spots appear; the thick epidermis is gradually pierced by frambœsial nodules similar to those found in other regions of the body. This affection of the soles is very painful; the natives of Ceylon call it 'dumas.' Similar lesions may occur on the hands. The granulomatous infiltration may attack the matrix and margins of the nails (frambœtic onychia and paronychia). The nails become thickened, dry, brittle, and may be cast off entirely, though later they grow again.

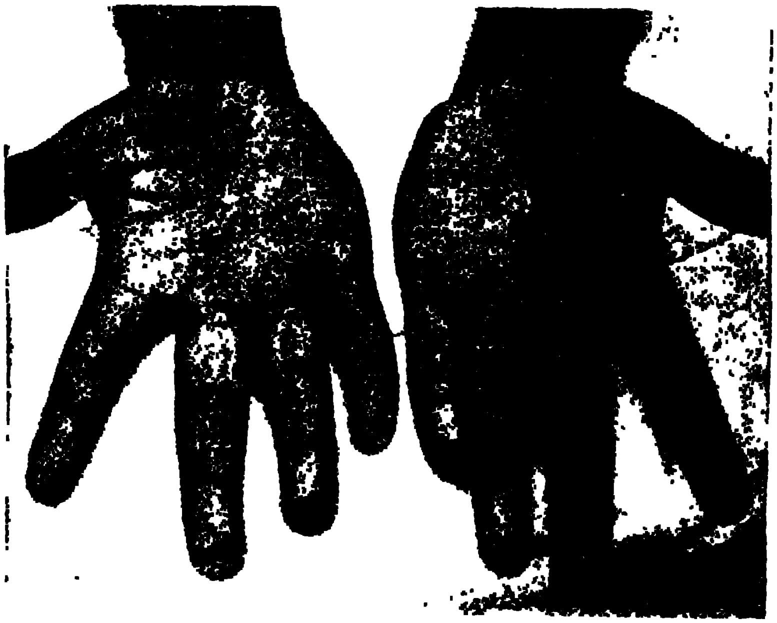

FIG. 698.—FRAMBŒSIA: PITTED APPEARANCE OF THE HANDS.

After the granulomata have disappeared, occasionally at the same time peeling, whitish patches may be seen on the palms of the hands and soles of the feet closely resembling the syphilitic *psoriasis palmaris and plantaris.*

PECULIAR PITTED FRAMBŒSIDE OF THE PALMS OF THE HANDS.—In several cases in the latter part of the secondary stage hard, round, flattened papules or small nodules, having a thick, hard, epidermic plug in their centre, may be observed on the palms and wrists. This plug falls off spontaneously or is easily pulled out, when a deep depression remains. The papules gradually disappear, but the depressions remain, and the palms acquire a peculiar pitted appearance. This condition of the palms may remain unchanged for several years after all symptoms of framboesia have disappeared. A somewhat similar appearance of the soles of the feet is occasionally met with.

Lesions of the Hair and Nails.—We have never noticed any change in the appearance of the hair, or alopecia. A few hair-follicles may be destroyed when the granulomata develop on the scalp, which, however, seldom occurs.

Lesions of Mucosæ.—These are not very common. During the secondary stage small granulomatous nodules may develop at the base of the tongue, also whitish patches closely resembling syphilitic leukoplakia. Small granulomata may develop on the nasal mucosa.

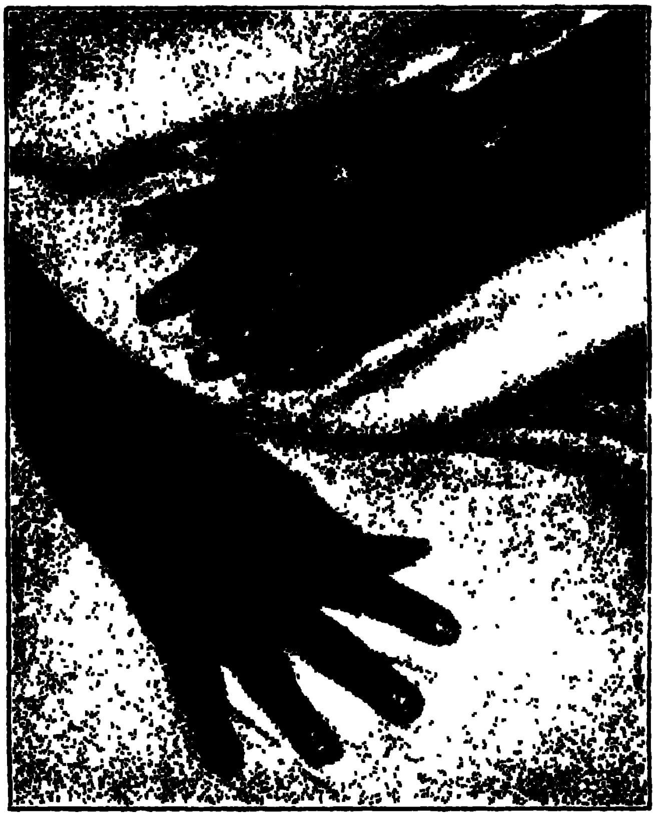

FIG. 699.—FRAMBŒSIA: DACTYLITIS.

Constitutional Symptoms—*Fever.*—As already stated, fever is frequently present, of intermittent or remittent type, before the general secondary eruption begins. During the secondary stage it is usually absent, unless complications supervene.

Lymphatic Glands.—In a number of cases in our experience various groups of lymphatic glands are found to be enlarged. The enlarged glands are roundish or spindle-shaped, hard, painless, and never come to suppuration, unless a secondary pyogenic infection is present. The cervical and inguinal glands are most frequently enlarged.

ALIMENTARY SYSTEM.—As a rule the digestive functions are not disturbed. In children slight diarrhœa may be occasionally noticed preceding the general eruption. The spleen and liver are frequently found enlarged in children, but this is probably due to preceding or concomitant malaria infection. The microscopical examination of the fæces of framboesia patients will frequently reveal ova of various worms—*Ascaris lumbricoides, Trichuris trichiura,* and occasionally *Ancylostoma duodenale*—but this is of frequent occurrence also in normal natives.

RESPIRATORY SYSTEM.—As a rule the respiratory, as well as the circulatory, system is not affected. Occasionally small granulomatous ulcers are to be found in the nasal mucosa and more rarely in the larynx.

LOCOMOTORY SYSTEM.—*Joints.*—In some patients several of the large articulations may become swollen and very painful. The condition is often of an acute character, and may be accompanied by fever, so that an attack of articular rheumatism complicating the frambœtic infection might be suspected. Sodium salicylate, however, is not beneficial, while the administration of large doses of potassium iodide speedily reduces the temperature to normal and cause the swelling of the articulation to subside. At other times one articulation only is involved, and the symptoms may become so serious as to suggest purulent arthritis. In many cases the smaller articulations become involved. The symptoms in such cases are not acute, and there is usually no fever.

Bones.—Inflammation of the periosteum of various bones is of common occurrence. Very frequent is a form of multiple periostitis of the digital phalanges, the cause of the multiple dactylitis so often seen in framboesia patients.

Maul has investigated the bone and joint lesions of Framboesia, and has noted that, in the Philippine Islands, 20 per cent. of the cases are suffering from such lesions, which may simulate tubercular or central septic abscesses, gummata, hydatid cyst, benign cyst, fibrous osteitis, enchondroma, endothelioma, secondary carcinoma, myeloma, and sarcoma. The same author has made a careful roentgenological survey, and has found that in the majority of cases the bone lesions appear as rarefied areas, irregularly oval, with the long axis parallel to that of the bone, from a few millimetres to 2 or 3 centimetres in length. Most of the lesions seem to originate in the interior of the bone, but some appear as small excavations on its outer surface.

Muscles.—Contractures of various groups of muscles may be observed. Fairly common is a contracture of the flexor muscles of the forearms. This contracture is often permanent, and in our opinion is probably due to pathological alteration of the peripheral nerves, rather than being of direct muscular origin.

NERVOUS SYSTEM—*Neuritis.*—Neuralgic pains are often observed, but also a true form of neuritis must be admitted. We have seen in several cases clear symptoms of neuritis of the sciatic nerve, with severe pain along the course of the nerve, and signs of motor and trophic disturbances.

Hyperidrosis.—In several of our patients we have noticed hyperidrosis. The phenomenon was limited to the face in some cases, to the hands and soles of the feet in others. It never extended to the whole body, and generally affected symmetrical regions. Hyperidrosis is more frequently observed in children than in adults. In a case at the Colombo Clinic a boy of fourteen, presenting a general eruption of framboesia, the hyperidrosis of the face was so marked that large drops of perspiration were constantly dropping down. He was treated with potassium iodide. After a month the granulomata had disappeared, and the hyperidrosis was no longer noticeable. In some cases the hyperidrosis ceases suddenly without any treatment. The condition, however, may last for some weeks or months.

The Eyes.—Granulomatous and papular eruptions may develop on the eyelids. A slight periostitis of the orbital margin is not rare, the margin becoming thickened and very painful on pressure. The occurrence of iritis is denied by most authors. In the Colombo Clinic two typical cases were observed during the general granulomatous eruption. In both cases the affection was of moderate severity. There was photophobia, ciliary congestion, discoloration of the iris. Pupillary reaction was almost absent. Both cases recovered on large doses of iodides without any local treatment.

The Genito-urinary System.—The primary lesion is rarely, if ever, found on the genital organs. In fact, in all the cases we have seen the primary lesion was always extragenital. Eruptions of the secondary stage, papular and granulomatous, frequently involve the skin of the penis and of the labia. Granulomatous ulceration may be found on the vaginal mucosa. The urine, as a rule, does not contain anything abnormal; only when there is fever—as, for instance, when the articulations are acutely involved—then a slight amount of albumen may be present.

The Blood.—There is often a certain degree of anæmia, never very severe. The number of red blood-corpuscles varied in our cases from 3,000,000 to 4,000,000, the hæmoglobin index (Fleischl) from 50 to 75. The red blood-corpuscles did not show anything abnormal in their shape. On several occasions a comparatively large number of polychromatic erythrocytes were noticed, staining blue instead of pink with Leishman's method. Many of these basophile red cells are micro-erythrocytes. The leucocytes varied from 7,000 to 11,000 per cubic millimetre. In the majority of cases an increase was noticeable in the number of the large mononuclears, even when there was no sign and no history of malaria. The number of lymphocytes is generally normal. Clapier and Violle have recently emphasized this, and note that it is in contrast to what one sees in syphilis, in which the lymphocytes are increased in number, while the large mononuclears are in normal amount. In many cases the eosinophiles are increased, this being probably due—in part, at least—to the presence of intestinal worms, as revealed by the microscopic examination of the stools, which shows frequently ova of *Ascaris lumbricoides*, *Trichuris trichiura*, and in a few instances of *Ancylostoma duodenale*. Density and viscosity of blood seem to be normal according to Violle, and the coagulability is not impaired. Auto-agglutination is generally absent, but has been recorded in certain cases.

Complement-Fixation Reactions.—Wassermann reaction is positive in the great majority of recent cases, but is fairly often negative in old cases. According to Schüffner and Violle, in frambœsia there is often fixation if an alcoholic extract of syphilitic liver is used as antigen, while there is no fixation if an aqueous extract is used. In syphilis there is generally complete fixation.

Cuti-Reactions.—The cuti-reaction with 'frambœsin,' prepared with cultures of *T. pertenue* according to the technique used by Noguchi in the preparation of luetin, is often positive. Luetin also may at times give a positive reaction, though less marked

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CEREBRO-SPINAL FLUID.—The liquid is in all cases perfectly clear, like distilled water. No cellular sediment on centrifugalization is found in most cases. In a few some rare mononuclear cells are found. The pressure is not increased. The physical and chemical characters do not show much variation from what is found in normal conditions. The density varied in our cases between 1003 to 1005. A certain amount of globulin was present, and a substance (dextrose?) reducing Fehling's solution. This reducing substance was in several cases distinctly in excess of what is observed in the normal fluid. No cholin is found. The reaction of the fluid is alkaline. The liquid is sterile; no treponemata can be detected.

Tertiary or Late Stage.—The disease often terminates with the secondary stage. In some cases, however, the infection does not become extinct, and tertiary lesions appear. These have been denied by many observers, but having been able to watch cases for several years through the whole course of the disease, we have no doubt as to their existence. Sometimes the secondary and tertiary stages merge into each other, but frequently the tertiary symptoms appear after the lesions of the secondary stage have undergone complete involution. The interval of time varies considerably in length, and may extend to many years. The characteristic lesions of the tertiary period are gummatous-like nodules and deep ulcerative processes. These gummatous nodules may develop in any tissues. When developed in the skin and subcutaneous tissues, they are indolent, and by their softening and breaking down ulcers are produced which may occasionally present clear-cut margins and a granulating fundus, and when several contiguous nodules break down, serpiginous ulcers are left. In other cases deep, irregularly shaped ulcerations with very thick and undermined edges are seen; in others —and these are the more numerous —large fungating ulcers are present. On healing, these various ulcers leave whitish scars, which are often thick and disfiguring. Frequently the scar-tissue undergoes retraction, and thereby causes permanent contractures and disfigurement. Lesions of the osseous type are very frequent, painful nodes developing under the periosteum of several bones, ribs, sternum, etc., and we are inclined to believe that *Gangosa* (p. 1876), an ulcerative condition of the palate, nose, and pharynx, is in reality a tertiary manifestation of yaws. In other cases a diffuse chronic periostitis is present, altering the normal shape of the bones. Contractures of various groups of muscles are frequently seen. Tertiary affections of the internal organs and of the central nervous system seem to be rare. Cases of aneurysm considered to be of frambœsial origin have been

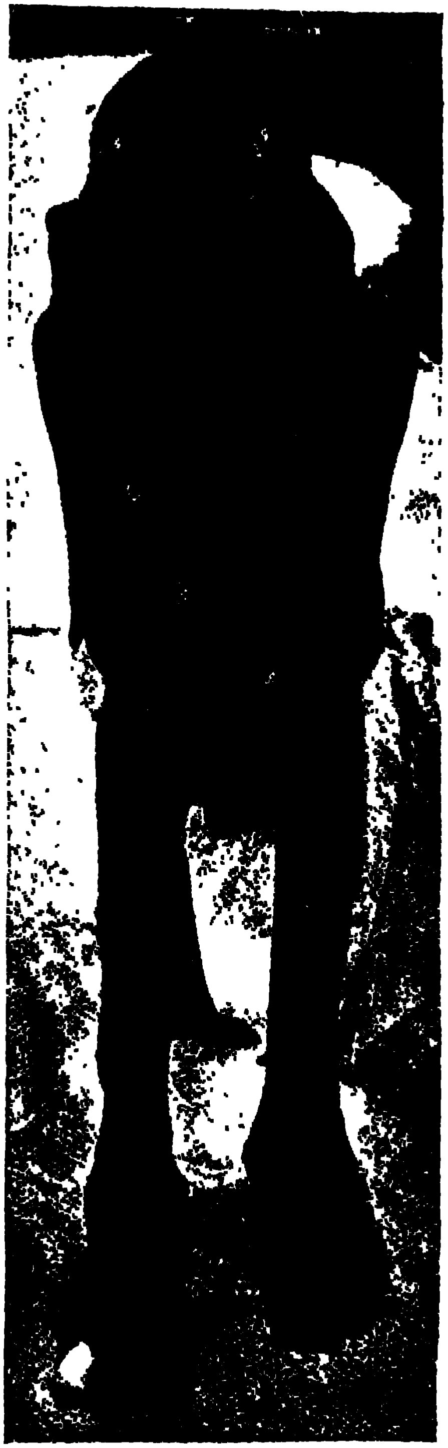


FIG. 701.—FRAMBŒSIA: TERTIARY STAGE.

observed. The malady does not appear to be hereditary; in fact, it is worth noting that, in contrast to syphilis, parents generally contract the malady from their children.

Fourth Stage: Paraframbœsial Affections.—Cases of tabetic symptoms and symptoms pointing to paralysis progressiva believed to be due to an old frambœsial infection have been placed on record by Harper and others.

Communicability.—Frambœsia is usually conveyed by direct contact from person to person. It appears, however, that the germ is unable to enter through the normal skin, and that there must be some pre-existing abraded surface, small wound, or ulceration. Women are frequently infected by their children, the primary lesion appearing often on the mammæ. In the native women of Ceylon the primary lesion frequently develops on the skin of the trunk just above the hip, slight abrasions caused by friction being usually present on this part, owing to the habit they have of carrying their children astride of the hip. Among certain Congo tribes it is a common dictum that a woman affected with the Nkoulou (yaws) should not sleep with her child, or he will certainly contract the malady. The natives, however, believe that the infection may be contracted also by partaking of contaminated food. In our opinion there can be little doubt that in certain cases insects may carry the disease. It is very noticeable that flies eagerly crowd on the open sores of frambœsia patients. In the hospitals, as soon as the dressings are removed, the frambœtic ulcerations become covered with flies, sucking with avidity the secretion, which they may afterwards deposit in the same way on ordinary ulcers of other patients. Ants also are occasionally seen to go on to the frambœtic

FIG. 702.—FRAMBŒSIA: TERTIARY STAGE.

ulcerations, as well as on to ordinary ulcers. In Nuttall's classical work on the rôle of insects as carriers of parasitic diseases several authors are quoted (Alibert, Hoish, Cadet, Wilson) who believe that the infection may be conveyed from one individual to another by flies. Wilson states that this belief prevails among the natives of the West Indies.

One of us made some experiments to prove that flies are instrumental in the dissemination of the disease. A number of flies were fed on scrapings from slightly ulcerated frambœtic papules. The flies (*Musca domestica* and allied species), before feeding on the frambœtic material, were examined. The examination showed that they did not harbour any treponemata, either on their mouth organs or on their legs. On examination after feeding, the majority presented coarse spirochætes, and a few of them also *T. pertenue.* In another experiment flies fed on yaws material were placed on scarified spots over the eyebrows of several monkeys, and kept there for two hours by means of strips of gauze smeared with collodion at their margins. One of the monkeys became infected. Sambon considers that a fly of the genus *Hippelates* plays a very important rôle in the dissemination of the disease in the West Indies.

Modder some years ago suggested that *Ixodes bovis*—*i.e.*, *Margaropus annulatus* var. *australis*—or some of the Argasidæ might be the transmitting agent. Bahr has suggested that the causative treponema may be transmitted by some blood-sucking insect whose range is definitely limited by the character of the vegetation or by climatic factors. According to certain authorities yaws may be communicated by means of food. R. P. Greggio states that natives of some Congo tribes suffering from yaws place inside the manioc they are selling portions of crusts removed from their own yaws lesions, in the belief that in this way the disease will leave them, will 'emigrate' to the buyers, who will become infected by eating the manioc.

Diagnosis.—In countries where the disease is endemic the diagnosis is generally easy, the large frambœsiform nodules, capped with thick yellow crusts, being typical. By some observers the disease has been confused with *verruga peruviana* and with *syphilis.*

Verruga Peruviana.—This disease is strictly limited to certain valleys of the Andes at an elevation of from 3,000 to 10,000 feet. Its eruptive elements, unlike those of frambœsia, frequently attack the various mucosæ, and bleed with great facility., The microscopical examination for spirochætes is negative.

Syphilis.—By some authors frambœsia has been looked upon as a form of syphilis. The results of experimental investigations of yaws and syphilis prove conclusively that the two diseases are distinct, inasmuch as (1) patients suffering from syphilis may contract yaws, and patients suffering from yaws may contract syphilis; (2) monkeys successfully inoculated with yaws do not acquire any immunity against syphilis; (3) mercury has practically no action on frambœsia.

Syphilis has a world-wide distribution; frambœsia, on the other hand, is restricted to certain parts of the tropics. Frambœsia is extremely common in Ceylon, extremely rare in India. Syphilis is common to both countries. In Samoa, according to Turner, syphilis was unknown up to at least 1880, while frambœsia has been endemic there ever since the group was discovered. In Fiji, too, up to a few years ago syphilis was not present, while frambœsia was almost universal. Daniels has made the interesting observation that in British Guiana frambœsia of late has disappeared, while syphilis is still rampant. As regards clinical features, frambœsia differs from syphilis by the following characters: the primary lesion is, as a rule, extragenital; the principal type of eruption is a papule, which proliferates into a characteristic frambœsiform granulomatous growth; there is an extremely well marked pruritus. The disease is apparently not hereditary; in fact, in contrast to syphilis, parents generally contract the malady from their children. The histopathology differs also in the two diseases. In frambœsia the proliferative changes of the epidermis are much more marked, the granulomata present a more diffuse plasma cell infiltration, and their bloodvessels have no tendency to the thickening of their walls, which is so characteristic of syphilis. Giant cells are generally absent. Naturally these differential histological details must be considered collectively, as there is no individual histological character which exceptionally might not be present in both syphilis and frambœsia.

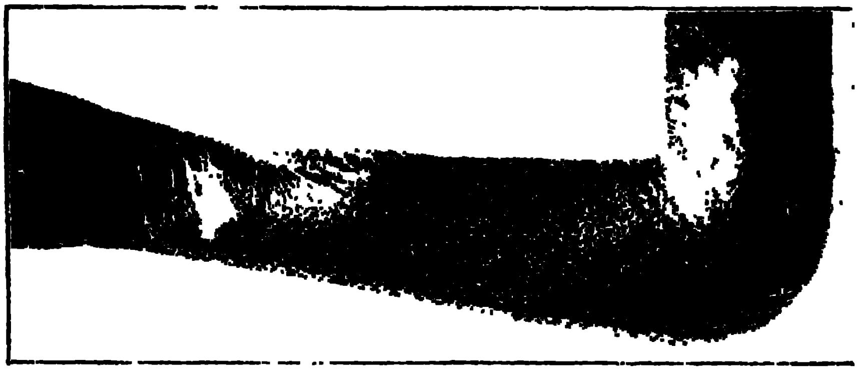
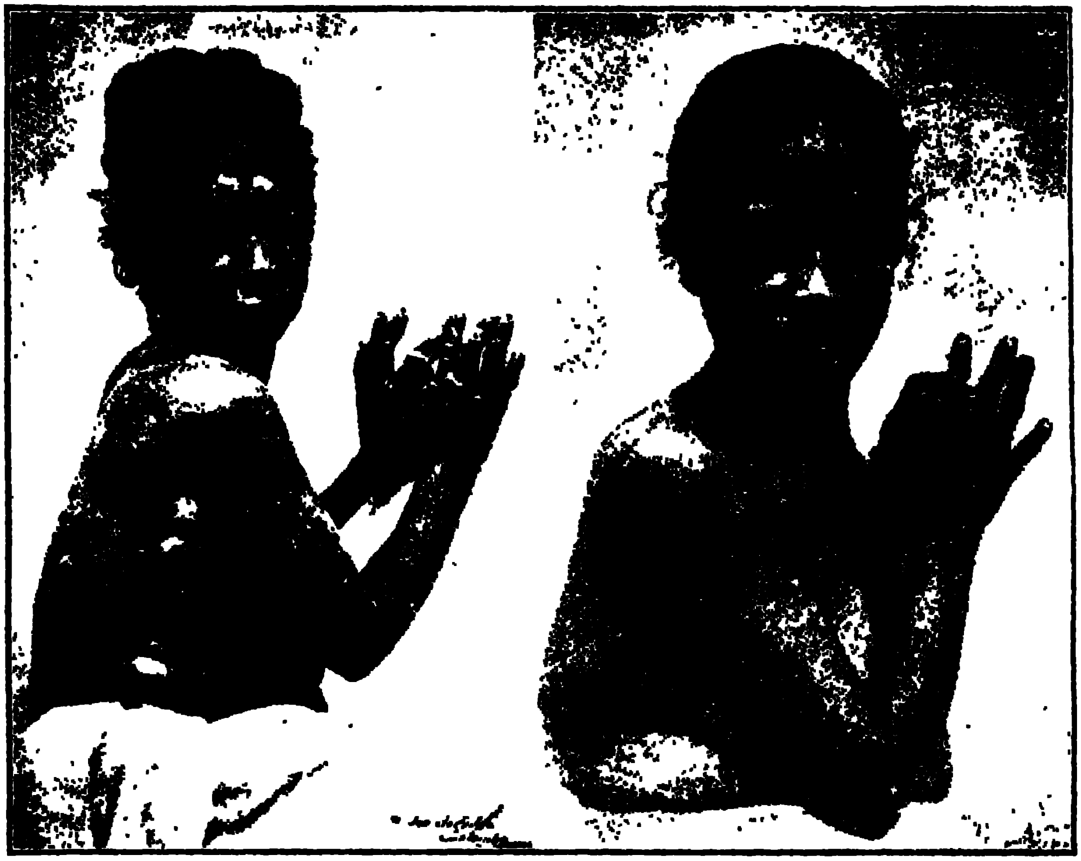


Fig. FRAMBŒSIA: TERTIARY STAGE.

Boubas and Pian.- Some of the older authors believed that under the names of yaws, boubas, and pian three different diseases were indicated. All those, however, who have had opportunity to investigate frambœsia in different parts of the tropics have come to the conclusion that these various denominations are simply local synonyms indicating the same pathological entity, though, of course, each of these terms is sometimes used by natives to indicate, besides frambœsia, other clinically similar conditions. Comparative experimental investigations made by one of us have led to the same result, inasmuch as he has been able to demonstrate that monkeys successfully inoculated with Ceylon frambœsia become immune to boubas and pian, and *vice versa.*

Breda and De Amicis, in Italy, have not found *T. pertenue* in

Italian emigrants returning from Brazil, and suffering from what they considered to be boubas; but Splendore has shown their cases to have been cases of leishmaniasis and blastomycosis. The fact is, that in South America the term boubas is used by the natives to cover several clinically similar diseases, while most medical writers use the term as a synonym for framboesia. Rivas, Linderman, and Robledo have found the *T. pertenue* in their cases of boubas in Venezuela, Brazil, and Colombia. It is not to be excluded, however—in fact, it is probable—that future investigation will show that there are several varieties of *T. pertenue*.



FIGS. 704 AND 705.—FRAMBOESIA BEFORE AND AFTER TEN DAYS' TREATMENT WITH CASTELLANI'S MIXTURE.

Cutaneous Leishmaniasis.—A type of cutaneous leishmaniasis (Bush-Yaws), fairly common in the West Indies, may simulate yaws, but the presence of leishmania bodies and absence of the *Treponema pertenue* will clear the diagnosis.

Prognosis.—The prognosis is not serious so far as life is concerned. In 1908, in the Ceylon hospitals, 3,246 cases were treated, with twenty-three deaths; in 1904, out of 3,591 cases, sixteen died; in 1903, out of 3,254 cases, ten only died. The prognosis is far more serious in children than in adults. When the disease ends fatally the termination is gradually due to secondary infection, the frambœtic ulcerated lesions becoming phagedenic, and giving opportunity to septicæmia and pyogenic processes to develop. Though framboesia rarely terminates in death, its long duration and great contagiousness render it a serious malady. The patients suffering from it are unable to attend to their work. Epidemics of framboesia, therefore, are of the greatest consequence on tea, sugar, and other plantations, as they reduce the supply of labour.

Treatment.—The most efficacious and quickest treatment is by Ehrlich-Hata salvarsan or neo-salvarsan, while potassium iodide and tartar emetic are fairly efficacious, and mercury practically useless. Salvarsan and neo-salvarsan and their substitutes seem to act in framboesia more quickly and more powerfully than in any other spirochætal and treponemal condition; in fact, in framboesia the *therapia sterilans magna* in Ehrlich's meaning, by a single dose, can at times be obtained. Salvarsan was first tried with good results in experimental yaws by Nichols, and in patients suffering from the disease by Strong in the Philippine Islands, and Castellani in Ceylon, while Alston in the West Indies made the interesting observation that the serum of patients treated with salvarsan showed remarkable curative powers when injected in framboesia patients. Recently the salvarsan treatment of framboesia has become general, having been used with very good results by De Gorge and Mouzels, Sabella, Born, and many others. The salvarsan treatment is especially efficacious in recent cases. Relapses, however, occasionally occur. In very old cases with tertiary lesions the treatment may fail. At the present time neo-salvarsan, instead of salvarsan, is generally used.

MODE OF ADMINISTRATION AND DOSAGE.—Neo-salvarsan and its substitutes novarsenobenzol, neokharsivan, novoarsenobillon, and to a certain extent galyl, are much more soluble than salvarsan and its substitutes arsenobenzol, kharsivan, etc., and are therefore used in practice in preference to salvarsan. Moreover, Castelli has shown that the *dosis tolerata* of neo-salvarsan in infected rabbits is nearly three times larger than for salvarsan, and that the *dosis sterilans* is one-tenth of the *dosis tolerata*.

The dosage of neo-salvarsan and most of its substitutes is, in adults, 0·4 to 0·6 gramme, though larger doses up to 1 gramme have been given with impunity. The dosage is therefore approximately 0·01 gramme per kilogramme of weight; in children half or one-third doses should be given. The best method of administration is by intravenous injection, and we have found Ravaut's method of concentrated solutions very convenient, although we do not use such highly concentrated solutions as does Ravaut, who recommends dissolving neo-salvarsan in only 1 or 2 c.c. of water. We generally dissolve 0·3 or 0·4 gramme of neo-salvarsan in 10 c.c. of sterile distilled water or sterile physiological salt solution, and make the intravenous injection, using a 10 c.c. syringe.

The patient is made to lie down quietly on a couch or in bed. The skin is painted with tr. iodi and the veins of the bend of the elbow made turgid by applying an elastic band round the arm. The needle, already attached to the syringe containing the solution, is inserted in one of the veins; if blood appears in the liquid, it means that the needle is in the vein, and the piston of the syringe is then very slowly and gradually pressed down until all the liquid has been injected.

Three to six injections of neo-salvarsan at three to six days' interval are generally sufficient to obtain a cure, though in a number of cases one injection is sufficient to make all the symptoms disappear. If one injection only is given, 0·4 to 0·6 gramme should be injected; when a course of three or more injections is carried out we often give 0·3 gramme the first time, 0·4 gramme the second time, and 0·6 gramme the third time and afterwards.

The patient should keep, if possible, at complete rest in bed for several hours after the injection, and in individuals with weak heart the injection of neo-salvarsan may be preceded by a hypodermic injection of caffein. The patient may complain at times of headache, and there may be a rise of temperature, but very seldom are serious symptoms caused by the drug, though cases of transient coma, delirium, epileptiform crisis, nephritis, and jaundice have been recorded.

Salvarsan.—Salvarsan may be given by intramuscular, subcutaneous, or intravenous injection; by the mouth in alkaline solution; and also by the rectum in the form of enemas or suppositories. We recommend the intramuscular and intravenous injections. The administration by the rectum in our experience does not give any good result, and of the oral administration we have no personal experience.

Intramuscular Injections.—The injection is generally given in the buttocks, with the usual precautions as regards the disinfection of the skin, and the use of a sterile all-glass syringe. The quickest method of disinfecting the skin is to paint it with tincture of iodine. The dose to be given in adult males is 0·40 to 0·50 gramme; in adult females and thin individuals 0·30 and 0·40 gramme. A dose exceeding 0·60 gramme should never be given either in males or females. In children the dose is 0·03 to 0·04 gramme for each year of age, or 0·008 gramme for each kilogramme of weight.

The injection of salvarsan in the same dose can be repeated after two or three weeks, if the first one has not been completely successful. The drug is not easily soluble, and various methods of preparing the liquid to be injected have been described. The simplest method is Ehrlich's. The salvarsan powder (0·30 to 0·60 gramme) is rubbed with a little methyl alcohol (pure) in a sterile vessel, and then mixed with 10 to 20 c.c. of normal salt solution.

An alkaline or neutral solution is preferable, and is prepared by rubbing the drug in a sterile mortar with 10 to 20 drops of a 15 per cent. solution of sodium hydrate, and adding 8 to 10 c.c. of sterile distilled water, stirring continuously. In order to prepare a clear solution, it generally requires 1 c.c. to 1·2 c.c. of the sodium hydrate solution for 0·6 gramme of salvarsan; a suspension of the drug in olive-oil or some other fatty material may also be used. A good preparation of this type, which we have often used, is by Pasini.

The suspensions in oil may often be given with advantage subcutaneously in the interscapular region. The intramuscular or subcutaneous injection of salvarsan, especially the acid solution, is generally painful, and is followed by a hard infiltration, which lasts for some weeks. Occasionally a slough forms, which has to be removed surgically.

Intravenous Injections.—The dose is smaller than for the intramuscular injection, 0·4 gramme for men and 0·3 gramme for women being sufficient.

The preparation of the solution to be injected is as follows. One of the glass phials in which salvarsan is put up in the dose of 0·6 gramme is broken, and the contents (0·6 gramme of salvarsan) is carefully added to 30 or 40 c.c. of physiological salt solution made with distilled water in a sterile stoppered vessel. It is dissolved by shaking thoroughly, and by adding 1·2 c.c. (about 23 drops) of 15 per cent. sodium hydrate solution. A precipitate is formed which redissolves. The solution should then be diluted to 300 c.c. with normal saline; 1 or 2 more drops of sodium hydrate may be required if the liquid is not clear. Each 50 c.c. of this solution contains 0·1 gramme of salvarsan. In man, 200 c.c. should be injected, in women 150, in children less, according to the rules given *supra*.

For the intravenous injections special apparatus have been devised, based on the principle of the Grantly douche. A convenient one, which may serve for all these forms of injection, has been placed on the market by W. H. Martindale.

Precautions to be Observed. - The solution should be prepared with sterile salt solution made with freshly prepared distilled water and chemically pure sodium chloride. It should be *perfectly clear*, it should be slowly infused into the vein (200 c.c. in about eight minutes); it should not be cold (about the temperature of the body if possible); the patient should be in bed, and should be kept there for a couple of days. If signs of collapse occur during the infusion, it should be stopped at once, and an injection of caffein given.

Tartar Emetic.—Broden, in 1910, and later on other observers, tried antimonial preparations by intravenous injection as in sleeping sickness. The results are much less satisfactory than with salvarsan or neo-salvarsan.

Intravenous Injections of Tartar Emetic associated with Other Drugs.- Potass. iodide and mercury were associated by one of us with tartar emetic, but the mercury did not seem to increase the action of tartar emetic. Herewith two formulæ:--

1.	Tartar emetic .	gr. iii.
	Potass. iodid. ..	gr. xxx.
	Aq. dest. ..	ad ℥i.
2.	Tartar emetic ..	gr. iii
	Potass. iodid. .	gr. xxx.
	Hydrarg. perchlor.	gr. ⅛
	Aq. dest.	ad ℥i.

One to 3 c.c. may be given diluted in 8 or 10 c.c. of sterile water by intravenous injection every other day.

Treatment by Oral Administration of Drugs.—When neo-salvarsan, salvarsan, or their substitutes, are unobtainable, or in districts where lack of medical men and skilled nurses makes any method of treatment by injections difficult or impossible, treatment by oral administration is very convenient, and the mixture known in the tropics as 'Castellani's yaws mixture' will be found effective in many cases.

This mixture contains tartar emetic, gr. i.; potass. iodid., ʒi.; sodium salicylate, gr. x.; bicarbonate of soda, gr. xv.; water or chloroform water, to 1 oz. One ounce is given three times daily diluted in three or four times the amount of water, to adults and youngsters of over fourteen years; half doses to children of eight to fourteen years of age, and one-third or less to younger children.

To Europeans it is advisable to give half doses, as they do not stand full doses so well as do natives.

The active drugs in the mixture are the potassium iodide and the tartar emetic; the salicylate of soda does not influence the yaws lesions, but seems to hasten the disappearance of the thick crusts, while the bicarbonate of soda, though rendering the mixture cloudy and inelegant, prevents to a great extent the symptoms of iodism and decreases the emetic properties of the mixture, in this way rendering possible the administration of massive doses of potassium iodide, and large doses of tartar emetic. In the few cases in which emesis is produced, the bicarbonate may be increased, or a small amount of liq. morphiæ or codein given before each dose; and in the comparatively rare cases in which severe iodism appears, epinephrine, as suggested by Milian, in grm. 0·002 doses, may be given by the mouth or by subcutaneous injection, twice daily.

The mixture as set down is cloudy, although it becomes clear when diluted with water at the time of administering it. At the suggestion of Dr. Dawson Williams some experiments were carried out to obtain a clear mixture, and it was found that the addition of sodium tartar. gr. x., or of glycerine ʒii. or of syrup ʒi. per dose, was sufficient to keep the mixture clear for weeks. The modified formula of the mixture is therefore as follows:- -Tartar emetic, gr. i.; potass. iodid., ʒi.; sodii salicyl., gr. x.; sodii bicarb., gr. xv.; sodii tartarat., gr. x., or glycerine, ʒii., or syrup, ʒi., Aq. ad ℥i. It is given in the same doses as the original mixture, and well diluted in water to prevent a severe sensation of burning in the stomach.

Either the original or the modified mixture is given in the doses mentioned for ten to fifteen days, then it is discontinued for about a week, and then given again for another ten to fifteen days. The results, as shown by Castellani, Spaar, Thomson, and more recently by Guerrero, Domingo, and Argüelles, who have carefully investigated this method of treatment in the Philippines, are usually very satisfactory in recent and fairly recent cases when they may be compared with those obtained by the salvarsan treatment. In chronic cases the results are not so striking, but as a rule much better than with any other known treatment, except salvarsan or neo-salvarsan.

The natives treat the disease in various ways. In Samoa the patient is rubbed down with sand and washed in the sea, after which the yaws are scraped with a shell. In the West Indies boiled and beaten-up leaves of the ' physic-nut ' are applied ,or powdered alum and sulphur used. In the Congo pieces of forge scoriæ are made incandescent and the yaws lesions touched with them. In Ceylon the *vedaralas* (native doctors) apply concoctions of various herbs, and give decoctions of sarsaparilla and other roots. They also use mercury disguised in various ways. The majority of European practitioners use potassium iodide. Others affirm this drug to be quite useless, and believe that cleanliness and good and abundant food are quite sufficient to bring about a cure.

In the Colombo Clinic for Tropical Diseases some experiments have been made on the various treatments, and the conclusion arrived at has been that the salvarsan and neo-salvarsan treatment is the most effective of all, while the mixture tartar emetic, potass. iodide, bicarb. of soda, and sod. salyc. is also very successful. Some cases may recover spontaneously, but this is certainly the exception, not the rule. Occasionally cases are met with refractory to any treatment, and tertiary lesions are often intractable. An important point often overlooked by the practitioner is that the oral treatment should be prolonged for a time after the complete disappearance of the eruption, inasmuch as clinical experience, as well as experiments on inoculated monkeys, prove that the specific treponemata may, and do, persist in the lymphatic glands and internal organs long after the cutaneous manifestations have disappeared. Atoxyl has been tried by Neisser in monkeys experimentally inoculated with the disease, and by one of us in human patients. The results are occasionally fairly good. Spittel has used, by intravenous injection, a solution of arsenious and mercuric iodide.

Local Treatment.—This consists chiefly in keeping the skin scrupulously clean, washing the eruption twice daily with a perchloride of mercury solution (1 to 1,000), which greatly allays the itching. The ulcerated lesions may be dusted with iodoform, europhen, xeroform, or boracic acid. Mercury ointments may be beneficial, but in our experience are not sufficient to hinder secondary pyogenic infections. Caustics are not called for unless the ulcers become phagedenic. In such cases pure carbolic acid is best. Though the external treatment may be useful, one must bear in mind that it is not, as a rule, sufficient alone to cure the disease.

Prophylaxis.—In countries where frambœsia is endemic the slightest abrasions of the skin should be taken care of and properly treated with antiseptics. Frambœsia patients should be prevented from mixing with the rest of the population, and should be isolated in special hospitals till the disease is cured. Their skin lesions should be properly dressed, and thus prevented from becoming a source of infection through the agency of flies and other insects. Their huts and belongings should be thoroughly disinfected.

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CHAPTER LXII

VERRUGA PERUVIANA

Synonyms — Definition — History — Climatology — Ætiology — Pathology — Histopathology — Symptomatology — Diagnosis — Prognosis — Treatment — Prophylaxis — References.

Synonyms.—Peruvian wart, Verruga Blanda, Carrion's Fever, Verruga de Castilla, Verruga of the Andes, Verruga de Zapo ó de Quinua, Verruga Andicola, Verruga Mular, Verruga de Sangre, Fiebre de la Oroya, Verruga de Crapaud, Bouton des Andes. The word 'verruga' signifies in Spanish a wart.

Definition.—Verruga peruviana is a chronic endemic specific general disorder of unknown origin, not contagious, but apparently inoculable, and characterized by an irregular fever associated with rheumatoid pains and anæmia, followed by granulomatous swellings in the skin, mucous membranes, and organs of the body.

History.—It is probable that the disease existed in South America before the advent of the Spaniards, for the earliest references to it are found in Spanish works on Peru in the sixteenth century. The first record is by Agustin de Zárate, Treasurer of Lima, in his 'History of the Conquest of Peru,' written in 1543, in which he relates that warts or small tumours appeared on the face and other parts of the body, which were more deadly than smallpox, and almost as fatal as plague.

Garcilas de la Vega records that a quarter of the small army of François Pizarre perished from this cause, while Gomara, Garcilazo (1617), and other early writers, also drew attention to the disease. After this period writers on Peru either fail to mention the disease at all, or only write short paragraphs such as that in Cosme Bueno's geographical description of the province of Canta, published in 1764, in which it is mentioned under its ancient name of 'berrugas.'

The modern descriptions of the disease begin with the works of Tschudi in 1843, Malo in 1852, Smith in 1858, Salazar and Manuel Odriozola in 1858, Velez in 1861, and Dounon in 1871, the last named giving a very clear account of the complaint.

But little interest was, however, taken in it until 1870, when a severe outbreak of fever took place among the workpeople laying the railway-line between Lima and Oroya. This complaint for some reason was called 'Oroya fever,' although it did not affect Oroya. About the same time Dounon's excellent paper appears to have interested French naval surgeons, so that numerous investigations as to verruga and Oroya fever were made both by Peruvian doctors, such as Pancorvo and others in 1875, and French surgeons, such as Fournier in 1874, Bourse in 1876, and Tupper in 1877. During this period there was much disputation as to whether Oroya fever was related to verruga, or was a distinct clinical entity. In 1885 Daniel A. Carrion, a student of the Faculty of Medicine of Lima, who had for some time been studying the disease, attempted to settle this question by vaccinating both his arms with the blood from a verruga tumour on August 27, 1885, and on September 17 he began to suffer from the symptoms of Oroya fever, from which he died on October 5. In honour of his noble attempt to elucidate the ætiology of the fever, his compatriots have since referred to Oroya fever as Carrion's disease.

The unfortunate death of this brave young man stimulated inquiry, and a very large number of investigations were published, of which it is only possible to mention a few.

In 1885 Izquierdo announced the discovery of a bacillus in some specimens sent to him in spirit, which, of course, prevented anything of the nature of a thorough bacteriological investigation.

In 1887 Florez grew a coccus on agar-agar inoculated with the blood from persons suffering from verruga. In 1898 a most elaborate monograph by E. Odriozola appeared, which the reader interested in the subject is strongly advised to peruse.

In the same year Nicolle and Letulle independently described bacilli resembling those of tuberculosis in the skin lesions. Barton, in 1902, published the first careful bacteriological examinations of Carrion's fever, and from 1903 to the present time Biffi has written a series of able papers on the disease.

We are therefore confronted with two conditions described by authors—viz., a disease which may or may not begin with fever, and which ultimately ends with a most peculiar and typical eruption, verruga peruviana, and another disease characterized by an incubation period of twenty-one days, as proved by Carrion's inoculation, and of a severe type often ending in death, without the appearance of any eruption. Are these two conditions one and the same disease—that is to say, is Carrion's fever Peruvian wart without an eruption, or are the two separate pathological entities? Tasset, in 1872, held that they were separate entities, and that Carrion's fever was a typho-malarial fever, but since the inoculation of Carrion most authors have considered the two diseases to be one and the same, though every now and again some author has objected, and has held that Carrion's fever was typhoid. In 1901-02, Barton, as the result of careful bacteriological researches, concluded that in the blood and organs of persons dying from Carrion's fever a micro-organism could be found which, though similar to *Bacillus coli communis* in many respects, was easily separable therefrom. This organism was fatal to inoculated animals, causing a septicæmia and, it is said, a verruga-like eruption in the skin. Biffi has carefully investigated this bacillus, and finds that it is present constantly and in abundance in persons suffering from Carrion's fever, but is absent in patients suffering from verruga peruviana without fever. It is agglutinated by the serum of persons suffering from Carrion's fever, but not by that of patients suffering from verruga who have not had fever. The micro-organisms are, however, not always of the same strain. Thus, Biffi has separated two different strains, one of which resembles Schottmüller's *B. paratyphosus B*, and the other Gärtner's bacillus. Biffi and Carbajal were unable to confirm Barton's results as to the presence of a skin eruption in animals inoculated by these strains. They therefore conclude that Carrion's fever is a separate pathological entity distinct from verruga, and that it is a fever belonging to the paratyphoid group, but differs from the usual types by being due to a different organism, and by occurring in patients suffering from verruga. In this finding they are supported by the clinical observations of several observers, among whom may be mentioned Eder.

The next question which must be considered is the nature of verruga peruviana, for it has been suggested that it is frambœsia, and this has been specially emphasized, since it has been realized that it may run its course without any fever. Biffi, however, has clearly shown that they are separate, frambœsia being contagious, verruga not; frambœsia beginning with an initial lesion, verruga not; frambœsia being due to *Treponema pertenue* Castellani, verruga not. We may therefore conclude that verruga peruviana is a definite pathological entity. Further researches in the disease have been made by Bassett-Smith, Mayer, and others.

In 1915 Strong, Tyzzer, Brues, Sellards, and Gastiaburu published a valuable report, pointing out that Oroya fever was distinct from verruga peruviana.

The former, according to these investigators, is due to *Bartonella bacilliformis* (*vide* p 502), which in many ways resembles *Theileria parva*, while the latter is probably caused by a filterable virus, and can be inoculated into monkeys; it resembles closely Bassewitz's angiofibroma cutis contagiosum tropicum (p. 2253). Verruga may be spread by a blood-sucking arthropod. Townsend, in 1914 and 1915, declared his belief that this arthropod was *Phlebotomus verrucarum*.

Climatology.—Verruga peruviana is confined to South America, and to the western slopes of the Andes in Ecuador, Peru, Bolivia, and the northern parts of Chili, the most important endemic area being Peru, where it is almost limited to the departments of Ancachs and Lima, lying north and south of the tenth parallel, and on the western side of the Andes. The department of Ancachs comprises seven provinces, of which the provinces of Pallasca, Huaylas, Huaraz, and Cajatambo, which are on the western slopes of the Andes, are most affected, while that of Santa, which runs along the littoral, is almost free. The disease is, however, peculiarly limited to certain places in these provinces. The heights of these places vary from Cochas, in the province of Cajatambo, which is only at an elevation of 406 metres, to Cajatambo, in the same province, which is at an altitude of 3,350 metres, but according to Monge it is never naturally acquired at an elevation below 2,800 feet or above 9,000 feet, nor does it originate in the main valleys.

One striking peculiarity common to all the places is that they are in narrow valleys along tributaries of rivers. The principal infected areas are Tablachaca, Pallusca, Corongo, Pacatqui, and Ninabamba, in Pallusca; Huaylas and Caráz, in Huaylas; Yautan, Pariacoto, Rurasca, Nanca, Jangas, Pongor, Anta, and another district on a branch of the River Huarmey, in Huaraz; Cochas, Huaylillas, and Cajatambo, in Cajatambo.

In the department of Lima there are six provinces, of which Chancay, Canta, Huarochiri, and Yauyos possess endemic areas, which vary in height from 900 to 2,030 metres. In Chancay there is Huaycho; in Canta, Acos, Viscas, Yasu, Magdalena, and Yangas; in Huarochiri, Santa Eulalia, Palle, San Gerónimo, San Pedro de Casta, Surco, Cocachacra, Santa Ana, and Sisicaya; and in Yauyos, Omas.

The best-known area is that which lies along the railway from Lima to Oroya, which begins a little below the division of the River Rimac into the rivers Santa Eulalia and Cocachacra, along both of which the disease is endemic for some distance, including Santa Eulalia, San Gerónimo, Cupichu, San Pedro de Casta, San Pedro de Mama, Santa Ana, Corcona Cocachacra, San Bartolomé (where the stream which runs into the Cocachacra River is called the Aqua de Verrugas, because the people believed the disease came from drinking the water), Cuesta Blanca, and Surco.

Here again, as in the department of Ancachs, the disease is restricted to certain deep, narrow valleys, locally known as 'quebradas,' along which streams flow, and which are some 28 to 60 kilometres distant from the littoral, where the disease never occurs. A very important epidemiological point is that the disease only occurs in the summer when the rivers are in flood, and when all sorts of insects abound. Monge points out that earthquakes are correlated with small epidemics, probably because the disturbed population becomes more exposed to the infection, whatever that may be.

Ætiology. The causation of verruga peruviana is unknown. Popularly the disease is believed to be conveyed by the drinking-water, which, however, has long been discredited. In 1875 Pancorvo, taking into consideration the well-known fact that the persons who mostly suffer are people who work in the fields or disturb earth, suggested that it was an intoxication due to sulphuretted hydrogen liberated from the earth, a view which never received any marked support. Odriozola and Tamayo have failed to find any bacteria in people suffering from the eruption of Peruvian wart. It is said to occur in animals, especially quadrupeds, and not to be contagious. Chastang believes that some germ is inoculated by the thorns of *Cactus opuntia*. Long ago Raymondi suggested that verruga would, like rabies and syphilis, be found some day to be due to a definite virus. Translating Raymondi's views into modern thought, it would mean that the three diseases would be found to be due to a parasitic protozoon, and, indeed, there is no doubt about the truth of this with regard to syphilis and with regard to rabies, and it is quite possible that verruga peruviana will some day be found to be of protozoan origin, thus confirming Raymondi's striking conjecture.

The study of the distribution of the disease in the various provinces of Peru, as detailed above, with the aid of a large-scale map, will impress the reader with the similarity to the distribution of Rocky Mountain fever, and will lead him to the conclusion that the ætiological cause must in some way be associated with some blood-sucking animal, perhaps an arachnid: and, indeed, this is supported by a fact well known - that the persons most prone to the infection are those who work in the fields. Such ideas must, however, be taken as mere suggestions, as at present there is no direct evidence in favour of them. Very minute bacillary-like rods, thicker in the middle than at the ends and variable in number, have been described in the red cells by Barton, Gastiaburu, Rabagliati, and Biffi. They become scanty after the eruption, and disappear during convalescence. Similar bodies have been seen by De Vecchi, Bassett-Smith, and Martin Mayer. De Vecchi considers them to be products of degeneration.

Strong, Tyzzer, Brues, Sellards, and Gastiaburu's experiments would point to the virus being a filterable one, and inoculable in monkeys. Inoculated in the testes of the dog and rabbit it induces characteristic changes. As already stated, these authors believe that the disease is not connected with Oroya fever, which, according to them, is due to *Bartonella bacilliformis* (p. 502), and is not inoculable in monkeys.

Age, sex, and race appear to have no influence, though it has been asserted that the coloured races have a partial immunity, which is due to mild attacks at a very early age, as nearly every inhabitant in the towns of the endemic areas acquires verruga, and if reinfected has only a very mild attack, for, as a rule, an attack confers a lasting immunity. Strangers visiting an endemic area are attacked almost at once with the disease in its gravest form. The disease may be acquired by travelling through an endemic area, but there is much more risk of infection if a night is spent therein, and if the endemic zone is quitted before sunset the risk of infection is greatly diminished. Another important point is that newly-born infants may acquire the disease. Cole has made some inoculation experiments in monkeys with a certain degree of success.

Pathology.—As the causation is unknown, the account of the pathology must be limited to very few remarks. There has been great doubt as to whether verruga can be transmitted to animals by inoculation, though Odriozola related that he inoculated a bitch with the blood from verruga lesions obtained from a post-mortem, with the result that the animal developed a typical skin eruption, and eventually died. The disease is said to occur naturally among animals—*e.g.*, horses, mules, asses, dogs, and fowls—but especially among quadrupeds, although Monge states that no one has definitely proved that this is the verruga of man, and the ordinary laboratory animals cannot be infected with the disease. According to some observers, the infection in man begins with a general illness, which would appear from the fever, the anæmia, and the pains in different parts of the body, to be of the character of a septicæmia, after which the typical eruption appears on the skin, mucous membranes, and internal organs, when as a rule the general symptoms of fever, etc., abate, from which one would infer that the organism had left the blood stream, and become located in the skin and other organs. It is possible that it leaves the body by way of the skin. If, however, the local lesion develops in such places as the meninges, the choroid plexus, the choroid coat of the eye, the intestines, the œsophagus, or larynx, severe symptoms are apt to appear, and complicate the illness. If at the same time a paratyphoid-like infection takes place during the febrile stage, the true symptoms are masked, and a peculiar and very deadly type of fever, called 'Carrion's disease,' is produced.

The morbid anatomy is characterized by marked pallor of the body, œdema and dropsy, hypostasis of the lungs, enlargement of the liver and spleen, and hyperæmia of the bone-marrow; but apart from these general signs, the characteristic features are the appearance of the verrugas in the skin and subcutaneous tissues, in the ocular and palpebral conjunctivæ, the mucosa of the nose, the lips, gums, palate, tongue, pharynx, larynx, trachea, œsophagus, stomach, small and large intestine, in the substance of the liver, spleen, lungs, thymus, thyroid, testicles, kidneys, and lymphatic glands, and at times in the leptomeninges, the choroid plexuses, the choroid coat of the eye, in the substance of the muscles, on the periosteum of bones, on the peritoneal coverings of organs, and on the pleura and pericardium.

Histopathology. -The histopathology of the disease has been carefully studied by Letulle, Jamayo, Escomel, Jeanselme, Hercules, Biffi, De Vecchi, and very completely by Strong and his co-workers. The miliary and nodular forms take origin around the capillary bloodvessels in the form of a neoplasm which is the reaction of the areolar tissue to some perivascular irritant. The connective-tissue fibres become swollen, and between them lie embryonic connective-tissue cells, while the interareolar spaces contain polymorphonuclear cells and macrophages. Microscopically a non-ulcerated skin lesion shows the cells of the surface epithelium swollen and distended with glycogen. The papillary layer of the cutis has disappeared, and the dermis proper is infiltrated with round cells, which are mostly mononuclear or polymorphonuclear leucocytes, separated by a slight amount of fibrillar connective tissue, which may in places be entirely absent. There is some doubt as to whether the connective-tissue corpuscles contribute to the round-celled infiltration, as has been asserted by Izquierdo; in any case, the recognizable connective-tissue cells are always swollen, and their nuclei are altered in various ways. The cellular infiltration is very vascular, and in the case of the older tumours almost cavernous in structure; hence the liability to haemorrhage, which is such a marked feature of the disease.

The subcutaneous fatty tissue is always inflamed. In addition to these features, Letulle describes and figures some most peculiar structures seen, under a magnification of 400 diameters, between the cells of the epidermis, which he considers to be clasmatocytes.

The growths appear to be often invaded secondarily with micro-organisms, especially if ulcerated, while the eosinophiles disappear and the mononuclears diminish. Myelocytes may be present, and may number 0·5 per cent., and there may be some large mononuclear cells like macrophages. The nuclei of the polymorphonuclears are simply bilobed.

Symptomatology. The incubation period is not definitely known, and is stated to vary from eight to forty days, but to be most usually from twenty to thirty days, during which time prodromata, in the form of malaise, lassitude, and depression, may be experienced.

Febrile Stage (*Orova Fever*). The invasion is gradual, the prodromal symptoms increasing in virulence, while anaemia becomes apparent, and peculiar rheumatoid pains appear in different parts of the body. These pains are very striking and very misleading, for they may in some cases be limited to a single region, or even to a single joint or muscle: on the other hand, they may be more extensive, and lead to a diagnosis of some nerve disorder. As a rule, but not invariably, fever appears, and varies in intensity with the severity of the attack. There is usually insomnia and often delirium. Usually it is intermittent in character, the paroxysm beginning about noon with chills, severe pains, much thirst, and a rise of temperature to about 104° F., with a quick, soft, compressible pulse, and ending in about twelve hours by crisis, associated with sweating and an amelioration of the pains. The liver and lymphatic glands enlarge, but according to some authorities the spleen is not palpable. The patient rapidly becomes very anæmic and feeble, and usually constipated, but may at times suffer from severe diarrhœa. The destruction of red cells, according to Monge, is enormous, the number falling to 900,000 per cubic millimetre, with microcytes in large numbers, macrocytes, normoblasts (2,000 per cubic millimetre), megaloblasts (200 per cubic millimetre), polychromatophilia, and poikilocytosis, while the hæmoglobin value is always increased. There is the picture of the blood in a pernicious anæmia. There is always a marked leucocytosis, the count rising to 20,000 per cubic millimetre after the first few days, and increasing later The polymorphonuclear leucocytes number about 75 per cent. The condition of the bone-marrow has been studied by Corvallo, who finds excess of normoblasts and neutrophile myelocytes.

Eruptive Stage (*Verruga, sensu stricto*).- In many cases, after the febrile stage has lasted from twenty days to eight months, the skin begins to itch, and an eruption appears on the face, neck, the extensor surfaces of the arms and legs, and at times on the conjunctivæ, the lips, tongue, gums, palate, and pharynx. This eruption shows itself at first as small, pinkish-red, erythematous spots, sometimes associated with small vesicles, or more rarely with bullæ or pustules. The erythematous areas speedily become papules, and finally nodules, which may vary in size and in number. The usual size is about that of a pea.

When fully developed, they appear as elevated, cylindrical, fungiform, or irregular wart-like bodies, usually discrete, red in colour, generally firm to the touch (though they may be soft), and very liable to bleed. This type of eruption is the *forme miliare* (miliary type) of the Odriozolas and Salazar. In addition to these superficial tubercles there are deep subcutaneous nodules (nodular type), which lie under the unaltered skin, and from which at first they are quite free. These nodules may reach a large size, and become adherent to the skin, ulcerate, and reach the surface as large red fungating masses, which readily bleed. This is the *forme mulaire* of the above mentioned authors. Both types appear on the skin, but the miliary type may also appear on the mucous membranes and internal organs, while the nodular type is confined to the skin, especially at the flexures of the elbows and knees. The first crop usually appears on the face, and the extremities may be discrete or confluent: in the latter case no healthy area of skin may be visible. The miliary eruption may appear when the general symptoms have abated, but the nodular is accompanied by fever.

The area of the skin on which the spots appear is usually œdematous, a feature most commonly observed on the legs. With the appearance of the eruption the fever declines, the general symptoms abate, and the patient feels better, but the blood shows a marked diminution in the red cells, some of which are nucleated, and a corresponding reduction in the hæmoglobin, and this anæmia may be aggravated by hæmorrhages from the nodules, which may be so severe as to cause the death of the patient. This blood condition has been carefully investigated by Monge, who finds that at the commencement of the illness there is oligocythæmia, microcytes, macrocytes, normoblasts, and megaloblasts (under 1,000 per cubic millimetre), with poikilocytosis, polychromatophilia, and granular red cells. The hæmoglobin value is raised. The white cells are increased, and there is slight polymorphonucleosis. The mononuclears have well-marked basophilic protoplasm. At this stage the verrugas may develop in the internal organs, and cause serious symptoms; thus in the larynx they will cause dyspnœa: in the bronchi, bronchitis: in the lungs, pneumonia: in the pleura, pleurisy; in the nose, epistaxis and difficulty in nasal breathing; in the œsophagus, dysphagia; in the intestine, bloody diarrhœa; in the meninges, brain symptoms: in the eye, amblyopia; and in the uterus, metrorrhagia.

After lasting from four to six months, during which several crops appear and disappear, each preceded by an attack of fever, the eruption finally disappears, and the nodules, becoming pale and drying up, disappear without producing a scar, while the ulcerated nodules dry up and heal by cicatrization, and the patient is left

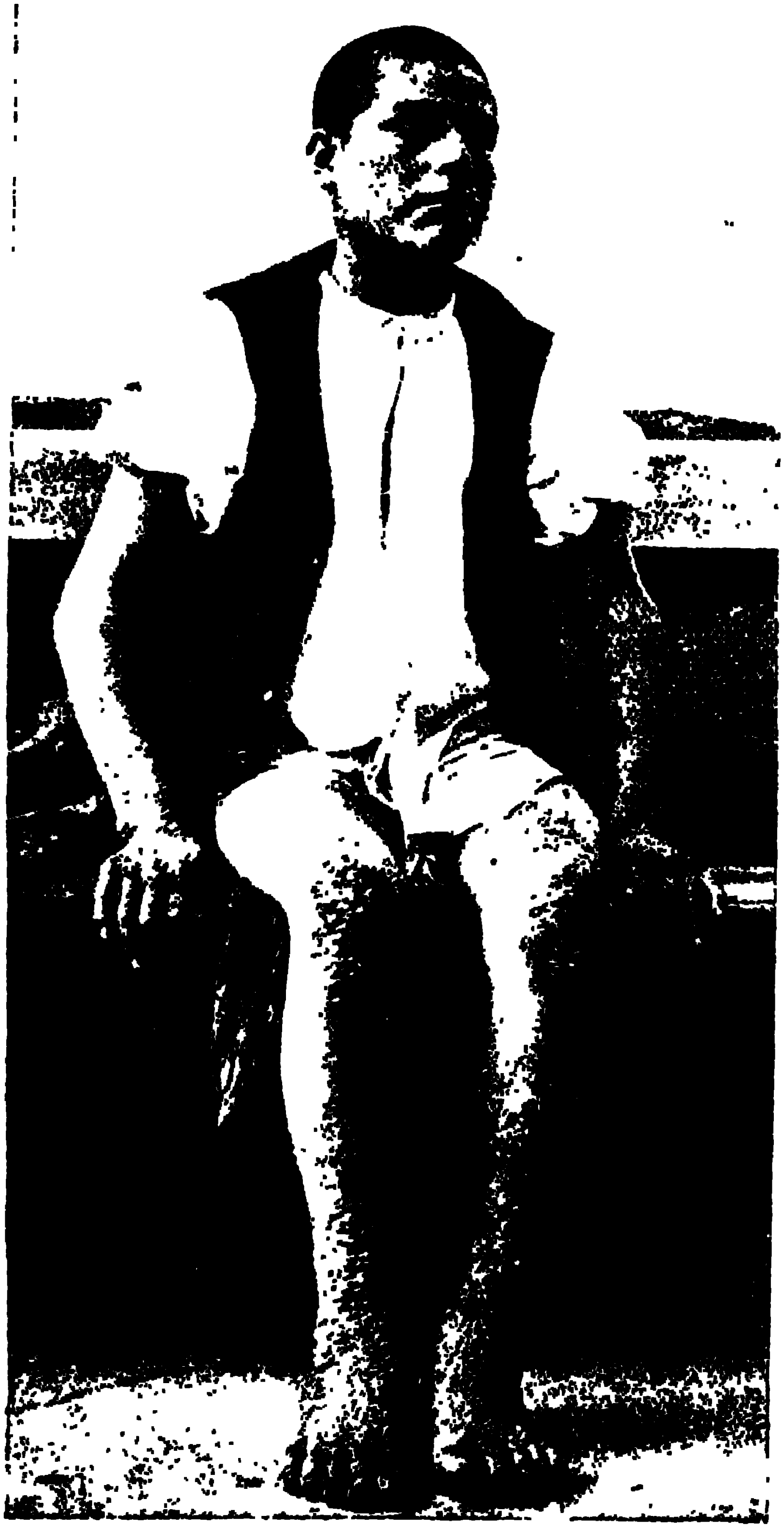

FIG. 706.—VERRUGA PERUVIANA: ERUPTION ON EXTREMITIES. (After Biffi, from the *Archiv fur Schiffs- u. Tropen-Hygiene.*)

convalescent, but anæmic and feeble. According to Monge, systematic examination of the blood reveals the fact that a time arrives, which he calls *the critical period*, when the leucocytes are reduced; the polymorphonuclear leucocytes also diminish in numbers, and the eosinophiles, which have been practically absent, reappear, and a definite mononuclear increase supervenes. This critical period lasts four to five days, and changes completely the blood picture.

During the decline of the disease there is slight oligocythæmia and granular red cells, while the mononuclear cells are increased to 50 to 60 per cent.; there is slight eosinophilia, and the hæmoglobin value is normal.

The course of the disease, however, is by no means as straightforward as depicted, for at times the eruption comes out poorly, and is limited in its distribution, or, having developed, may disappear, in which cases the general symptoms, which may have improved, are apt to return and cause a serious illness.

Acute or Severe Form. This form Carrion's disease, *sensu stricto* is considered by many authorities to be a condition separate from verruga, and when present in verruga to be merely a complication. It seems to be a fever of the enteroidea group. The temperature becomes almost continuous, the pains and the diarrhœa severe, the urine dark and scanty, acid in reaction, with high specific gravity, increased indican and urobilin, but rarely albumen, and never blood. It contains something which reduces Fehling's solution. According to some observers the anæmia becomes profound, the red cells being reduced to 500,000, according to Monge, nucleated red cells appearing, while death results in about two or three weeks.

Varieties. Slight cases may pass through the whole illness without fever, while more severe cases show intermittent or even remittent fever.

Complications. The complications are numerous, and include septic poisoning, malaria, tuberculosis, and syphilis.

The observers who consider Oroya fever a separate entity from verruga, admit that it is not rarely complicated with the latter.

Sequelæ.—The usual sequelæ are anæmia, dropsy, and affections of the nervous system.

Diagnosis. The most important feature in the diagnosis is residence in one of the endemic areas, when a person complaining of vague pains and illness, with distinct anæmia, with or without febrile symptoms, should be regarded as most likely to be suffering from the febrile or anæmic stage of verruga. The rapidity with which the anæmia is developed is an important point in the diagnosis, for in the severe forms of the disease the number of the red cells will fall in three to four days to less than 1,000,000 per cubic millimetre, and even in slight cases there will be a marked diminution. Concurrently in the severe forms all the signs of the blood picture of pernicious anæmia will develop This anæmia imprints a typical facies upon the patient. The febrile stage must be differentiated from malaria by the absence of the parasites in the blood, from typhoid by the serum reactions, from tuberculosis by skin and ophthalmic reaction, from rheumatism by the absence of the swelling of the joints, and from histoplasmosis by the absence of the parasite. The stage of eruption must be distinguished from framboesia by the absence of the eruption on the trunk, by the tendency to hæmorrhage, and the absence of *Treponema pertenue*.

It should be remembered [illegible] ding to Strong, Tyzzer, Brues, Sellards, and Gastiaburu's valuable [illegible] s, Oroya fever and verruga are two separate diseases. Oroya fev[illegible] haracterized by the profound anæmia, the fever, the presence of *B* [illegible] *acilliformis* in the blood, its non-inoculability in monkeys, while uncomplicated verruga is clinically identical with angiofibroma contagiosum; there is no fever, no severe anæmia, there is absence of *B. bacilliformis* and the condition is inoculable in monkeys and human being.

Fig. [illegible] GA PERUVIANA ERUPTION ON THE FACE, LIPS, AND TONGUE.
(After Bahr from the *Archiv für Schiffs- u. Tropen-Hygiene*.)

Prognosis.—With the possibility of such a serious complication as Carrion's fever arising, or in later stages of internal verrugas forming, the prognosis must be very guarded. A good sign is an early appearance of a widely-spread eruption, while a poorly-developed eruption associated with anæmia and marked weakness is of grave import. Monge states that the difference between two consecutive blood counts is of importance in deciding the prognosis, as an increase in the mononuclears and of the erythrocytes and the appearance of eosinophile cells marks an improvement.

The appearance of the eruption *per se* should not be considered a good sign if there is still marked oligocythæmia and polymorphonucleosis.

Especially serious is the disappearance of a poorly-marked eruption, and the reappearance of fever pains, etc. Cold weather and high altitudes are unfavourable, and complications increase the gravity of the case considerably, the former because it delays the development of the eruption and may cause it to abort, and the latter because it increases the tendency to hæmorrhage. The mortality varies from 10 to 40 per cent.

Treatment.—No specific treatment is known, but Odriozola recommends hypodermic injections of arsenic, and removal from the endemic region to the warm countries along the littoral will also be of benefit. Atoxyl, salvarsan, and neo-salvarsan may be tried. Chills and cold baths must be specially avoided as being apt to stop the development of the eruption, and hence to endanger the life of the patient. Drugs appear to be useless in the febrile stage, and though decoctions of maize, of *Buttneria cordata* (Buttneriaceæ), *Buddleia incana* (Scrofulariaceæ), or *Schinus molle* (Terebinthinaceæ), have been popular, they are now believed to be useless.

Tonics of iron and arsenic are useful during convalescence, but the iron is best administered by hypodermic injections. Carrion's fever must be treated in the same manner as typhoid fever.

Prophylaxis. In the present state of our knowledge the only possible prophylaxis is to avoid the endemic regions, and to protect the body against biting arthropods, especially at night.

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CHAPTER LXIII

RHINOSPORIDIOSIS AND SARCO-SPORIDIOSIS

Rhinosporidiosis—The Sarcosporidioses—Sergentelliasis—References.

RHINOSPORIDIOSIS.

Definition. Rhinosporidiosis is a chronic infection caused by *Rhinosporidium seeberi* Wernicke, 1900, and characterized by the production of polypi on mucous membranes and papillomata on cutaneous surfaces.

History. The disease was first recognized by Malbran in South America in 1892, then by Seeber in 1896 in Buenos Aires, in a nasal polypus occurring in a young man aged nineteen years. In 1900 he gave a description of the parasite and its development, which we have been unable to obtain, but which is said to be a most excellent account. Later he found two other cases in the same town, and in 1900 the parasite was named *Coccidium seeberi* by Wernicke.

In 1903 Kinealy reported to the Laryngological Society a peculiar case of a polypus which he had found in 1894 growing from the septum of the nose of an Indian in Calcutta in the form of a pedunculated, raspberry-like body, with whitish spots on the generally red surface. On section this tumour was found to have peculiar bodies embedded in it. It was then carefully examined and described by Minchin and Fantham, who came to the conclusion that the peculiar bodies were Haplosporidians, and named them *Rhinosporidium kinealyi*. In 1905, Nair of Madras found similar nasal polypi in several people, who all came from the small native State of Cochin, on the west coast of India. These polypi were carefully described by Beattie in 1906.

In 1910 we observed the same parasite in a nasal polypus in Ceylon, and in the same year Ingram published an account of its occurrence in a conjunctival polypus and in a papilloma on the penis.

In 1914 Tirumurti gave a most excellent account of the disease.

In 1918 Chelliah, in Ceylon, not merely confirmed our original discovery of the disease in that island, but reported several more cases in Singhalese and moormen.

Climatology.—Rhinosporidiosis occurs in South America, in India, and in Ceylon, and quite possibly in other regions.

Ætiology.—The cause of the disease is *Rhinosporidium seeberi* Wernicke, 1900 (p. 533), which is present in the growths in the form of clear hyaline roundish cysts of varying diameter.

The life-history in man appears to be as follows:—

The free spores, which are small spherical ovoid bodies with single chromatinic masses, grow into sporocysts which have a few chromatinic granules. These sporocysts grow into larger bodies containing a few centrally placed pansporoblasts. When these cysts are mature they are filled with pansporoblasts which have formed spore morulæ containing some fourteen to sixteen clear shining spores.

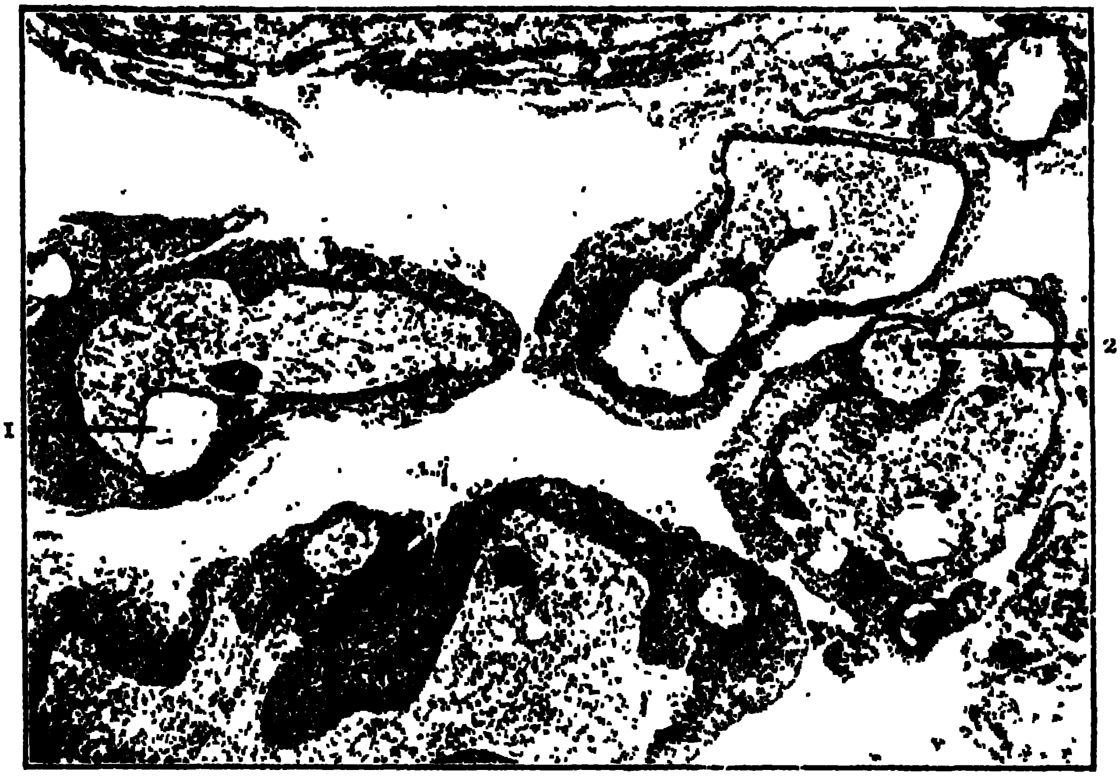


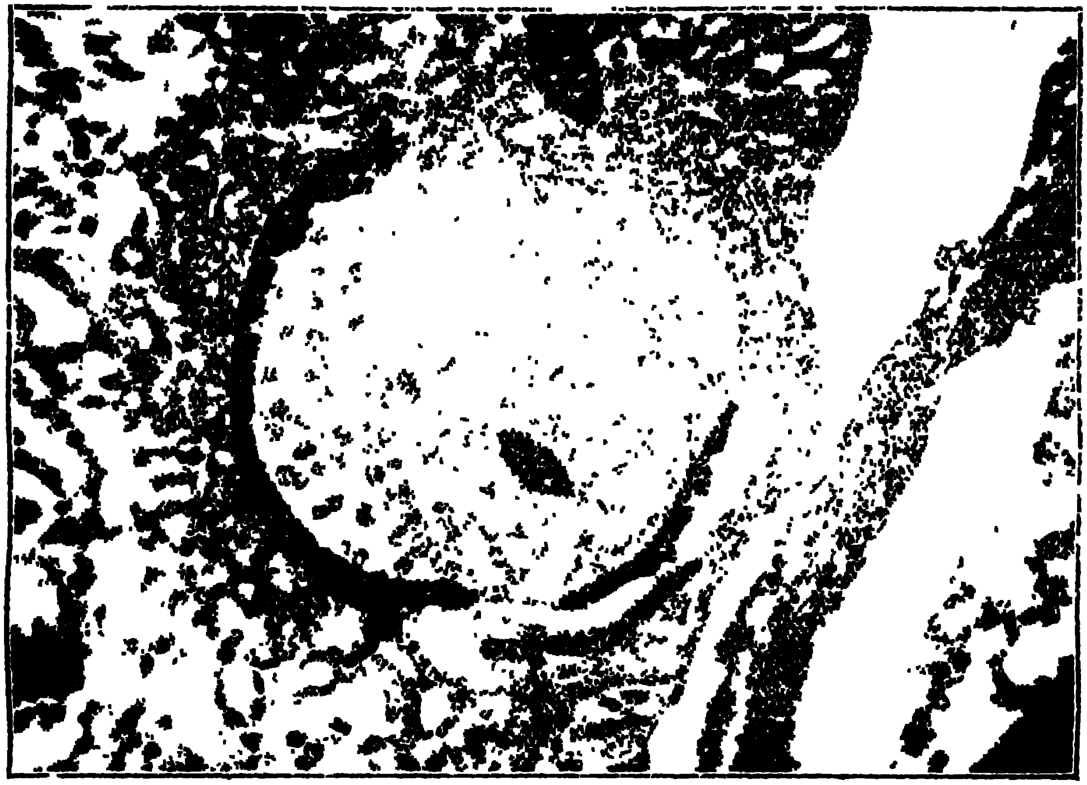
FIG. 708 SECTION OF NASAL POLYPUS SHOWING *Rhinosporidium seeberi* AT 1 AND 2. (× 30) CEYLON CASE. (PHOTOMICROGRAPH.)

1 is reproduced much more highly magnified in Fig 709.

The cyst ruptures, the pansporoblasts escape and rupture, and so allow the spores to be liberated. Spores probably escape from the nose and other parts, and possibly infect man in this way, because there is some slight evidence of transference direct from man to man, though we were unable to trace any such cause in our Ceylon case. Probably the reservoir for the parasite is in some unknown animal. Spores which do not escape from the body propagate the parasite in the patient.

Morbid Anatomy.—When a polypus is teased out in the normal saline it will be observed that it is stalked, and that from this central peduncle strands of fibrous tissue branch out into processes. The tissue is studded with pin-head sized white dots which represent the cysts.

As can be judged from Fig. 708, the mucous membrane is thrown into folds which form papillomatous-like processes, in which, here and there, the epithelium is thin or wanting. The subepithelial tissue is very vascular, and is infiltrated with polymorphonuclear leucocytes, and shows small hæmorrhages at times, and in the nose may also be myxomatous in places. The cysts may be seen lying in this tissue or bulging through the epithelium (*vide* 2 in Fig. 708 and also in Fig. 709, which shows a cyst full of pansporoblasts, which appear under higher magnification in Fig. 710.



Pathology.—The parasite spreads in the body by the rupture of the cyst and the liberation of the spores. We suspect that it may, at times, give rise to a condition resembling a septicæmia.

Symptomatology. The patient has his attention drawn to his nose by profuse bleedings, and in a little time notices a growth. On examination this is found to be a small vascular pedunculated tumour, about the size and shape of a pea, freely movable and painless, attached to the anterior and upper part of the cartilaginous septum. In appearance it resembles a strawberry or a raspberry.

It may, however, form polypi in other regions, as, for example, on the conjunctiva, or papillomata on cutaneous surfaces, as, for example, on the penis.

Diagnosis.—The diagnosis can only be made by removal of the whole or a portion of the growth, which in most cases has the appearance of a nasal polypus, followed by a microscopical examination, when the parasite will be easily seen as a roundish cyst filled with granules which, when examined under a higher power, are seen to be the pansporoblasts.

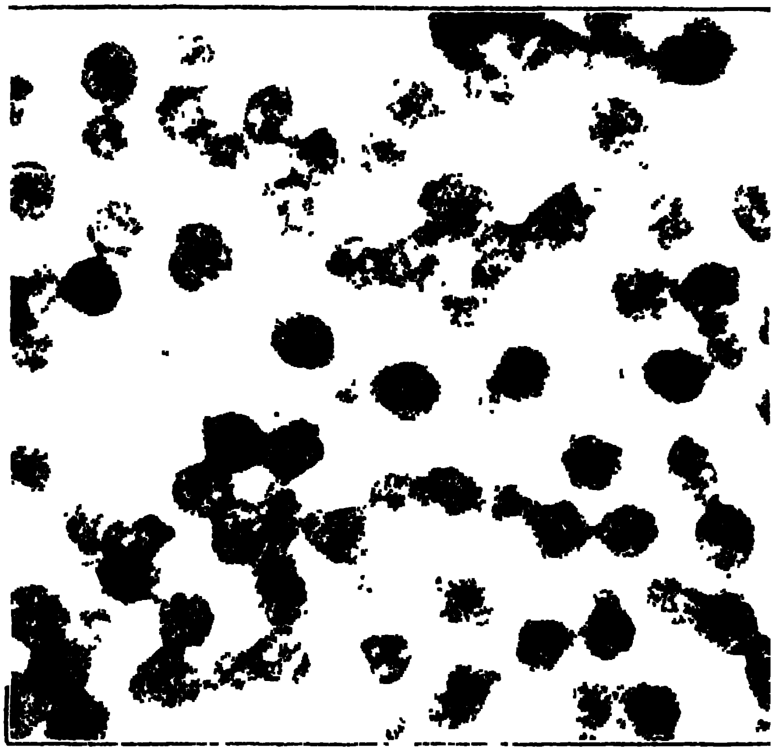


Fig. 711.—*Rhinosporidium seeberi* Wernicke as seen at 2 in Fig. 708 (×1,000.) Ceylon Case. (Photomicrograph.)

Prognosis. This is usually said to be good, but if it can cause, as we suspect, a general infection, it may be dangerous to life.

Treatment. The treatment is to remove the growth and cauterize its base.

Prophylaxis. As we are entirely ignorant of the life-cycle of the parasite or where it exists outside the human body, no remarks can be made as to the prophylaxis.

THE SARCOSPORIDIOSES.

Definition. Sarcosporidiosis is a chronic infection caused by the invasion of the body by *Sarcocystis lindemanni* Rivolta, 1878, *Sarcocystis muris* R. Blanchard, 1885, and perhaps other allied organisms.

History. In 1868 Lindemann found some indefinite bodies in the myocardium and on the valves of the heart of a person who had died of dropsy. It is thought that these bodies may possibly have belonged to the genus Sarcocystis, but it is very doubtful what they really represented. In 1887 Koch described the first genuine case in Egypt. In 1894 Baraban and St. Remy found these parasites in the laryngeal muscles of a man who had been executed. In 1902 Rosenberg reported a doubtful case, and Kartulis another doubtful case. In 1903 Et. and Ed. Sergent described a parasite which later was called *Sergentella hominis* Brumpt, 1910, in the blood (*vide* p. 537), and in 1905 Castellani and Willey described rather different bodies also in the blood (*vide* pp. 537 and 538), which they were inclined to consider of protozoal origin, and later similar, but somewhat larger, forms were found by Castellani and Sturgess in the blood of *Bos indicus* (Fig. 189, p. 531). In 1909 Darling described a case of sarcosporidiosis in a Barbadian negro in which the parasite appeared to be *Sarcocystis muris* Blanchard.

Climatology.—Sarcosporidiosis being only a chance infection in man, and the parasite normally occurring in monkeys, buffaloes, cattle, sheep, pigs, rats, and other animals, it is obvious that not merely will the disease be very widespread, but that different varieties will occur in the different zoological regions. The cases so far described are in Central America, Europe, and Egypt, and doubtful cases in Algeria and Ceylon. We are suspicious that the Ceylon case may have some connection with *S. tenellæ*, var. *bubalis* Willey, Chalmers, and Philip, 1904, which is very commonly found in buffalo meat in Ceylon.

Ætiology.—The causation of sarcosporidiosis is the presence of some species of sarcocystis in man, but the method of entry is not obvious. It would seem possible that eating undercooked meat infected with *Sarcocystis* might produce the infection, as Darling has shown that guinea-pigs can be infected by feeding them with rat's muscle containing *S. muris*, and by feeding them with the ripe sporozoites of the same species. In our opinion this is a very probable method of chance infection, because the buffalo meat in Ceylon is heavily infected (*vide* p. 531).

Morbid Anatomy. The spores can be found in the blood and the parasites in the muscle fibres.

Symptomatology. The incubation period in animals appears to be very long, some 152 to 104 days. During the invasion the patient suffers from an irregular fever, which may resemble enteric fever, and in severe cases this fever may be complicated with myositis and even necrosis of the muscles.

Diagnosis.—The symptoms are those of an irregular fever, which in some cases may be typhoidal-like, and in others of a very low type without much general disturbance, while some cases may never show pyrexia. The nature of these fevers may be suspected by finding bodies resembling the spores of *Sarcocystis* (*vide* Fig. 189, p. 531) in the blood. Failing this, and especially if there are any signs of myositis, the diagnosis can be cleared by excision and examination of a piece of diseased muscle.

Prognosis.—This is good after the parasites have become quiescent, for no one has so far been known to die of the disease.

Treatment.—The treatment is entirely symptomatic.

Prophylaxis.—Meat should be carefully inspected, and any found heavily infected with *Sarcocystis* should be condemned, while all meat should be well cooked.

SERGENTELLIASIS.

The brothers Sergent, in 1903, described a peculiar parasite (the description of which is found on p. 537) in a person suffering from night sweats and attacks of nausea. There was apparently no fever, and the general condition was good. This parasite, to which Brumpt has given the name of *Sergentella hominis*, might be the free spores of a species of *Sarcocystis*.

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CHAPTER LXIV

PARAGONIMIASIS

Synonyms—Definition—History—Climatology—Ætiology—Pathology—Morbid anatomy—Symptomatology—Complications—Diagnosis—Treatment—Prophylaxis—References.

Synonyms.—Parasitic hæmoptysis, Pulmonary distomatosis, Endemic hæmoptysis.

Definition. Paragonimiasis is a chronic or subacute general or local infection of man by means of *Paragonimus ringeri* Cobbold, 1880, which produces cystic lesions, containing a thick, opaque, reddish fluid, in which are found at times the parasite or its eggs.

History. In 1879 Ringer discovered the parasite of this disease in a patient at Tamsui in Formosa, and it was named *Distomum ringeri* by Cobbold in 1880. In 1878 Kerbert had discovered similar parasites in the lungs of two Bengal tigers which died in the Zoological Gardens of Amsterdam and Hamburg. Subsequently it was considered that the two parasites were one and the same species, and as Kerbert had named his species *Paragonimus westermani* in 1878, this name was applied to the human parasite until Ward and Hirsch stated that the spines which cover the cuticle and which are arranged in groups are different in the two species. Thus *Paragonimus ringeri* has chisel-shaped moderately heavy spines, while *P. westermani* has lancet shaped and very slender spines. The human species is, therefore, known by Cobbold's name of *P. ringeri*.

In 1880 Baelz found bodies in cases of hæmoptysis which he thought were psorosperms, and, therefore, he called the disease 'gregarinosis pulmonum,' but when the bodies were shown to Leuckart he said that they were ova of a distomum.

In the same year (1880) Manson found the eggs in a case of hæmoptysis in a Chinaman from Northern Formosa, and later in a Portuguese with similar symptoms from Tamsui in Northern Formosa. This Portuguese died in Formosa, and Ringer discovered in the lungs during the post mortem examination a minute fleshy oval body, grey in colour. This specimen was forwarded to Manson, who sent it to Cobbold, who named it *Distomum ringeri*.

In 1883 Baelz also found adult specimens in the lungs, and gave them the name *Distomum pulmonale*. In 1890 Otani and Yamagiwa showed that it could give rise to a general infection and could be found in the brain. In 1902 Musgrave gave a very complete account of the disease as seen in the Philippine Islands. In 1910 Nagano reported upon the prevalence of the disease in Northern Formosa, around the prefecture of Shinchika; and Nakagawa in 1913 and 1914 found 1,249 cases, of which 922 occurred in that prefecture, and believes that there are not less than 13,000 cases therein. In 1912 Masuo and Yokokawa found the disease in Sansaka, Koryo, Jukirin, and Nansho. In 1914 Nakagawa investigated the inhabitants of the lowlands occupied by savage tribes, and found that about 50 per cent. of the population were infected: but in the highlands the cases were less in number.

In the meanwhile observations had been made as to the development of the worm in the egg by Nakahama in Japan, by Manson in China, and by Garrison and Leynes in the Philippines. In 1914 Nakagawa found that the cercariæ developed in the mollusc *Melania libertina* Gould, which lives in pools and sluggish streams: in *Melania obliquegranosa* Smith, which inhabits slowly moving streams; and in *Melania tuberculata* Mueller.

The life-history would be as follows: The miracidia attach themselves by means of suckers to the head, jaws, and feet of these molluscs, and then bore their way by means of their proboscis into the liver, the heart, and the kidneys, where they become sporocysts and cercariæ. These latter possess an unforked tail and measure 0·12 × 0·09 mm., and a tail of 0·054 mm. They also show a spine, two suckers, three pairs of poison glands, and a heart-shaped excretory vesicle. They encyst on the gills of certain crabs—viz., *Potamon* (*geothelphusa*) *obtusipes* Stimpson, the red crab; *Potamon* (*geothelphusa*) *dehaani* White, the dung crab; *Eriocheir japonicus* de Haan, the hairy crab; and perhaps on those of *Sesarma dehaanii* Milne Edwards, and *Potamon* (*parathelphusa*) *sinensis* Milne Edwards.

Dogs fed upon these crabs showed eggs in ninety days after infection. The young distome escapes from the cyst in the intestine of the dog, pierces the wall of the jejunum and passes into the peritoneal cavity, pierces the diaphragm and pleura and enters the lungs, where it encysts and becomes adult.

More recently other observers have doubted the necessity of the crab in the case of the infection of man, which apparently can take place via the skin.

Kobayashi believes that the cercariæ observed by Nakagawa in molluscs of the genus *Melania* are not those of *P. ringeri*.

Climatology.—Paragonimiasis is found in China, Corea, Japan, Formosa, the Philippine Islands, and Sumatra. The infection is more prevalent among people living along large rivers, according to Nakagawa, and less so among people who use well water.

Ætiology.—The causal agent is *Paragonimus ringeri* Cobbold (p. 573), which lives not merely in man, but also in the cat, the dog, and the pig. The intermediate hosts are molluscs of the genus *Melania*, in which the cercariæ are developed, and these pass to man either directly or through the agency of certain crabs, in which they become encysted. Infection may be by the alimentary canal, and also perhaps by the skin. The worms become adult in the lungs and other organs.

The disease appears to be very widespread in certain districts, and the old idea that it is more common in males than in females requires reinvestigation.

Pathology.—The pathology of the disease is by no means clear, and how the various pathological changes are evolved is unknown.

Musgrave has classified the lesions into:—

1. The non-suppurating lesion.
2. The tubercle-like lesion.
3. The suppurating lesion.
4. The ulcerative lesion—
    (*a*) in the skin:
    (*b*) in the bronchial mucosa;
    (*c*) in the intestinal mucosa;
    (*d*) in the bile-duct.

The simplest lesion appears to be an infiltration of the connective tissue of an organ with eggs, without any histological changes at first, but later with a proliferation of the connective tissue and the formation of a cirrhosis or a round-celled infiltration, with sometimes many eosinophiles, which may lead to abscess-formation, and finally to ulceration. The abscess-formation may at times produce caseous material, giving a tubercular appearance.

The non-suppurating lesion may therefore be simple infiltration of the tissue by eggs, with or without inflammation. On the other hand, cirrhotic changes may be seen, especially in the liver. In serous membranes an adhesive inflammation is often produced, associated with the presence of eggs in brown patches at the points of contact.

The inflammation of the organ may, however, proceed to pus-formation, resulting in a typical abscess. On the other hand, the tissues generally attempt to circumscribe this abscess by a fibrous wall, and thus produce what is called the typical lesion of the disease. In the centre of the abscess will be seen degenerated cells, blood, eggs, and perhaps a parasite. Then comes a capsular wall of fibrous connective tissue, smooth towards the centre, and joining the rest of the organ externally. Around this wall the connective tissue of the organ is proliferating and congested. In this way the typical little cysts, with dull blue-grey walls, smooth internally, and containing a thick, reddish fluid, with or without eggs or a parasite, are formed. These lesions may work their way to a cutaneous or mucous surface, and so open into a bronchus, or into the intestine, or the bile-duct, or on to the skin, thus giving rise to ulcers in those regions. The intestinal ulcers closely resemble dysenteric ulcers, and, indeed, may become secondarily infected with amœbæ or bacteria.

In course of time these lesions may show some attempt at healing and scar-formation, but generally this is not very successful.

The blood may show a deviation of complement with worm-body used as antigen.

Morbid Anatomy.—The body may be well nourished, but more usually is emaciated and anæmic. Ulcers can be seen at times in the axillæ and groin, leading into diseased glands. The muscles may contain abscesses. The pleura, pericardium, peritoneum, and, more rarely, the meninges, show the chronic inflammations and the non-suppurative lesions mentioned above. The lesions found in the lungs are diffuse cirrhosis, bronchiectatic cavities, pneumonia, and caseous abscesses, while those of the liver are cirrhosis, perihepatitis, and abscess-formation. The typical lesions mentioned above may be found in the spleen, pancreas, small and large intestines, kidneys, bladder, epididymis, prostate, and in the choroid plexus of the brain.

Symptomatology.—As the invasion of the body is so generalized, the symptoms are very varied. Musgrave differentiates four varieties—the generalized, the thoracic, abdominal, and cerebral; but there is nothing very characteristic about any of these types.

In *the generalized type* there may be fever, enlarged lymphatic glands, general muscular pains, and ulceration of the skin.

In *the thoracic type* there will be cough, with the expectoration of purulent or, more generally, blood-stained sputum, in which the eggs may be best seen by the addition of a little 0·1 per cent. solution of sulphuric acid. More rarely an adult parasite appears in the sputum, which also may contain Charcot-Leyden and creatinin crystals. The patient generally complains of pain in some part of the chest. The physical signs may indicate broncho-pneumonia or pleural effusion, which may be serous or purulent.

In *the abdominal form* of the disease there are only the vaguest symptoms of dull, aching pains and tenderness, while diarrhœa, appendicitis, epididymitis, or cirrhosis of the liver, may be demonstrated by the usual physical signs and symptoms. When diarrhœa occurs, the eggs may be found in the fæces

The cerebral type is associated with epilepsy, which may be Jacksonian in character, while neuritis or paralysis may also be present.

The blood and urine have not yet been fully examined. Though generally chronic, the course may be acute if complicated by septic or other diseases.

Complications.—The most usual complications are tuberculosis and entamœbic dysentery.

Diagnosis.—With the above symptomatology, it will be obvious that the diagnosis depends entirely upon finding the eggs of the parasite in the sputum, the fæces, the scrapings from the ulcers, or the fluids obtained by puncture of a hydro- or pyothorax. Suspicions as to the presence of the disease will be strongest when cases showing any of the above signs occur in the endemic area.

Treatment.—The treatment must be devoted to relieving individual symptoms, but Musgrave recommends treatment by iodide of potash. Removal from the endemic area is, of course, indicated. Perhaps tartar emetic injected intravenously might do good.

Prophylaxis.—In the endemic region drinking and bathing water should be boiled or filtered, and crabs should not be eaten.

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CHAPTER LXV

KATAYAMA DISEASE

Synonyms — Definition — History — Climatology — Ætiology — Pathology — Morbid anatomy — Symptomatology — Varieties — Complications — Diagnosis — Prognosis — Treatment — Prophylaxis — References.

Synonyms. Urticarial fever, Asiatic schistosomiasis, Schistosomiasis japonica, Kabure (cutaneous symptoms).

Definition.—Katayama disease is caused by *Schistosoma japonicum* Katsurada, 1904, and is characterized by urticarial and dysenteric symptoms, painful enlargement of the liver and spleen, with or without fever, dropsy, progressive anæmia, and sometimes pulmonary and brain symptoms.

History.—In 1887 Mazumi drew attention to a peculiar form of cirrhosis of the liver which was found in certain districts in Japan, and was caused by the ova of some unknown parasite. His discovery was confirmed, and the ova were found in other organs besides the liver; and the disease, which became well known among Japanese medical men, was named 'Katayama disease,' from a town in Bingo, one of the districts in which it is common. In 1904 Katsurada, who was resident in the infected area, discovered that the ova were those of a *Schistosoma*, and, further, found the adults in the portal vein of a cat. He named the parasite *Schistosoma japonicum*. In the same year Fujinami discovered a female worm in a human being. Meanwhile Catto found the same parasite in a Chinaman from Fukien, and described it in 1905, and in the same year Stiles and Looss gave accounts of the disease. In 1906 Woolley, in a most excellent paper, described its occurrence in the Philippine Islands. Logan has found it in a Chinaman from Hunan, and in 1909 Peake recorded three cases from a small town on the Siang River, in the Hunan province of Central China. In 1911 Houghton, Logan, and Lambert, drew attention to cases of fever with urticaria, and eosinophilia connected with infections with *S. japonicum*.

In the same year Edgar drew attention to this fever in the Yangtze Valley, near Hankow, and noted that nearly every patient had bathed or waded in marshy ground near the river.

In 1912 Miyagawa did not believe that the worm was the cause of the dermatitis.

In 1913 Miyairi and Suzuki noticed that the eggs of the worm, when kept for one to two hours in fæces and water at a suitable temperature, hatched out, the shell being broken. The newly-born miracidia swim about vigorously and enter a snail, said at the time to be a species of *Limnæus*, in which after twelve days rediæ appear in the liver. They further found that mice placed in the same vessel with these snails for three hours a day develop *S. japonicum* in their livers.

Also in 1913 Katsurada found that the worms reached maturity in two weeks and produced eggs in three weeks, and that the method of infection of the vertebrate was by the skin, as could be demonstrated by producing the disease in cats and dogs (Katsurada), in cattle (Fujinami), in man (Matsura in himself).

In 1914 White gave an account of a case of the disease, as seen on H.M.S. *Cadmus*, under the term *urticarial fever*. The patient suffered from fever about 102° to 103° F. in the evening and normal in the morning, pains in the lumbar and epigastric regions, pulse-rate 90, with a temperature of 103° F., slight reduction of the red corpuscles, 4,800,000 per c mm., and 50 per cent. to 70 per cent. of eosinophiles, and loss of weight associated with the appearance of urticarial eruptions in various parts of the body.

In the same year Lanning noted that it was not uncommon for a fair proportion of the crews of gunboats patrolling the Yangtze River to become infected after wading through the water-covered paddy fields in search of snipe.

Miyairi's work induced Leiper and Atkinson, in 1914, to proceed to Shanghai and later to Katayama in Japan to investigate the parasite. Their results were published in 1915. At Katayama they found a small brown snail, with eight spirals and an operculum, known at that time as *Katayama nosophora*, which had an extraordinary attraction for the miracidia, its small head and foot becoming festooned with white specks (the miracidia), which appeared to irritate the snail. Later the liver was found to be full of cercariæ with bifid tails, which infected laboratory-bred mice by passing through the skin, male and female adult worms being found in the portal vessels one month after infection.

In 1916 Koiki drew attention to the fact that in forty-two cases found near Shushin, in Japan, all but three were farmers, and most had had an itchy eruption on the legs about a year before. In the same year Mann reported upon the disease, and said that salvarsan was beneficial in the second stage; and Narabayashi studied the life-history of the parasite (*vide* p. 592) and pointed out the relationship between it and the skin disease called kabure.

Climatology.—It occurs in Japan, China, and the Philippine Islands: in the first in the provinces of Bingo, Yamanashi, Hiroshima, and Saga; in the second it is reported up to date from Hunan, Honan, Hupeh, Kiangsi, and Anhwei provinces, and from Fukien. In Wuhu 8 per cent. of all male cases entering the General Hospital show either latent, active, or overwhelming infection. In China only the low-lying lands appear to be infected; no cases from the hills or mountains are known.

In the Philippine Islands one case has been reported by Woolley as occurring in a Filippino who had never left the islands.

Ætiology.—The cause of the disease is *Schistosoma japonicum* Katsurada, 1904, which is spread by *Blandfordia japonica*, in which the worm develops into cercariæ which penetrate the skin. The vertebrate reservoirs are cats, dogs, and pigs. For description of the worm see p. 590.

Pathology.—After penetrating into the skin the parasites enter either veins or arteries. In the former case they pass to the right heart and hence to the lungs, at the bases of which they collect, and then, passing through the mediastinum, diaphragm, and liver, reach the portal system. Sueyasu, in 1916 obtained complement fixation with the blood of immune animals.

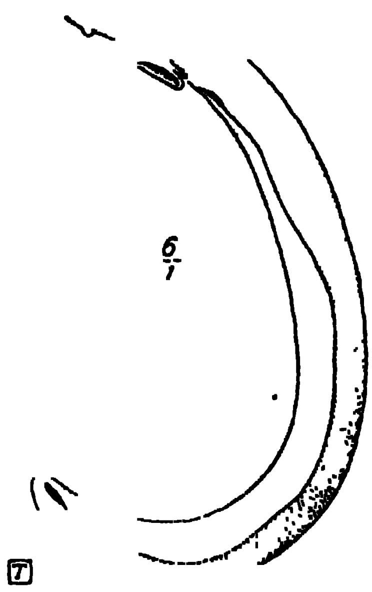

Fig. 711 — *Schistosoma japonicum* Katsurada. (After Manson.)

Morbid Anatomy.—On opening the abdomen, signs of old peritonitis may be seen, the appendices epiploicæ being matted together, and at times there are also signs of old pelvic peritonitis. The liver is cirrhotic and less than its normal size, and its surface is studded by nodules, usually larger than those of alcoholic atrophic cirrhosis. Glisson's capsule is thickened, and shows much connective tissue with round-celled infiltration, in which lie the ova of the worm.

The small and large intestines and appendix may be thickened, and their mucosa is swollen and hyperæmic, and shows patches of ulceration and necrosis, and, in addition, papillomata, resembling those of bilharziosis. The eggs may also be found in the mesentery and in the mesenteric glands, the wall of the gall-bladder, the pancreas, the walls of the mesenteric vessels, and the pylorus. The adult worms may be found in some of the veins of the portal system, especially at the bifurcations of the smaller mesenteric vessels.

In addition, the eggs may be found in fibrous and round-celled infiltrations in the lungs and in the brain. This infiltration often takes the form of nodules.

Symptomatology.—The early symptoms of the disease may be slight, or perhaps it may begin with attacks of fever, with urticarial rashes, in which there is marked eosinophilia, and this may be associated with cough, scanty expectoration, some impairment of resonance over the bases or other parts of the lungs, with fine crepitant râles on deep inspiration, and a diminution of the breath-sounds.

About two years later there are diarrhœic or dysenteric symptoms, with or without fever, and the presence of the ova in the fæces. Associated with these symptoms are abdominal pains, enlargement and tenderness of the liver, the hypogastrium shrinking, and the epigastrium enlarging and giving rise to a characteristic abdominal appearance. At the same time the dysenteric symptoms cease, and an irregular chronic diarrhœa sets in, with motions containing much undigested food, and associated with dyspepsia.

In course of time the preliminary enlargement of the liver may cease, and the organ may begin to shrink, but in any case the spleen becomes tender and enlarges, ascites appears, and the patient becomes steadily weaker, more and more anaemic, emaciated, and incapable of mental or physical work. The average of three differential blood-counts by Peake is as follows: Polymorphonuclears, 56·6 per cent.; mononuclears, 13·2 per cent.; lymphocytes, 15·6 per cent.; eosinophiles, 14·1 per cent., but the eosinophilia may reach 50 per cent. Attacks of fever may occur nightly, otherwise the temperature may be subnormal. The vascular, respiratory, nervous, and urinary systems are usually normal. If, however, the ova affect the lungs, there may be signs of bronchitis, broncho-pneumonia, and fibrosis; and if the brain, those of Jacksonian epilepsy. In children the development is stunted. Death may result directly from the action of the parasite, or be due to some intercurrent disease.

Lanning distinguishes three stages in the disease, viz.:-

Initial Stage.—This lasts three to six weeks, and is characterized by high afternoon temperatures, with slow pulse-rate, evanescent œdemas and urticarias, pains in the abdomen especially in the upper part, diarrhœa or constipation, marked eosinophilia, and often mental depression.

Second Stage.—During this stage the liver and spleen are enlarged with anaemia; there is loss of weight, slight fever at times, and the passage of blood-stained mucus, associated with more or less tenesmus and straining, and either diarrhœa or constipation. The characteristic ova can be found in the motions.

Third Stage.—This may or may not be present, and then only after three to five years, and especially if frequent reinfection takes place. It is characterized by cirrhosis of the liver, which may be enlarged or shrunken, ascites, œdema of the extremities, emaciation, anaemia, weakness, passage of blood and mucus in the motions, and a little fever.

Termination.—Death may occur from exhaustion or some terminal infection.

Varieties. Houghton recognizes the following types of the disease: (*a*) Typical cases, with enlarged liver and spleen, ascites, and blood in the motions; (*b*) cases with only splenic enlargement, and with or without blood in the motions; (*c*) cases with cerebral symptoms and marked eosinophilia, to which may be added—(*d*) urticarial fever, with marked eosinophilia in the early stages; (*e*) cases only showing eosinophilia, often associated with some other concurrent disorder; (*f*) latent cases showing ova in the motions, but no bodily disturbance.

The splenic type, when present without blood in the motions, may give rise to difficulties of diagnosis, which may be cleared up by an examination of the blood and fæces. The eosinophilia in these cases is from 25 to 51 per cent.

The cerebral type is exemplified by partial hemiplegia and slight disturbance of speech after high fever, and associated with an eosinophilia of about 50 per cent. Jacksonian epilepsy has also been reported as due to this parasite.

The urticarial fever is characterized by a remittent type of fever, usually ranging at first from 99° to 100° F. in the morning to 102° to 103° F. in the evening, and after a time from normal to about 100° F., associated with marked urticaria, followed by pale raised blotches on the arms, trunk, and legs, and associated with a marked urticarial rash. The fever lasts some weeks, and very closely resembles malaria at first, because the daily fall of temperature is associated with sweating.

Complications. The infection is generally complicated by the presence of *Trichuris trichiura*, *Ancylostoma duodenale* or *Necator americanus*, and *Ascaris lumbricoides*. Dysentery is a complication which may occur and prove fatal to the patient.

Diagnosis. The characteristic signs are chronic painful enlargement of the liver and spleen, associated with ascites and chronic irregular diarrhœa, and marked eosinophilia (10 to 50 per cent.). A definite diagnosis is to be effected by finding the ova in the fæces. These ova are large (0·1 by 0·07 millimetre), oval, non-operculated, laterally spined (75 per cent.), smooth, and transparent, with a double contour sometimes showing a *Miracidium*, and when kept in water for a short time give rise to a free-swimming ciliated *Miracidium*. These ova are apt to be mistaken for *Ascaris lumbricoides*, or less likely for an *Ancylostoma* ovum. The ova require to be looked for carefully.

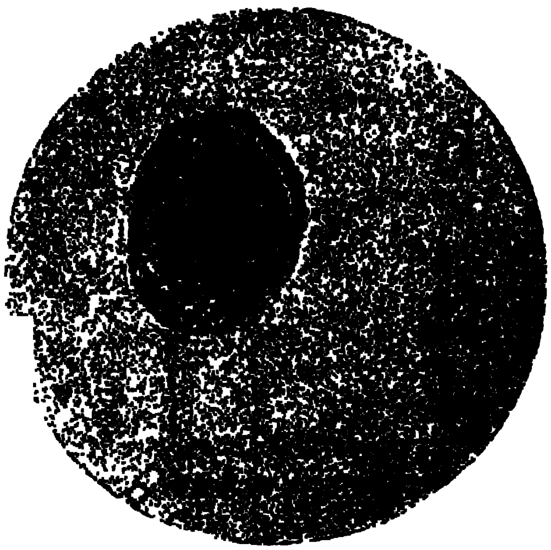

FIG. 712.—EGG OF *Schistosoma japonicum*.

(From a photomicrograph by J. J. Bell.)

Other points which assist in the diagnosis are the greatly exaggerated knee-jerks, the peculiar muddy complexion suggestive of anæmia, the lack of leucocytosis (the counts in uncomplicated cases being about 2,000 to 8,500 per cubic millimetre), and the emaciation without obvious cause.

Prognosis.—The prognosis is very bad, as the parasite directly or indirectly leads to the death of the patient. The mortality is not known, but Katsurada met with between thirty to fifty-four cases every year for five years in the infected area in Japan, and saw three to five deaths per annum, which he considered directly due to the parasite—*i.e.*, a mortality of about 10 per cent.—but he thinks that the indirect mortality would raise the percentage considerably.

Treatment.—The only treatment that can be suggested is to administer salvarsan or tartar emetic.

Prophylaxis.—Avoid contaminated water in drinking and bathing —*i.e.*, use boiled water in infected areas for both purposes. Wading in swamps, lakes, and paddy fields, is very dangerous, and is the method of infection of man.

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CHAPTER LXVI

THE FILARIASES

Synonyms—Definition—Filariasis caused by *Filaria bancrofti* Cobbold, 1877—History—Climatology—Ætiology—Pathology—Clinical description—Filarial lymphangitis—Filarial orchitis and hydrocele—Lymphatic varix—Varicose lymphatic glands—Chylous effusions—Elephantiasis—Rarer affections—Filariasis caused by other Filaridæ—References.

Synonyms.—Filarial disease. *French*, Filariose, Maladies filariennes; *Italian*, Filariasi; *German*, Filaria Krankheit.

Definition.—Filariasis is a term denoting the infection of man or animals by any species of *Filaria*—*e.g.*, *Filaria bancrofti* Cobbold, 1877, and some others.

FILARIASIS CAUSED BY FILARIA BANCROFTI Cobbold, 1877.

The diseases produced in man by *Filaria bancrofti* Cobbold, 1877, include lymphangitis, orchitis, varix in lymphatics and lymphatic glands, chylous and lymphatic extravasations, and elephantiasis.

History.—The appearance of the huge leg of elephantiasis is so striking that it was early noticed by ancient Indian writers, who give descriptions of diseases which clearly refer to elephantiasis of the leg and of the scrotum, and also less clearly to lymph scrotum. Further, they appear to have known that elephantiasis could affect the hands and other parts of the body.

The word 'elephantiasis' was first used by Celsus to indicate leprosy, and in this he was followed by most writers until Galen, who included true elephantiasis under the same term, an error which became firmly established as time passed. In the ninth and tenth centuries Rhazes and Avicenna, and other Arabian physicians, described true elephantiasis of the leg under the term 'da-fil' or 'dau-ool-fil,' or elephantine disease, which, however, only served to make the confusion between the two diseases more complete. In the seventeenth century Leonicenus and Varandaeus pointed out that they were two distinct clinical entities, and in 1709 Clarke described elephantiasis on the Malabar coast of India under the term 'Cochin leg.' In 1712 Kaempfer described endemic hydrocele, under the term 'andrum,' as occurring in India, and being associated with erysipelatous eruptions on the scrotum, which recurred at the time of the new moon. He also described a large foot under the term 'perical,' but his description agrees more with Madura-foot than with elephantiasis, though it is probable that he was confusing both diseases under the same term. In 1750 Hillary, a most careful and skilled observer, gave the first full and accurate account of the evolution of the large leg of elephantiasis, which he clearly differentiates from true leprosy, describing the successive attacks of fever, the lymphangitis and lymphadenitis, and the swelling of the limb, which, gradually becoming permanent and slowly increasing, produces the well-known condition.

He was ably supported in 1784 by Hendy, who, in a subsequent treatise in 1789, gave the first full account we have been able to trace of the development of elephantiasis of the scrotum, which he clearly recognized to be the same disease as that affecting the legs. He describes and figures an elephantiasis of the scrotum 24 inches in height and 6 feet in circumference at its base, and he further notes cases of spontaneous cure by sloughing. In 1809, and again in 1824, Alard wrote most excellent treatises on the elephantiasis of the Arabs.

In 1812 Chapotin was the first to describe hæmatochyluria in Mauritius, and he was followed by Salese in 1832, whose paper aroused so much interest in Brazil, where the disease had for long been well known, that in 1835 a conference on the subject was held in Rio de Janeiro, after which there were many investigations, among which may be mentioned those of Rayer in 1838, Quevenne in 1839, Siguad in 1844, and Mozae-Azema in 1858, the last-named observer reporting it in Réunion. In 1854 Jamsetjee described lymph scrotum. The result of all this work was to produce a consensus of opinion among Brazilian, French, and Indian physicians that hæmatochyluria and elephantiasis were merely different aspects of the same disease, and at the same time the classical researches of Danielssen and Boeck in 1848 on leprosy, and of V. Carter in 1860 on mycetoma, ended the confusion of these two diseases with elephantiasis.

In 1863 Demarquay, in Paris, discovered a *Microfilaria* in the fluid from a hydrocele in a person who had come from Havana, but this discovery passed unnoticed at the time. In 1866 Wucherer, stimulated by the discovery of *Schistosoma hæmatobium* in hæmaturia in Egypt, found a *Microfilaria* in the urine of a case of hæmaturia in Brazil, but at first thought it to be of no importance, but when, after two years of careful work, he regularly found the same small worm in the urine of persons suffering from hæmatochyluria, he published his discovery in 1868, in the same year in which Lewis independently found the same parasite in the urine of a case of chyluria in India. Lewis also found the same small worm in the blood and lymph of persons suffering from elephantiasis of the leg, and concluded that it was the cause of the chyluria and the elephantiasis. In 1876 Winckel found the same small parasite in the fluid from a case of chylous ascites.

In 1876-77 Bancroft discovered adult female worms in a lymphatic abscess in the arm, and in a hydrocele of the cord, and these worms were later described by Cobbold, who gave them the name *Filaria bancrofti*. About the same time Manson found the *Microfilariæ* in the lymph from the enlarged lymphatics of a lymph scrotum and from varicose lymphatic glands, and suspected that the so-called malarial orchitis must be of filarial origin. He also obtained a female worm from a case of elephantiasis of the scrotum, and in 1879 Lewis found pieces of male and female worms; while in 1888 Sibthorpe obtained perfect specimens of a male and female from a lymph scrotum, the former being described by Bourne. Lastly, in 1898, Maitland drew attention to the occurrence of synovitis in cases of filariasis, which he considered could not be looked upon as accidental, and must be held to be of filarial origin, but this view cannot be regarded as proved.

In this way arose the knowledge that the causation of a form of lymphangitis, of lymphatic abscesses, of varices of lymphatics, and of lymph glands, of hæmatochyluria, of chylous extravasations, and of elephantiasis, was the invasion of the body by *Filaria bancrofti* Cobbold, 1877.

In the meanwhile the epoch making discovery of the agency of the mosquito in the dissemination of *Filaria bancrofti* was made by Manson in 1878, as well as the periodicity of the *Microfilariæ*, which only appear in the blood in large numbers at night, and in 1899 he discovered that they retire to the vessels of the lungs during the day. With regard to this periodicity, Bahr has shown that it does not depend upon the human host, but upon the habits of the insect host being nocturnal when the host is *Culex fatigans*, and nocturnal and diurnal when the host is *Stegomyia pseudo-scutellaris*, which is a day-feeding mosquito. Thorpe's view with regard to the diurnal and nocturnal periodicity is that it is caused by the irregular habits of the human hosts, but this latter theory has not been supported by Fülleborn's observations on Samoan natives. Low, Grassi, Noé, and Fülleborn, have supplied the information as to the method by which the *Filaria* escapes from the mosquito and enters man during the act of biting. While, therefore, much has been done to elucidate the nature of the lesions due to the worm, researches are still required with regard to the method by which the worms produce the various pathological phenomena attributed to them, especially elephantiasis, and the rôle of a secondary bacterial infection in the production of the lymphangitis, abscesses, and elephantiasis.

The morbid anatomy has been investigated by but few observers, notably by Mackenzie, Manson, Low, Young, and Bahr.

Climatology.--The fact that ancient Indian writers were acquainted with elephantiasis of the leg and scrotum, while Celsus does not appear to have known the disease, and the further fact, mentioned by both Hillary and Hendy, that elephantiasis was rare in Barbados at the beginning of the eighteenth century, together with Hillary's views that the disease was introduced into that island by negro slaves from Africa, awaken suspicions that the endemic home of filariasis is Asia, and that it has spread from thence to Africa, and from Africa to America. If this gradual dissemination of filariasis is correct, it may explain many features of the epidemiology which are difficult at the present time to comprehend.

Be this as it may, filariasis is now widely distributed throughout the tropics and the subtropics, extending from about 41° N. to about 28° S. in the Eastern Hemisphere, and from about 31° N. to about 23° S. in the Western Hemisphere.

In *Asia* it is known in Arabia, India, Ceylon, Burma, Indo-China, the Philippine Islands, Guam, China, and Japan.

It is known in *Australasia*, especially in Queensland, and in Oceania, especially in Fiji, in Samoa and the Friendly Islands, but is absent in the Sandwich Islands. It is also known in New Guinea.

In *America* it occurs in the Southern United States, in Central America, the West Indies, in Guiana, Venezuela, Brazil, Peru, and Columbia.

In *Africa* it is common on the West Coast, in South Africa, East Africa, Madagascar, Réunion, Mauritius, Morocco, and Egypt and Northern Africa.

In *Europe* it is said to exist near Barcelona and in Turkey.

In these countries its distribution is unequal, being in general more common along sea-coasts and the banks of large rivers, but presenting peculiar circumscribed endemic areas. Thus, Daniels points out that in the Shiré Highlands filariasis and elephantiasis are only found in immigrants, while along the lower Shiré River both are common.

Still more interesting is his observation that at the southern end of Lake Nyassa there was only one case of filariasis met with, and none of elephantiasis, while at the northern extremity both were frequently seen.

Low has also studied the distribution in the West Indies. Here, again, this is very unequal, some of the islands—Barbados, for example—being heavily infected, while in others, Grenada, the infection does not appear to exist.

The distribution must depend upon the presence or absence of mosquitoes capable of disseminating the worm, but this aspect of the epidemiology still requires a considerable amount of research; further, the distribution of the suitable mosquitoes must depend upon many factors concerning which we are quite ignorant. When these conditions are better understood, the climatology will be rendered more explicable.

Two atmospheric conditions—viz., high air-temperature and considerable atmospheric humidity—have long been known to be associated with the prevalence of filariasis and elephantiasis, and the reason of this has recently been explained by Fülleborn's experiments on *Dirofilaria immitis*. This observer found, as the result of most careful experiments, that the *Dirofilaria* developed better in mosquitoes if the air-temperature was high, and in that respect resembled the malarial parasite; and, further, that at high temperatures the *Dirofilariæ* are able to leave the proboscis more easily, and to penetrate the skin more quickly than at a low temperature.

Further, the moisture in the air is of importance, as the *Dirofilaria* passes from the proboscis on to the skin, and either makes its own way through this into the tissues, or enters the aperture of the mosquito's bite after it has withdrawn its stilettes, and, therefore, has to be for some time in contact with the skin, which, if dry, will have a harmful effect upon it, but if moist, will not be injurious to it.

With reference to Fiji, Bahr concludes that it is possible that at one time or another nearly every Fijian is the subject of filariasis, because 27·1 per cent. were found to harbour *Microfilariæ* in their blood, and adult worms could be found in the lymphatics and other tissues, and others (25·4 per cent.) were found to suffer from filarial disease when no *Microfilariæ* could be found in the blood; and, lastly, in patients while still under observation the *Microfilariæ* have disappeared from the blood.

Ætiology.—The causation of the various pathological phenomena mentioned above is *F. bancrofti* Cobbold, 1877 (p. 633), introduced into the body by the bite of a mosquito.

The known carriers of the worm, as given by Theobald, are *Culex fatigans* Wiedemann, 1828; *Mansonia uniformis* Theobald, 1901; *M. pseudotitillans* Theobald; *Pyretophorus costalis* Loew, 1866; *Myzomia rossii* Giles, 1899; *Myzorhynchus nigerrimus* Giles; *M. minutus* Theobald, 1903; *Cellia albimana* Wiedemann, 1821; *Stegomyia pseudo-scutellaris* Theobald, 1910; while the worm is known to be capable of undergoing a part of its development in certain other mosquitoes already mentioned in Chapter XXIV.

The reason of the non-completion of full development in any and every mosquito is not known.

After development in the thoracic muscles of the mosquito the embryo passes into the labium, and when the mosquito bites, it works its way through Dutton's membrane on to the skin, its passage being favoured, according to Fülleborn, by high air-temperatures and moist conditions of the skin. Arrived on the skin, it may work its own way into the body through the skin like an Ancylostoma embryo; or it may enter through the aperture of the mosquito-bite when the stilettes have been removed, for before this takes place it is impossible for it to pass through this aperture, which is completely filled by these appendages.

Its further history and wanderings in the body are quite unknown until the adult condition is reached. The adults (males and females) are generally found lying together, though the females appear to be in preponderant numbers in lymphatic vessels, but they can also be found in the lymphatic glands; while dead and calcified worms have been found not merely in lymphatic glands, but also in the testes, epididymis, spermatic cord, and tunica vaginalis. Here the female produces the thin *Microfilariæ*, which pass through the lymphatic glands and thoracic duct into the blood stream, in which they are found in large numbers at night, retiring in the day-time mostly into the bloodvessels of the lungs.

When taken into the mosquito's stomach they escape from their enclosing egg-shell, and, entering the thoracic muscles, complete the cycle of development.

It is interesting to note that in various parts of the tropics natives believe that elephantiasis and other filarial diseases may be transmitted through sexual intercourse.

The adults lying in the lymphatic vessels may mechanically cause obstruction to the flow of lymph, and thus produce varices, inflammation of vessels and glands, and if the varicose vessels rupture, extravasation of lymph or chyle.

While this ætiological relationship of the worm to the lymphangitis and lymphatic abscesses, to the varices in lymphatics and lymphatic glands, to hæmato-chyluria and chylous extravasations, is admitted by all observers, there are those who doubt this relationship with regard to elephantiasis. These authors base their objections upon the facts that the worm and its larvæ may be absent in well-developed cases, and that the disease can occur in countries in which filariasis is believed not to be present, both of which are quite true, but are capable of explanation. There is an undoubted general relationship between the number of cases of filariasis and of elephantiasis in a district. Where there is no filariasis, elephantiasis is either extremely rare or unknown; where there is abundant filariasis, there are also many cases of elephantiasis.

In investigating this point in a locality care must be taken to exclude immigrant cases of both filariasis and elephantiasis. Thus, Low failed to find either condition in the inhabitants of the forests of British Guiana and in the Wagandas, natives of Uganda, though immigrant cases were met with.

The adult *Filaria* has been found in the tissues removed by operation from a case of elephantiasis of the scrotum; and, further, the condition of elephantiasis is produced as a rule by a series of attacks of lymphangitis, which in every particular resemble undoubted filarial lymphangitis.

It is true that a secondary bacterial infection may possibly assist the development of the disease, for a diplococcus has been found by Dufogeré, which he calls the 'lymphococcus,' and his findings have been confirmed by Foulerton. Le Dantec describes a similar organism, which he calls the 'dermatococcus'; but the main cause of elephantiasis in the tropics is *Filaria bancrofti*, though it is quite possible that, exceptionally, other causes may lead to occlusion of lymphatics and the formation of elephantiasis.

Pathology. -If the parent worms live in positions in which they do not obstruct the flow of the lymph, and if they are not accidentally injured, no pathological effects will be produced on the host: and our observations support Manson's theory that the presence of the worms may produce no ill-effect upon the host, for we know of a case where for years they have produced no symptoms.

But if the parent-worms obstruct the circulation of the lymph mechanically—for example, when three or four come together in an important main lymphatic trunk then the retained lymph is certain by mechanical pressure to damage the tributary channels. Further, if any accidental injury is inflicted upon the female parent-worm, this may cause abortion, and as a result the production of oval eggs instead of elongated embryos (Fig. 268), and these, as will be explained below, are liable to block up the small lymph channels of the skin or of a lymphatic gland. Therefore Low is quite correct in his statement that 'the *Filaria* is not entirely compatible with health,' for very slight causes will produce disease.

In certain districts from 5 to 27 per cent. of the population is infected with filariasis, and therefore if there are many mosquitoes capable of carrying the worm, there ought to be multiple infection of the individual host; and one would also assume that the heavier the infection, the greater the liability to obvious disease. Multiple infection would be more liable to occur in natives than in Europeans. As a matter of fact, heavy infections with the parent-worms have not yet been described, though it must be admitted that but few post-mortem examinations are on record; and, moreover, as Fülleborn has shown, it is at times by no means easy, even with the utmost care, to find the adult worms, though they may be found even in fair numbers after considerable search in those parts of the lymphatic system which appear to be least affected. When the case is one of varicose lymphatics, or lymphatic glands with clear lymph, the obstruction must be looked for below the junction of the lacteals with the receptaculum chyli, but when the fluid is milky, it is obvious that the obstruction must be beyond this point. The cause of the obstruction may be a coiled-up mass of worms—

e.g., Young found six females and one male in such a bundle— and they may be discovered behind a valve or in a dilated sinus. A single female worm may, however, be found lying in a dilated lymphatic, the draining gland being probably blocked by the aborted ova. The irritation caused by the worms may lead to a permanent blocking of a main lymph channel, which will persist even after the irritating worms have died and disappeared, as has been observed by Mackenzie; or, again, the thoracic duct may be found dilated in part of its course, but quite patent throughout, though associated with enormous varicose glands and vessels and a complete absence of worms, which simply means that the parasites having caused the lesions have died and disappeared.

Low and Bahr have shown that the worms lead to great fibrosis in the glands, and that lymphocytes are collected in clusters between the strands of this tissue. This fibrosis is associated with an excessive number of eosinophile cells in the glandular substance.

In chylous extravasations the blocking of the thoracic duct leads to engorgement of the renal, the lumbar, and the pelvic lymphatic channels with lymph, as well as that of engorgement and dilatation of the lacteal vessels themselves.

If the lymphatic vessels of the bladder or other parts of the urinary tract rupture as a consequence of this pressure, the result will be chyluria, and if, as often happens, some bloodvessels also rupture, there will be hæmato-chyluria. Wise states that in chyluria the milky opacity is due to a large amount of proteid, and not to fat, and this observation has been confirmed by Low, who in one case found the lacteals normal, and showed that the milky fluid was lymph proceeding from dilated lymphatics in the kidneys, ureter, and bladder. If the abdominal lymphatics rupture, there will be chylous ascites, if those of the tunica vaginalis, there will be chylocele.

If, on the other hand, the obstruction is posterior to the junction of the lacteals with the receptaculum chyli, then ordinary ascites, hydrocele, and varicose lymphatics of the scrotum (lymph scrotum), of the leg, and varicose groin glands, will result. More rarely the lymphatics of the arm may be affected in the same manner.

The lowered resistance of the tissues engorged with lymph renders them specially liable to inflammation, which may at times go on to abscess-formation, and which, if often repeated, will end in elephantiasis.

Manson believes that elephantiasis arises by a damage to the female worm, causing her to produce immature embryos, which lie coiled up in the egg-shell, instead of stretching it considerably. The immature egg is 50 μ in length by 34 μ in breadth, while the fully-developed *Microfilaria* is 250 to 300 μ in length by 5 to 8 μ in breadth; therefore it is not difficult to imagine that a lymphatic, along which the slim *Microfilaria* passes with ease, might be quite blocked by the immature egg, and that if sufficient channels in the skin or in the lymphatic glands were blocked, lymph stasis would occur, and, as a result, the connective tissue would become inflamed and hypertrophied, which, together with the excess of lymph, would increase the size of the part. Manson bases this theory on his observation of eggs escaping from the ruptured vesicles of a lymph scrotum. Bahr is of the opinion that tropical elephantiasis can best be explained by the blockage of the lymphatic channels of the diseased area by the frequent and long-continued invasion of the adult *Filariæ*. He finds that the *Microfilariæ* may not reach the blood, but die in the gland or organ in which they are lying. He also finds that the periodical discharge of these *Microfilariæ* may be a factor in the production of lymphangitis, orchitis, and funiculitis, and that the parent-worm may die after these inflammatory attacks.

It is believed that the smooth elephantiasis (elephantiasis glabra), in which the skin is smooth, is due to blocking of the channels in the groin glands, and rough elephantiasis (elephantiasis verrucosa), in which the skin is very nodular, is due to blocking of the small skin capillaries, but we are not acquainted with definite proofs of this theory.

The Blood. The blood in filariasis does not exhibit anaemia unless there is hæmato-chyluria or diarrhœa: the number of leucocytes is normal, but there may be leucocytosis during the attacks of fever. The eosinophiles are at times increased.

Morbid Anatomy. The morbid anatomy naturally varies with the variety of the pathological lesion produced.

In lymphangitis the lymphatic vessels will be found enlarged and inflamed, and abscesses of varying size may at times be found containing the dead worms, which are apt to become calcified by the deposition of lamellar plates of calcium carbonate in the interior of the worm. The calcified worms were first described by Wise as small yellow bodies, with the shape and structure of *Filariæ*, which he found in the pelvis of the kidney. Bahr states that at a later stage the calcareous deposit may be gradually absorbed until only minute yellow spicules are left. The calcified (and also the living) worms are surrounded by eosinophile cells in large numbers. Bahr has found filarial abscesses to be of common occurrence amongst the Fijians in the substance of the gastrocnemius, the popliteal space, the groin, and in the quadriceps extensor in the leg, and over the internal condyle, in the axilla, in the latissimus dorsi and serratus magnus muscles in the arm. In these abscesses the dead worm was found associated with *Staphylococcus pyogenes aureus* and *Streptococcus pyogenes*.

With regard to the lymphatic vessel, Bahr is of the opinion that the worm, both during its lifetime as well as after its death, exerts an influence on the vessel wall, leading to proliferation of the endothelium and to an invasion of the vessel wall with fibrous tissue. In this manner the lymphatic becomes thickened, but shows also numerous cyst-like dilatations in which the dead worms may be found.

The fugitive swellings found in filariasis have been proved by

Young to be composed of dilated lymphatic tissue. Inflammatory masses adherent to the skin in various parts of the body have been found to contain the adult worm.

In lymphatic varix or varicose lymphatic glands the obvious lesions may, and generally do, form part of a much larger dilatation of the pelvic and lumbar lymph vessels and glands. The vessels are found enormously dilated with thickened walls, while the glands are riddled with dilated channels. At first the appearance of the gland may not be much altered, and on section it may show the appearance of a sieve riddled with holes, but in more advanced cases all appearance of a lymphatic gland disappears, and it is transformed into a large sac divided by fibrous tissue, septated into numerous compartments.

In chylous extravasations the thoracic duct may or may not be found impervious, but in any case the lacteals, the lumbar, pelvic, pudendal, and crural lymph vessels will be found enormously dilated, and the lumbar lymph glands converted into septated sacs. The site of the ruptured lymphatics is, however, by no means easy to find.

In elephantiasis the lymphatic vessels will be found dilated and thickened, and in early cases a round-celled infiltration may be seen in the connective tissue of the part: but in later cases this has led to a hypertrophy of the connective tissues of the skin and the fasciæ, including those around the muscles, the vessels, and nerves, while all the tissues are sodden with retained lymph. The muscles of the affected regions are found to be in a state of fatty degeneration; the bones may be thickened and covered with osteophytes, or more rarely atrophied, and still more rarely invaded by caseous abscesses.

Microscopically the epidermis may be normal, or thickened with atrophied or elongated papillæ; the sweat glands and hair follicles may or may not be degenerate.

In cutting into the tissue of a region affected with elephantiasis the skin may be noted to be thickened, and below it there will be found dense fibrous trabeculæ, with the spaces filled with yellow, oily, fatty substance, which exudes lymph, while the vessels and nerves will be found much increased in size.

THE CLINICAL DESCRIPTION.

General Remarks.—The clinical description of the various lesions will be arranged under the headings Filarial Fever, Filarial Lymphangitis, Orchitis, Lymphangiectasis, Phlebectasis, Varicose Lymphatic Glands, Chylous Effusions, and Elephantiasis of various parts of the body—*e.g.*, scrotum, leg, etc. and, finally, a few remarks will be made with regard to rarer lesions. As regards *general treatment*, salvarsan, neosalvarsan and galyl have been recommended and tartar emetic might be tried, but no good results have so far been obtained in our experience. *Prevention* is to be based on antimosquito measures as described in the chapter on malaria, p. 1202.

FILARIAL LYMPHANGITIS.

Synonyms.—Elephantoid fever, Liliwa (Fijian term for a rigor), fever and ague (Barbados).

Definition.—Filarial lymphangitis is an inflammation of lymphatic vessels in any part of the body caused by *Filaria bancrofti.*

Remarks.—Attacks of lymphangitis, associated with an erysipelatous eruption of the skin, are extremely common in the tropics, and are often of a filarial nature, and by their repeated recurrences produce elephantiasis.

Symptomatology.—The attack often begins with a shivering fit, and a rise of temperature to any degree from 101 to 104° F., with vomiting and headache. In some cases there is no pain in the affected area, but a careful examination, or the sensation of pain on the part of the patient, will lead to the discovery of a red oedematous area of skin, from which the inflamed lymphatic may be noted extending towards the nearest lymphatic glands, which may or may not be inflamed and painful. Usually the temperature falls quickly in a couple of days to normal, and does not rise again, though it may be several days before the erysipelatous rash disappears and the lymphatics return to normal.

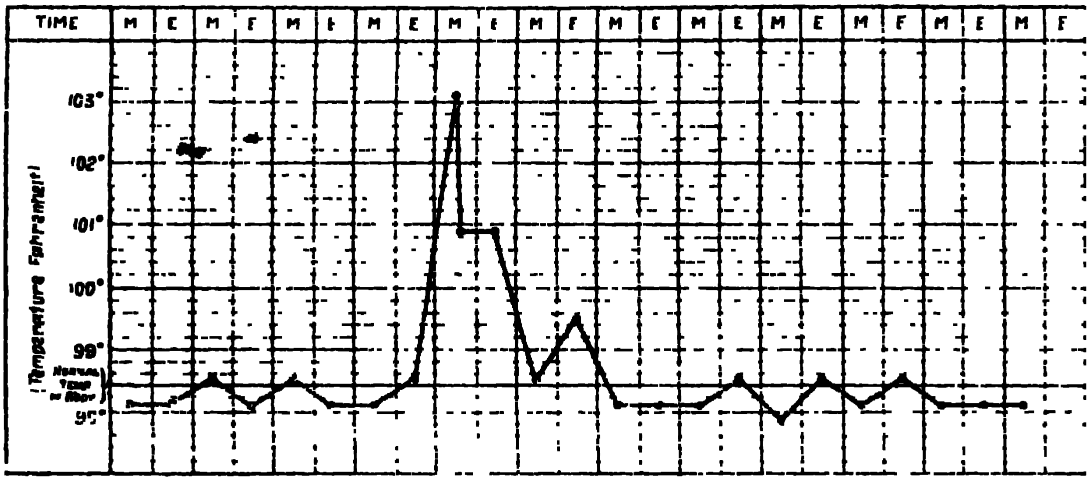

FIG. 713.—TEMPERATURE CHART OF A CASE OF ELEPHANTIASIS OF THE LEG DURING AN ATTACK OF FILARIAL FEVER.

Complications.—Rarely does this condition go on to abscess, which may be caused by a dead filarial worm or a secondary infection.

Sequelæ.—Sometimes, after the acute inflammation has subsided, a lymphatic can be felt as a hardened cord, which, if excised, will be found to contain adult *Filariæ*.

Diagnosis.—The only condition which could reasonably be mistaken for this affection is a caterpillar sting, which closely resembles it in all details. The history of the case will indicate the correct diagnosis.

Treatment.—The treatment consists of rest in bed, a mild purgative, and a little phenacetin and caffeine to relieve the headache, while some of the old authors advise arsenic or tinctura ferri perchloridi, ♏x.-xx., given three times a day, well diluted. Locally, at first lead and opium lotion, and later an ointment, composed of ichthyol and lanoline, gives relief. If an abscess forms, it must be evacuated and treated on ordinary principles.

FILARIAL ORCHITIS AND HYDROCELE.

Symptomatology.—This complaint begins with pains in the testicle, fever, and at times rigor, pains in the back and lower part of the abdomen and groins, and bilious vomiting. The testicle enlarges, and is tender and painful, while an effusion forms in the tunica vaginalis of either lymph or chyle. The lymph thrown out is at first inflammatory, and may coagulate, and is usually absorbed after the fever subsides, but may persist and form a filarial hydrocele. The effusion of chyle is, however, more usually permanent, and forms one of the varieties of chylocele to be mentioned later.

Treatment. The treatment consists of rest in bed and the application of lead and opium lotion, and cool applications, together with fairly vigorous purgation of the bowels.

FILARIAL LYMPHANGIECTASIS.

Synonyms. Lymphatic varix, Lymph scrotum.

Definition. Filarial lymphangiectasis is the dilatation of lymph vessels brought about by obstruction to the flow of lymph, due to the presence of *Filaria bancrofti*.

Remarks. Filarial lymphangiectasis can, of course, take place in any part of the body, but the most common situations are in the scrotum, where it is called 'lymph scrotum,' in the spermatic cord, in the leg, and in the arm.

FIG. 714.—FILARIAL LYMPHANGIECTASIS.

Symptomatology.—In the scrotum the affection begins with an attack of fever, associated with redness, swelling, and pain in that region. When the fever has subsided, the whole scrotum is found swollen and elastic. It may be smooth or rugose, and on inspection the skin shows a number of small clear vesicles, which, if ruptured, discharge either lymph or chyle containing filarial embryos, or, much more rarely, eggs.

If the vesicles are ruptured, the discharge of lymph may be quite considerable in the twenty-four hours, and may produce such marked exhaustion in the patient as to necessitate an operation.

In the spermatic cord the disease begins with pain and swelling in the testicle, cord, and lower part of the abdomen, associated at times with fever. When the acute symptoms have subsided, a swelling like a varicocele, which disappears in the prone position and reappears when standing erect, will be noticed along the cord, but the vessels constituting the swelling will be noted to be softer, less tortuous, and more like a series of pouches than a true varicocele.

FIG. 715.—FILARIAL LYMPHANGIECTASIS.

In lymphangitis of the leg there is the same fever, with swelling of the glands, leaving a soft swelling in the groin, which disappears on lying down and reappears on standing up, and which has no impulse on coughing.

Treatment.—As the local condition is simply part of a much more generalized varicosity of the lymphatic vessels, it is best to treat it symptomatically with antiseptic dusting-powders, such as boracic acid, zinc oxide, and dermatol, etc.

If, however, lymphorrhagia is taking place and the patient is becoming exhausted, it is necessary to remove some of the diseased tissue and to ligate the dilated vessels, but in so doing it is as well to warn the patient that this will not cure the disease, and, indeed, may be followed by elephantiasis or even chyluria.

FILARIAL ABSCESSES.

Manson, Low, Wise, Bahr, and others, have called attention to the frequency of filarial abscesses in various parts of the body. The most important are those found in the thorax and in the retroperitoneal tissues. In the latter situation the symptoms may be those of peritonitis.

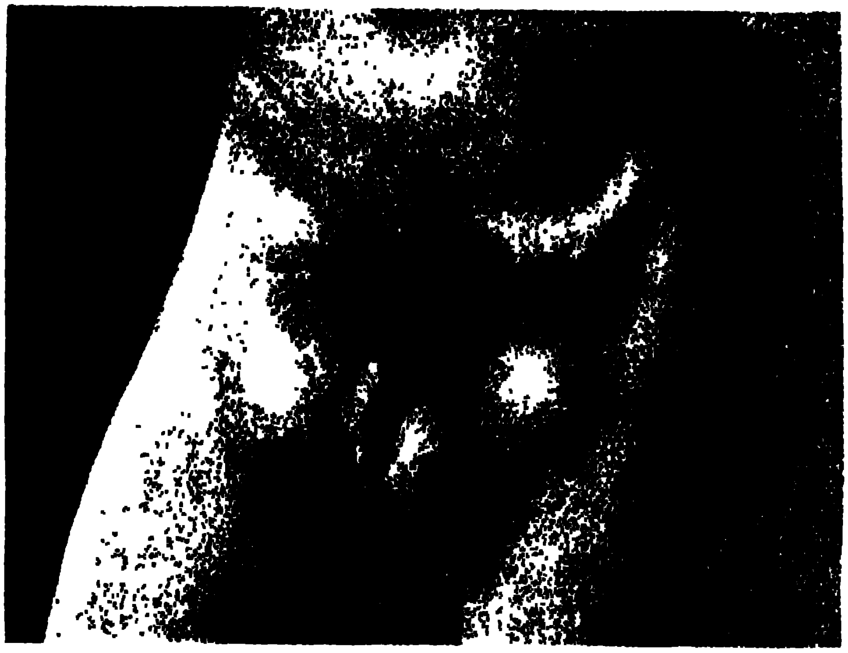

FIG. 716.—FILARIAL PHLEBECTASIS SIMULATING VARICOSE LYMPHATIC GLANDS, AND VARICOCELE: PATIENT IN THE UPRIGHT POSITION.

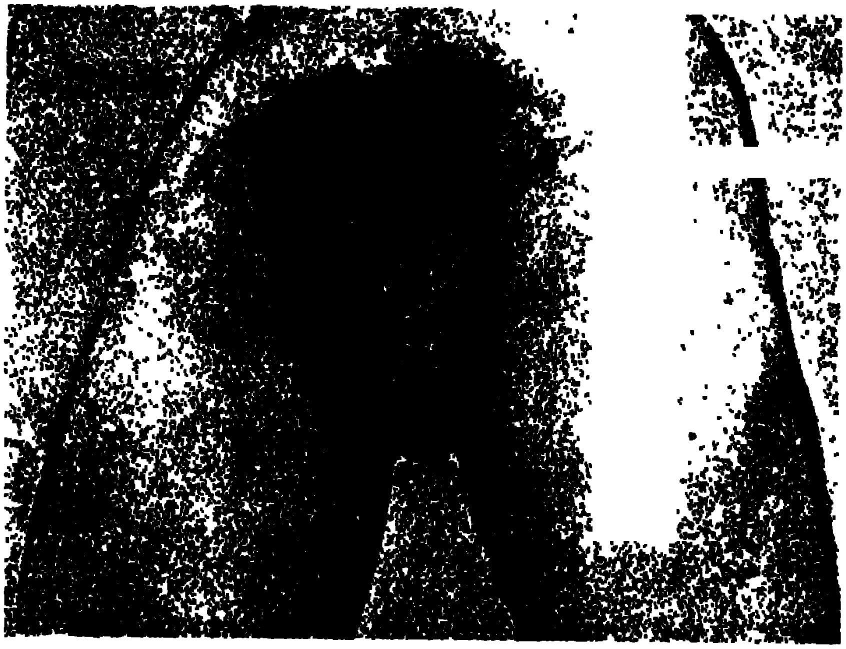

FIG. 717.—FILARIAL PHLEBECTASIS: SAME PATIENT LYING DOWN. (Photograph taken from above. Note the disappearance of the swellings.)

FILARIAL PHLEBECTASIS (FILARIAL VARIX).

At times persons suffering from filariasis exhibit, as observed by us, marked varicose conditions of various veins. Occasionally in association with enlarged superficial veins large masses are to be seen in the axilla, groins, and other regions, which on superficial examination might be taken for enlarged glands, but on palpation it can be ascertained that they are composed of veins, the same sensation being obtained as that experienced when palpating a varicocele. When these masses occur in the groins they disappear when the patient lies down.

VARICOSE LYMPHATIC GLANDS.

Synonyms. Helminthoma elastica, Adenolymphoceles.

Definition. Varicose lymphatic glands are glands enlarged, sometimes to an enormous extent, by dilatation of their lymph paths, brought about by obstruction to the flow of lymph.

Remarks. The glands most commonly found enlarged in patients are the groin glands, less frequently those of the axillæ, while even the parotid lymphatic gland has been recorded to have been affected. In post-mortems, as already noted, the lumbar glands may be found converted into septated sacs.

Symptomatology. The glands enlarge after attacks of fever, and are usually found as soft, elastic swellings, which are easily movable when small, and are covered with normal skin. They are found in the groin, inguinal or femoral regions, and in the axilla. If punctured with a hypodermic needle, lymph or chyle can be obtained at times containing *Microfilariæ*. Usually small, they may assume enormous proportions, reaching below the knee, and seriously impeding locomotion.

Treatment. They may be removed if necessary, but this should not be done without due cause, as they are only part of a more widespread disorder. Radium treatment has been advised by Sir Havelock Charles.

FILARIAL LYMPH AND CHYLOUS EXTRAVASATIONS.

Lymph and chylous extravasations are due to the rupture of dilated lymph or lacteal vessels into the urinary passages, the bowel, the tunica vaginalis, or peritoneum.

They may, therefore, be considered under the headings of Chyluria and Lymphuria, Chylous and Lymphatic Diarrhœa, Chylocele, and Chylous Ascites. Perhaps further investigations will show that Wise and Low are correct, and that in addition to hæmato-chyluria and other chylous conditions there may also be a pure hæmato-lymphuria, lymphatic diarrhœa, lymphocele, and lymphatic ascites.

Chyluria and Lymphuria.

Definition.—Chyluria is the passage of chyle with the urine, and is due to the rupture of dilated chyle-containing lymphatic vessels; when mixed with blood it is known as hæmato-chyluria. When lymph only is passed the term lymphuria, suggested by Low, should be adopted, and if mixed with blood, hæmato-lymphuria.

Pathology. This has been worked out principally by Mackenzie and Manson, and more recently by Low and Wise. The presence of chyle in the urine is due to the rupture of dilated chyle-containing lymphatic vessels. Owing to some obstruction in the thoracic duct with varicosity of lymphatics below the seat of obstruction, the lymphatics in the bladder walls become dilated and rupture, and so the chyle passes into the bladder.

Low has demonstrated that *lymphuria* takes place when the blockage of the lymphatics is below the thoracic duct and receptaculum chyli. Chemically the only difference between lymph and mesenteric lymph or chyle is that the latter contains a much larger amount of fat, which is derived from the lacteals of the intestine. According to Delamere, the fat contained in lymph does not exceed 5·0 per mille, while in chyle it may be as much as 0·5 per mille.

Symptomatology. The onset of the attack is usually abrupt, without marked symptoms, though vague pains may be felt, and at times there may be fever, pains in back, perineum, and thighs. Usually, however, the patient simply asks advice because he is passing milky or bloody urine.

As a rule the urine clears in the course of time, but it is merely an intermission, and the symptoms will in due course recur, and intermissions and attacks will follow each other for years; on the other hand, however, it may be continuous, and not intermittent. The duration of the intermissions may be days, months, or years, while the attacks may be attributed to exertion or emotion. After continuing for some time it may lead to exhaustion, neuralgic pains in different parts of the body, disordered bowels, coated tongue, dry, harsh skin, and a state of cachexia.

If the urine clots in the bladder, there may be severe pain and strangury. The urine generally presents the appearance of milk, but may be pinkish in colour from admixture with blood, and a large portion may clot into a semitransparent gelatinous mass. It is usually passed in fair quantity, and it will be noticed that the morning urine is usually very clear, while that at night is much more milky or red. On standing, in true chyluria, the fat accumulates on the surface, giving rise to a cream-like appearance. Under the microscope, as a rule no fatty globules, however minute, are observed, but white corpuscles, especially lymphocytes, and red corpuscles, and at times *Microfilariæ* and crystals of calcium oxalate, may be seen. The specific gravity is low, varying from 1015 to 1020. The reaction is usually acid. On shaking the urine with ether, the fat can be removed and estimated, when it will be found to vary from 0·8 to 1·8 per cent. After the removal of the fat, the urine can be tested for albumen, which is always present, and which usually persists for some time after the fat has disappeared. The quantity of albumen varies from 0·6 to 0·9 per cent. Albumoses and sugars are absent.

When the urine does not contain any distinct amount of fat one speaks of lymphuria, and if blood is present hæmato-lymphuria. The same patient may have at times attacks of chyluria and hæmatochyluria, and at other times attacks of lymphuria and hæmatolymphuria.

Treatment.—The treatment is purely symptomatic, and consists of rest in bed, lying as much as possible in the prone position, while in some cases methylene blue may be given in 2-grain doses, together with salol, 5 grains, or urotropine in 5-grain cachets. The diet must be bland, non-irritating. Astringent injections into the bladder have been used, and gallic acid, nitrate of silver, acetate of lead, iodide of potassium, and thymol have been administered internally, but have not been found to be efficacious. Indeed, there is no justification for their use. Administration of quinine, combined with exposure to X rays, has been recommended by Musgrave and McDill.

If the urine clots in the bladder, it must be washed out under chloroform by means of an aspirator, and if this is not successful, the bladder may have to be opened and drained.

Chylous and Lymph Diarrhœa.

Diarrhœa with chyle or lymph and blood in the motions has been recorded, but is rare.

Chylocele or Lymphocele.

This may develop gradually, the tunica vaginalis filling up with an opaque fluid, which on tapping is found to be chylous, and may contain *Microfilariæ*. It may, however, be preceded by an attack of fever and orchitis. It is said that the sac is less tense in the morning, and more so at night.

Treatment. A chylocele does not grow to any large size, and only requires occasional tapping.

Chylous Ascites.

Chylous ascites is rarely met with in human beings, though we have seen two cases. It is common in animals as the result of filarial infection.

ELEPHANTIASIS.

Synonyms. Elephant Leg, Cochin Leg, Barbados Leg, Galle Leg, Glandular Disease of Barbados, Elephantiasis Arabum, Da-Fil, Dau-ool-Fil, Pes Febricitans, Perical, Phlegmasia Malabarica, Elephantiasis Indica, Bucnemia Tropica, Morbus Elephas, Spargosis Fibroareolaris, Pachydermia, Hernia Carnosa, Elephantiasis Tuberosa et Scrotalis, Hypersarcosis, Mal de Cayenne, Sarcocèle d'Egypte, Roosbeen von Surinam. Shlipada, Kosharriddki, Barawa (Sinhalese).

Definition.—Elephantiasis is a chronic inflammatory hypertrophy of the fibrous connective tissue of a region of the body induced by lymph stasis, and resulting in a considerable hypertrophy of the skin and subcutaneous tissues.

Varieties.—The most common varieties of elephantiasis are the affection of the leg, scrotum, vulva, arm, and breast, while other regions are much more rarely affected. The different varieties must now be briefly described.

Elephantiasis of the Leg.

Symptomatology.—During attacks of filarial lymphangitis of the leg it is noticed that the limb becomes swollen, and though after the first attack it may resume its normal size, this does not happen after repeated successive attacks, and gradually the limb becomes

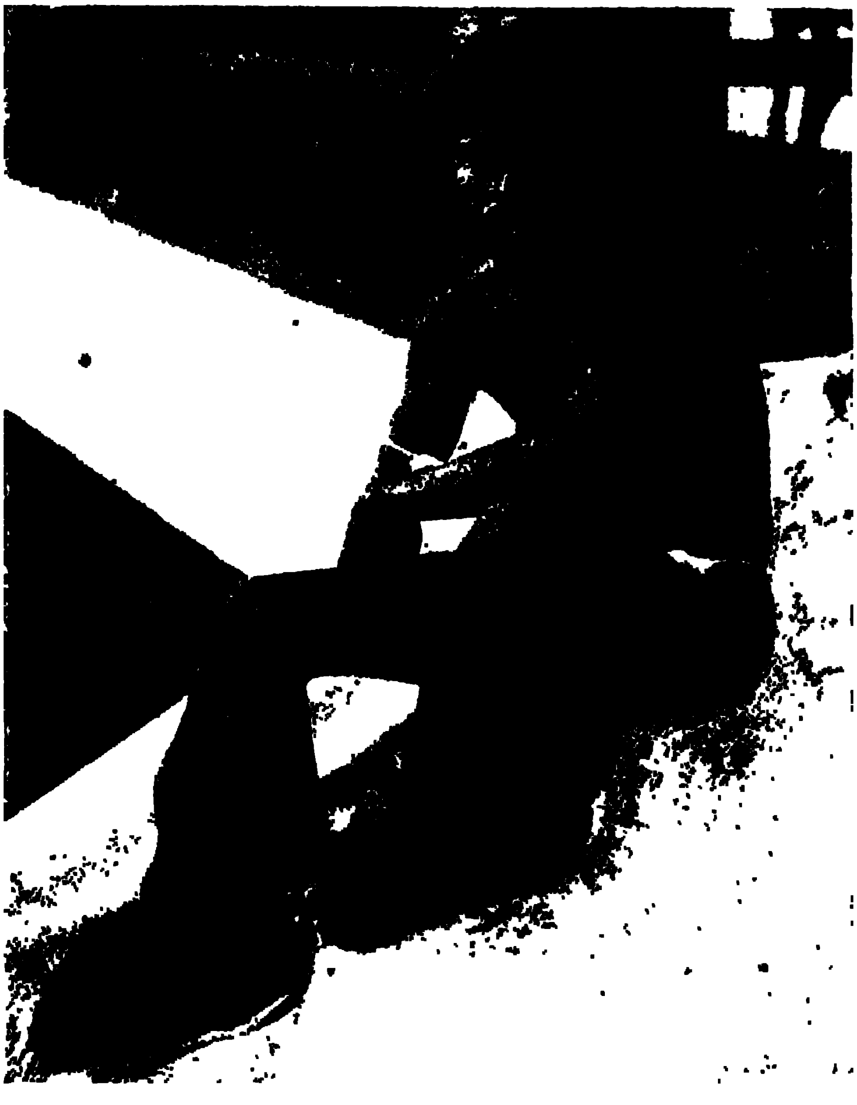

FIG. 718.—ELEPHANTIASIS OF THE LEGS.

more and more swollen, while the natural folds, especially the ankle fold, become much exaggerated by the swelling on either side, so that deep sulci are formed. The dorsum of the foot becomes swollen and puffy, and is separated by the deep ankle sulcus from the swollen lower part of the leg. In these sulci the débris of the cast-off epithelium, together with the excretions of the skin, accumulate and give rise to a foul smelling discharge, and ulcers may form. At first the skin is smooth and soft, forming the smooth variety of the complaint, which may persist, or it may become dark, hard, thick, and rough, being elevated into bosses or warty elevations, forming the verrucose variety. The appendages now atrophy from malnutrition, the hairs may drop off, and the nails become rough and thickened, while the skin perspires less and the sensibility is diminished. Ulcers may now form on almost any part of the foot. The swelling is more commonly met with below the knee, but the whole thigh may become implicated.

ELEPHANTIASIS OF THE LEGS.

If left untreated, the size of the leg gradually increases with repeated attacks of fever, and may reach considerable dimensions.

After some years the attacks of fever may cease altogether, though the condition of the leg usually remains unchanged. In some rare cases elephantiasis may develop without the patient ever having an attack of fever.

Treatment. —A radical method of treatment has yet to be found. Of the various palliative ones the most satisfactory is perhaps that introduced by Castellani, which consists in keeping the patient at complete rest in bed, with thiosinamin or fibrolysin injections and methodical bandaging. The details of the treatment are as follows: The patient is kept in bed and an injection of 2 to 4 c.c. of fibrolysin Merk (which consists of thiosinamin and salicylic acid dissolved in water) is given daily for three to six months, the injections being interrupted for a few days from time to time. The injections may be made in the affected parts, or deeply into the gluteal region, where they cause much less pain. After each injection the whole limb is tightly bandaged with flannel bandages, which are kept in place day and night. In some cases rubber bandages may be used with great advantage, especially in cases of verrucose elephantiasis, because they render the skin much smoother. Unfortunately, many patients cannot stand rubber bandaging. To increase the pressure on the hardest parts pads of inelastic material may be applied before bandaging, and for this purpose small cylindrical

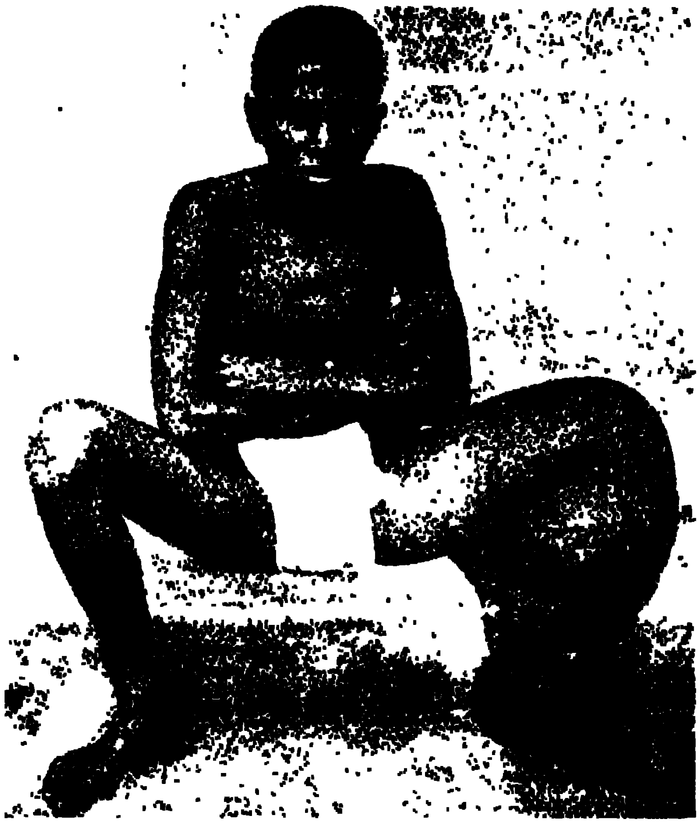

FIG. 720.—ELEPHANTIASIS OF THE LEG: BEFORE TREATMENT.

gauze bags filled with ordinary small lead shot are found especially useful. In some cases massage of the whole limb before bandaging is useful. It is of the utmost importance that the pressure on the whole limb should be well distributed, otherwise the parts on which insufficient pressure has been made will be found to become swollen. It is also useful to keep the affected limb continually elevated by means of pillows, etc. In cases of verrucose elephantiasis in which the skin is covered with numerous horny masses, a spirit lotion of resorcin and salicylic acid (ac. salicylici, resorcin, āā gr. xxx.; sp. rect., ℥iv.) is useful in removing these horny masses.

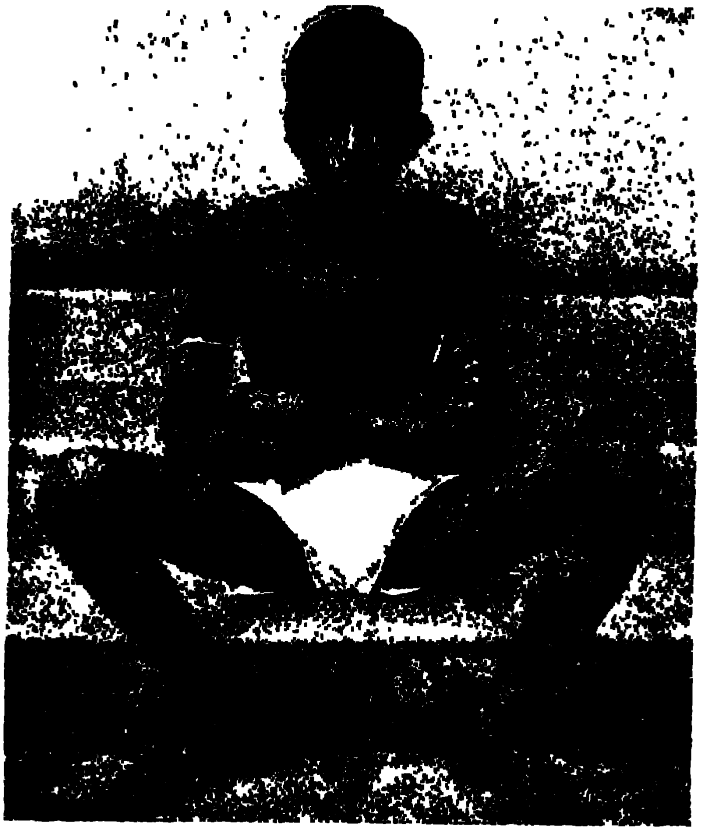

FIG. 721.—THE SAME CASE AS IN FIG. 720: AFTER TREATMENT BY FIBROLYSIN AND BANDAGING, AND WITHOUT ANY OPERATIVE MEASURES.

In successful cases after three to six months of this treatment the affected parts are of much smaller size, the skin is smoother, more elastic, and can be pinched into folds. Long elliptical strips of the redundant skin and subcutaneous tissue may then be removed, the margins of the wound being stitched together. This would not be practicable before the medical treatment, as the skin being enormously thickened and inelastic, the coaptation of the opposed surfaces could not be obtained.

In our experience this treatment has generally only a slight and temporary effect in recent cases when the disease is in the acute stage with frequent attacks of filarial fever. On the other hand, the treatment gives much better and more lasting results in old-standing cases, especially in those of the verrucose type, characterized by the enormous new formation of fibrous tissue and absence of fever. After treatment the patient should wear puttees or elastic stockings, and the rubber bandage should be applied from time to time.

Handley has treated cases by first preparing a vaccine from the diplococcus which he found in the blood, and administering this until the blood and lymph become sterile, and then performing his operation of 'lymphangioplasty,' by silk introduced by means of long probes, which are pushed along the subcutaneous tissues, through small incisions, until a path is made from the affected region to one with a normal lymph circulation. In the cases so far reported there was marked improvement at first after operation, but this did not last long. Madden and Ferguson report unfavourably on lymphangioplasty as a treatment for elephantiasis of the legs, as they find the temporary improvement not maintained, because the reactive changes in the tissues immediately around the thread eventually obliterate the new vessels. Sistrunk reports favourably on the Kondoléon Operation, the aim of which is to establish by a wide excision of the aponeurosis, a communication between the superficial and deep lymphatic channels.

Other methods of treatment consist in bandaging, massage, tapping with Southey tubes, and even amputation, but none of these are satisfactory.

Elephantiasis of the Scrotum.

The disease may begin as a lymph scrotum, or with recurring erysipelatous attacks, with a red inflammatory blush on the skin, and fever. After each attack the scrotum is larger than it was before, and it goes on growing, if left alone, until it may reach the weight of 224 pounds, as mentioned by Chevers, which is probably the largest ever described. When well developed it forms a triangular-shaped mass hanging down between the legs, with the base downwards, and the apex upwards towards the pubes. On its anterior and upper aspect there is an aperture which leads into a canal, formed by the inverted prepuce, at the bottom of which is the glans penis. The penis itself is buried in the tumour. The testicles are situated at the upper and back part of the tumour, and are usually surrounded by hydroceles.

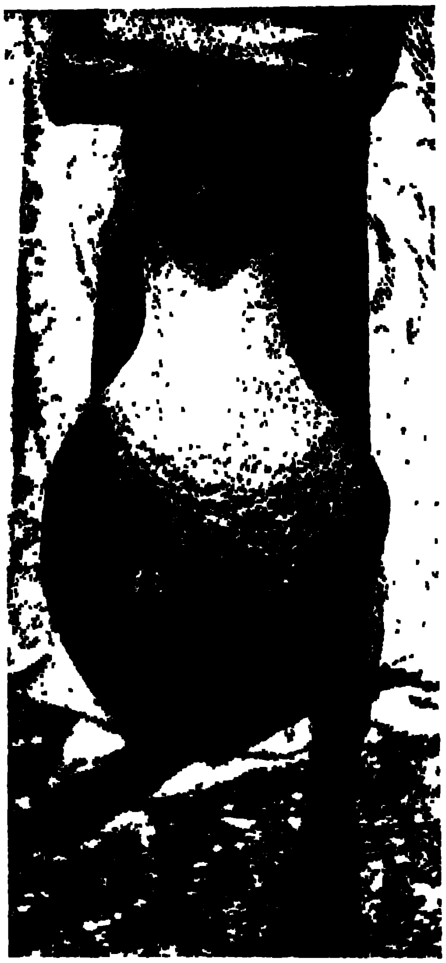

Fig. 722.—Elephantiasis the Scrotum.

If large, the base of the tumour is frequently ulcerated.

Treatment.—The treatment is removal, which is a very easy operation, and very successful, following either Manson's or Charles's method. Manson says that the mortality need not exceed 5 per cent.

The most important feature of the whole operation is to have the skin perfectly clean and aseptic, and to carefully choose the parts of the skin which are to be used as flaps.

An elastic tourniquet in a figure of eight is applied round the pelvis and the neck of the tumour. The skin flaps are now marked out and deepened, the vessels being carefully ligatured as they are exposed.

The testicles are then dissected by perpendicular cuts, and the penis is set free by dissection, after cutting down the canal already mentioned as formed by the prepuce. This is best done with a pair of scissors.

The general mass of elephantoid tissue is now cut away, gradually ligaturing the vessels as the cutting process goes on, this preventing any of the vessels being passed over. The tourniquet is now loosened, and any bleeding spot secured.

If there are hydroceles present, these are opened, and the sac turned inside out, and after any redundancy has been removed, it is stitched around the testicle in the inverted condition. The flaps are now brought together and stitched over the testes, a drain of some description being introduced at the lower portion of the wound if this is considered to be necessary. Skin flaps should, if possible, be made for the penis: failing this, the raw area must be covered with protective, and allowed to granulate. The whole wound must now be antiseptically dressed, and usually heals without difficulty.

Sir Havelock Charles' Operative Method.—After the usual preparation an incision is made in the median line from near the pubis to the preputial mouth deepening it to the dorsum of the penis. Enucleation of the organ is performed from the suspensory ligament to its free extremity. There the glans is still separated from the finger by the lining membrane of the prepuce. The head of the penis is pulled up and this cap of mucous membrane is cut through in front of the glans, which is easily palpable through it. The organ is now free, with its head, covered with a sort of cap, which is next slit up, and the parts thoroughly cleaned. Now the mass is pulled to the patient's right, exposing the left side of the neck of the tumour. Cut from above, near external abdominal ring, curving towards the median line in front of the anus. Deepen this incision gradually with finger and scalpel to near the bulb, avoiding hurting it. The trunks of the vessels can be seized with pressure-forceps before section or after cutting. The same procedure is repeated on the right side of the neck of the tumour. The two incisions will meet in front of the anus, all the main vessels will be seized and divided, and the bulb almost cleared on both sides.

Then the testicles are enucleated, and after wrapping them, as well as the cords, in gauze, they are placed on the pubis. The flaps are now made, practice determining the amount of covering necessary. Place the right testicle under the skin flap on the thigh. Repeat the same with the left testicle and draw the flaps to the median line. A few temporary stitches to keep them in position, whilst a continuous suture run quickly up holds them firmly. Lastly flaps are stitched to the body of the penis.

After the operation careful dressing, well and equally applied, is of great practical importance.

Elephantiasis of the Vulva.

This arises in the same manner as elephantiasis of the scrotum, and may affect the labia majora or the clitoris. It is, however, very rare. The tumour, according to Manson, may weigh 8 to 10 pounds, or more. The treatment is removal.

Elephantiasis of the Breast.

Elephantiasis of the breast is very rare, but does occur, and the enlarged breast may reach to the pubes or the knee. It may affect one or both breasts. The treatment is removal.

Elephantiasis of the Arm.

This is rare, but may arise in the same manner as in the leg. One arm or both arms may be affected. Bahr reports that the natives of Fiji and probably of other South Pacific Islands are, in comparison with natives of other regions, peculiarly liable to this form of elephantiasis.

Elephantiasis of the Scalp.

Rarely the whole scalp is enormously thickened, and presents deep furrows.

Circumscribed Elephantiasis.

Large pendulous tumours of filarial origin, one to several, may be found. These are commonest in the upper part of the thigh, just below the groin.

RARER AFFECTIONS.

Lewis has recorded a case of filariasis in which chyle containing *Microfilariæ* was discharged from both conjunctivæ, while Maitland has described cases of acute synovitis of the knee associated with filariasis as being of too frequent occurrence to be looked upon as merely coincidences.

FILARIASIS CAUSED BY OTHER FILARIIDÆ.

The lesions produced by *Dracunculus medinensis* (Linnæus, 1758), *Loa loa* (Guyot, 1778), *Onchocerca volvulus* (Leuckart, 1893), and other filarial worms, are described in Chapters LXXXVII., p. 1964, and LXXXVIII., p. 1968, while the zoological account of these worms can be found in Chapter XXVI., p. 621. It will be remembered that *Filaria immitis* Leidy, 1856, found in the dog, does not occur in man, the supposed case being wrongly quoted.

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CHAPTER LXVII

THE MYIASES AND ALLIED CONDITIONS

The Myiases: Rhinal; Aural; Ocular; Urinary; Vaginal; Oro-gastro-intestinal; Dermal—Allied conditions—References.

THE MYIASES.

Definition.—The myiases are the invasions of any part of the body of man or animals by dipterous larvæ.

Nomenclature.—In 1815 Kirby and Spence suggested the name 'scholechiasis' for the infestations of man and animals by insects and their larvæ. In 1840 Hope proposed a series of terms applying to various groups of insects, some of which have come into general use, and all of which are employed in this chapter. Thus he names the invasion of dipterous larvæ 'myiasis,' while that due to the larvæ of lepidoptera he calls 'scolechiasis,' and that brought about by beetles 'canthariasis.' In the present chapter we utilize all these old terms and keep the names 'diplopodiasis' and 'chilopodiasis,' which we have already used in previous editions, while we increase the number by turning one of Hope's terms into 'dermapteriasis.' Some of these old terms may not appear very suitable, but they are the first to be suggested.

Historical.—The history of the myiases may be divided into 'ancient knowledge' and 'modern knowledge.'

Ancient Knowledge.—As the disease is much more frequently found in animals than in man, it is not surprising to find that it was first recorded in them. According to Sambon, it was well known in animals to the Babylonians, and to the Ancient Egyptians, Greeks, and Romans. According to the same authority, it was recognized in man even in the Middle Ages. In the tenth century there appeared a book entitled 'The Leech Book' of Bald, or *Medicinale Anglicum*, which described the 'ana-worm' as growing in man and eating through to the outside and shedding itself out of the hole so made. Sambon says this may well have been the larva of *Hypoderma bovis*. In the eleventh and twelfth centuries the Arabian physicians mention a malady called 'bovine disease,' which may have been an infestation with the larva of the same fly. In the sixteenth century Ambrose Paré gave an account of several infestations by larvæ, and illustrated the paragraphs with fanciful drawings of maggots.

In 1589 Father Pedro Simon wrote an account of the occurrence of the fly which we now call *Dermatobia hominis*, as seen along the banks of the Rio Magdalena and in the low plains to the east of the Andes. This appears to be the first reference to the subject as seen in the tropics.

These observations were extended in 1653 by Father Bernabé

Cobo, who states that in each wound caused by the common mosquito there grows a *spine-covered worm* the size of a haricot bean or larger.

About this time Fernelius described some form of nasal infestation—perhaps a myiasis—as occurring in soldiers.

In 1687 Leuwenhoek, in Europe, mentions two cases, one of dermal myiasis in the leg of a woman who made a good recovery, and another in the mouth of a second woman, who died. The larvæ are thought by Hope to belong to the Muscidæ.

Modern Knowledge.—With the appearance of the work of Antonio Vallisneri in the early years of the eighteenth century, a much better conception of these infestations of animals and man became possible, and from this time onwards the knowledge of the subject increased and improved. In 1745 there appeared a work entitled 'Relation abrégée d'un voyage fait dans l'intérieur de l'Amerique Méridionale,' by De la Condamine, where, on p. 170, he mentions the 'ver macaque'—*i.e.*, the larva of *Dermatobia hominis* (Linnæus junior), and says that it takes its birth in the wounds made by a kind of mosquito, but from whence its egg comes is unknown. This observation has since been fully confirmed by recent research. In 1757 Arture drew attention to the occurrence of *Dermatobia hominis* in Cayenne, and in 1781 Linnæus junior did the same as regards Peru in a letter addressed to Pallas, in which he gave the fly its present name. Gmelin subsequently published this letter.

Somewhere about this time Turner described two cases of urinary myiasis in England.

In 1770 Wohlfart published an account of rhinal myiasis in his work entitled 'De Vermibus per nares excretis.'

In 1809 Azara gave a history of his journey in 1781-1801 into Paraguay, and wrote an account of a rhinal myiasis, most probably due to the larvæ of the fly we now call *Chrysomyia macellaria.*

About the same time Lemprière described the same condition in Jamaica, where it caused the death of a woman, and Sells gave an account of probably the same larva causing infestations of the eyes, ears, nose, and mouth in the same islands. Some of Sells's cases ended in recovery and others in death. Also about the same time (1806) comes the case of the soldier believed to be infested with *Œstrus hominis* Curtis in the skin near the scapula in Surinam.

In 1817 Schock studied gastro-intestinal myiasis.

In 1830 a sailor in Demerara is noted to be suffering from myiasis in the arm. This was thought to be caused by a species of Œstrus. In 1832 Howship recorded *Œstrus hominis* in the scrotum of a carpenter in Colombia; in 1835 Guyon mentioned a dermal myiasis in a negro in Martinique; in 1837 Hope described *Dermatobia hominis* in the head of a man, and called it *Œstrus guildingii*, after L. Guilding of Trinidad, who found the case.

In 1840 there appeared the classical and much neglected work on the whole subject by Hope, in which not merely are the older accounts gathered together, but also clear definitions of the various conditions are provided.

From this time onwards the observations on myiasis increase in number—*e.g.*, Duncan in 1854, while in 1856 Lahory described 'peenash,' an East Indian name for an infection due to the larvæ of sarcophaga, while in 1879 Portschinsky again drew attention to gastro-intestinal myiasis. From 1890 to 1896 there appeared a series of classical works by R. Blanchard on myiasis in general. From 1895 to the present time Austen has contributed many valuable articles dealing with these infestations. In 1903 Ward gave an excellent and well-illustrated account of the larva of *Dermatobia hominis*, Kayser in 1905 of ocular myiasis, Henneberg in 1903 and Vesescu in 1906 of aural myiasis, the Sergents in 1907 of thim'ni, and in 1908 Austen and Smith gave accounts of infestation with *Cordylobia anthropophaga*. In 1913 Rodhain, Pons, and others, studied the method of infection by this maggot. Finally, in 1915, Sambon gave an interesting account of *Dermatobia hominis* and its larva.

The above history is sufficient to indicate the large amount of scattered literature in existence dealing with the subject of myiasis in one or more of its phases, and of which Peiper's book, published in 1900, gives a summary.

Ætiology.—At the present moment too little is known as to the characters of the larvæ of the diptera to permit their recognition, unless belonging to a well-known species, and it is obviously incorrect to assume that larvæ are those of a given fly. It is therefore necessary for the medical observer to:—

1. Preserve specimens of the larvæ, as little damaged as possible, in 4 per cent. formalin, and held in position in the tube by means of fine tissue-paper.
2. Rear the larvæ or pupæ and so obtain the imago, which should be fed for a day or so before being killed, and should then be carefully mounted and preserved. Mr. Austen has asked that some of the larvæ should be placed at once on the top of a pot of fairly dry earth, which is then covered with muslin. After the flies have appeared they should be allowed to remain undisturbed for about twenty-four hours in order that they may dry themselves, and in order that they may develop their specific colours, after which they may be killed with chloroform, screwed up in cigarette-paper, packed in small metal boxes, and forwarded to England for identification.
3. Label all the specimens, especially noting the part of the body infected, the locality of infection, and the time of the year.
4. Send the complete collection to the British Museum, Natural History Section, Cromwell Road, London, S.W.

If this is done systematically it will be possible to obtain a correct diagnosis as to the fly causing the myiasis.

The lists of flies known to cause the various forms of myiasis will be given under the different diseases, but it may be noted that the principal families concerned are:—

1. *Muscidæ* (Subfamily: Muscinæ).—Genera: Musca, Calliphora, Chrysomyia, Cordylobia, and Lucilia.

2. *Sarcophagidæ.*—Genera: Sarcophaga, Sarcophila, and Cynomyia.

3. *Anthomyidæ.*—Genus: Fannia.

4. *Œstridæ.*—Genera: Hypoderma, Gastrophilus, Œstrus (Cephalomyia), Œstromyia, Spilogaster. For zoological details on flies see Chapter XXXIII., p. 814.

Less important families are:—*Tachinidæ, Micropezidæ, Syrphidæ, Phoridæ, Therevidæ, Sepsidæ,* and *Drosophilidæ.*

The larvæ appear to be attracted by fæcal or urinary substances, and also by any purulent or putrefactive discharges.

Pathology.—The changes produced in the body by these larvæ appear to depend upon the question of food. In such positions as the alimentary tract they appear to do little harm, probably because there is plenty of food available without hurting the tissues of the host; on the other hand, in the nose, ear, and eye they may cause much destruction of tissue, firstly by eating into the tissues, secondly by the microbic infections which follow in their track, and in this way they may cause the death of the host.

Symptomatology.—As may be expected from the last paragraph, the symptoms of the victim may vary from nil, local signs of destruction of tissue, with inflammation and pus formation, to signs of general septicæmia.

Diagnosis.—This is usually easy, and depends upon the discovery of the larvæ, which, indeed, are usually sufficiently obvious to the patient and practitioner alike.

Treatment.—When the larvæ live in passages such as the nose or ear it is usual to expel them by douches of chloroform water; when in the alimentary canal, by anthelmintic treatment: when in the skin, by the knife and forceps, or simply by the latter. The associated inflammation as well as the conditions causing the original stinking discharge which attracted the flies require treatment, otherwise the patient will again be in danger of infection.

Prophylaxis.—Any person suffering from a purulent or odoriferous discharge in any part of the body should be especially careful to avoid myiasis by sleeping under mosquito curtains until this disease is cured. Other people should be careful not to sleep in the open without some protection, especially in the daytime, and in certain cases—as, for example, *Dermatobia cyaniventris*—to use mosquito curtains.

Varieties.—The various forms of myiasis may be classified as follows:—

A. *Internal or Cavity Myiases* :—

I. Rhinal myiasis.
II. Aural myiasis.
III. Ocular myiasis.
IV. Urinary myiasis.
V. Vaginal myiasis.
VI. Gastro-intestinal myiasis.

B. ***External or Dermal Myiases*** :—

VII. Traumatic dermal myiasis.
VIII. Subcutaneous myiasis.

With regard to the ocular myiases, they may be a true cavity myiases if the larva lives in the lachrymal sac, but they may resemble a cutaneous myiasis if the larva penetrates into the tissues under the conjunctiva, when, indeed, it may destroy the eye.

THE INTERNAL OR CAVITY MYIASES.

RHINAL MYIASIS.

For purposes of description this may be divided into the American rhinal myiasis, the African rhinal myiases, the Asian rhinal myiases, and the European nasal myiases.

American Rhinal Myiasis.

BICHEIRO.

Definition.—Bicheiro is a rhinal myiasis found in Tropical America, and caused by the larvæ of *Chrysomyia macellaria* (Fabricius, 1794) and allied species.

Climatology.—The causal fly extends really from Canada to Patagonia, but is so much more common in the tropical regions as to justify the definition. In Canada it is diminished in numbers by the cold of the winters. In the Southern United States it is met with principally in the months of July to October.

Ætiology.—*Chrysomyia macellaria* (p. 847) usually deposits its eggs in some wound in cattle—*e.g.*, in the wounds after castration, spaying, branding, dehorning, in barbed-wire wounds, and where ticks have been burst or in the vulva, especially if there is a retained placenta, or in the navel or mouth of young calves. More rarely they lay eggs in the wounds of horses and mules produced by barbed wire, in the sheaths of horses, the vaginæ of mares, and the navels of colts. Hogs are also liable to be infested, but sheep are rarely attacked unless they have been worried by dogs.

In place of these more natural hosts the fly may at times attack man, probably being attracted by the odour of what to the human being is an offensive breath, or by an ozæna, or even a chronic catarrh. The fly then passes into one nostril, and if it is expelled dashes into the other nostril, and quickly deposits its eggs, sometimes in large numbers.

In Trinidad, Lawrence reports that the disease may be caused by *Chrysomyia viridula* Robineau-Desvoidy.

Pathology.—The eggs deposited in the manner just described become larvæ in the course of a couple of days. The larvæ proceed to feed upon the tissues of the nose and to burrow deeply into this mucous membrane, down to and even through the bone. The feeding excites a violent reaction on the part of the body, which can be exemplified by the fever, the discharge, the pains, etc.

Morbid Anatomy.—The morbid anatomy includes the destruction of the nose, pharynx, hard and soft palates, larynx, etc. Fistulous channels may be seen packed with larvæ and extending in all directions.

Symptomatology.—Some couple of days after a person suffering from a chronic catarrh, foul breath, or ozæna, has slept in the open, or has been attacked by a fly when riding or driving—*i.e.*, when the hands are engaged—signs of a severe catarrh appear, accompanied with inordinate sneezing and severe pain over the root of the nose or the frontal bone. Quickly the nose becomes swollen, and later the face also may swell, while examination of the nose may show the presence of the larvæ. Left untreated, the patient rapidly becomes worse, and pus and blood are discharged from the nose, from which an offensive odour issues. Cough appears as well as fever, and often some delirium. If the patient lives long enough, the septum of the nose may fall in, the soft and hard palates may be pierced, the wall of the pharynx may be eaten away, exposing the vertebræ, and even the hyoid bone may be destroyed. By this time, however, the course of the disease will have become quite evident by the larvæ dropping out of the nose, and if the patient continues to live all the larvæ may come away naturally.

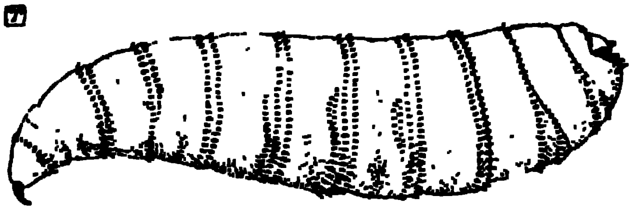

FIG —*Chrysomyia macellaria*: LARVA. (×4.) (After Blanchard.)

Diagnosis.—Any case with the history of a fly having darted into the nose should be assumed to be a case of nasal myiasis until proved by careful nasal examination not to be so. The onset of peculiar sensations at the root of the nose and along the orbital processes, together with the signs of an aggravated nasal catarrh occurring in the endemic region especially in the months of July to October, when the fly abounds in the Southern United States, makes the diagnosis probable, and this becomes a certainty on finding a larva by examination or douching. The onset of the severe symptoms will clear the diagnosis if not evident at an earlier stage.

Prognosis.—The prognosis is always serious, as it is difficult to be sure that all the larvæ have been removed.

Treatment.—The best treatment is to douche out the nose with chloroform water or a solution of chloroform in sweet milk (10 to 20 per cent.), and to follow this with douches of mild antiseptics.

Calomel may be insufflated after douching. It may be necessary to open the frontal or other sinuses, and to irrigate the passages.

Prophylaxis.—The prophylaxis consists in the avoidance of sleeping in the open air except under a mosquito curtain, and in the prompt treatment of any case in which a fly has been known to enter the nose.

The African Rhinal Myiasis.

THIM'NI.

Synonym.—Tamné (Ahaggar Mountains).

Definition.—Thim'ni is a facial myiasis—that is to say, an ocular, rhinal, and oral myiasis—found in certain parts of Algeria and the Ahaggar Mountains of Central Sahara, where the human population is relatively great and the numbers of sheep relatively small. It is caused by the larvæ of *Œstrus* (*Cephalomyia*) *ovis* Linnæus, 1761.

Historical.—In 1881 Kirschmann in Russia reported a case of myiasis due to *Œstrus ovis*, but was disbelieved. In 1907 the Sergents drew attention to the disease thim'ni, and in 1913 to tamné.

Climatology.—It occurs in Algeria, but not everywhere, being confined to certain mountainous regions where the ovine population is relatively little numerous as compared with the human population, and the fly is compelled to find new abodes for its larvæ. These regions are, La Grande Kabylie, La Petite Kabylie, and Le Dahra Oriental. It also occurs in the Ahaggar Mountains of the Central Sahara.

Ætiology.—*Œstrus ovis* (pp. 826, 827) should lay its eggs in the nasal cavities of sheep, and is only driven by force of circumstances to occasionally attack man. It only infests the shepherds and their dogs, being, it is thought, attracted by the cheese which both eat. It appears in the hottest part of the day in the warm weather, and, flying swiftly, deposits its egg, while still on the wing, into the nose, on to the conjunctiva or lips. The larva enters these cavities and causes much pain and inflammation.

Symptomatology.—In the nose it causes severe pain and inflammatory swelling of the whole organ. Frontal headache is intense, sleep is impossible, while a serous discharge runs away from the nose. In the eye vision is impossible, the eyelids and conjunctivæ swell, and little worms are seen on their surface. In the mouth there is much inflammation of the throat, which renders swallowing a difficult proceeding.

The duration is from three to ten days, being longest in the nose.

Prognosis.—This is quite good, as all cases recover.

Treatment.—The essential treatment is tobacco, as smoke or as injections or washes, but in the eye gentle removal is all that is required.

OTHER AFRICAN RHINAL MYIASES.

In addition to thim'ni, rhinal myiasis in Africa is known to be due to:—*Lucilia hominivorax* (*vide* Bouchet at Barika in 1895);

Sarcophaga nura Rudolphi, by Mouchet at Katanga; *Pycnosoma putorum* Wiedemann, 1830, in Abyssinia, Belgian Congo, and Lorenzo Marques. The condition has been reproduced experimentally in animals by Wellman, in 1906, with *S. regularis* Wiedemann in a goat.

Asian Rhinal Myiases.

PEENASH.

Definition.—Peenash is a word which may be used for the Indian rhinal myiases caused by the larvæ of species of *Pycnosoma* Brauer and von Bergenstamm, and by larvæ of species of *Sarcophaga* Meigen, especially by those of *Sarcophaga carnaria* Linnæus, 1758.

Climatology.—The disease is spread throughout India and Assam.

Symptomatology.—As far as is known, the symptoms resemble those produced by other forms of rhinal myiasis.

Treatment.—This is the same as for other forms (*vide supra*).

European Rhinal Myiases.

These are known to be caused by *Piophila casei* and by species of *Sarcophaga* Meigen, 1826, while *Calliphora limea* is also said to be causal.

AURAL MYIASIS.

Definition.—Aural myiasis is the invasion of the external auditory meatus, the middle ear, and associated cavities, by the larvæ of certain dipterous flies, especially those of the Muscidæ and Sarcophagidæ.

Historical.—Aural myiases have been recorded by Taschenberg in 1870, Blake in 1872, Johnson in 1892, and Austen in 1912, but the most complete study is that by Francaviglia in 1914.

Ætiology.—The following larvæ have been noted as causal agents:—

Muscidæ (Subfamily: Muscinæ):—
- *Musca domestica* Linnæus.
- *Musca vomitoria* Linnæus, 1758.
- *Calliphora erythrocephala* Meigen.
- *Chrysomyia macellaria* Fabricius, 1794.
- *Lucilia cæsar* Linnæus.
- *Lucilia nobilis* Meigen.

Sarcophagidæ :—
- *Sarcophaga carnaria* Linnæus, 1758; synonym, *S. carnosa* L., 1758.
- *Sarcophaga magnifica* Schiner, 1862; synonyms, *S. wohlfarti* Portschinsky, 1875, *S. ruralis* Meigen, *S. meigeni* Portschinsky.

Anthomyidæ :—
Fannia scalaris Meigen.
Fannia canicularis Linnæus.
Fannia incisurata Zett.
Hydrotæa meteorica Linnæus.

Syrphidæ :—
Syrphus, sp.??

Œstridæ :—
Œstrus ovis Linnæus, 1761.

Symptomatology.—If lodged in the external auditory meatus, they may simply cause deafness and ringing in the ears, but if eating into the middle ear they may give rise to a discharge of blood and pus.

Treatment.—It is usual to drop into the ear warm olive or carbolic oil, and then to syringe out the larvæ by means of boric lotion. If the larvæ are outside the tympanum, inject a few drops of chloroform dissolved in water.

Prophylaxis.—Some protection such as wool is necessary when suffering from an aural discharge.

OCULAR MYIASIS.

Definition.—Ocular myiasis is the invasion of the spaces under the eyelids, the lachrymal sac, the subconjunctival tissue, or the eyeball itself, by dipterous larvæ usually belonging to the families Sarcophagidæ or Œstridæ.

Historical.—In 1905 Kayser studied this form of myiasis and Portschinsky in 1913 reported some cases. Malgahaes has investigated this disease in Brazil. In 1913 Grünberg found a larva of a species of hypoderma in the anterior chamber of the eye of a girl.

Ætiology.—The larvæ so far recognized as causing this form of myiasis are:—

Sarcophagidæ :—
Wohlfartia magnifica (Schiner, 1862).
Necrobia, sp ?

Œstridæ :—
Œstrus ovis Linnæus, 1761.
Dermatobia cyaniventris Macquart, 1843.
Hypoderma, sp. ?

Symptomatology.—This varies from the discovery of a larva lying like a foreign body under the eyelid, to infection of the lachrymal sacs or the tissue under the palpebral or ocular conjunctiva, to the total destruction of the eyeball.

Treatment.—This consists of the prompt removal of the larva by surgical means.

Prophylaxis.—The prophylaxis consists of prompt treatment of conjunctivitis and the protection of the head when sleeping out of doors. Natives wrap themselves up completely when sleeping out of doors.

URINARY MYIASIS.

Definition.—Urinary myiasis is the invasion of the urinary passages, particularly the urethra and bladder, by dipterous larvæ, especially those of the Anthomyidæ.

Historical.—This form of myiasis is rare, but has been recorded by Ambrose Paré in 1582 and by Turner in the seventeenth century, when he recorded two cases, while in 1909 René Chervel analyzed all cases reported up to that date, and concluded that, of twenty reported cases, six were genuine, ten were probable, and four were doubtful. He also added one of his own observation. King, in 1914, reported an American case. Palmer and Austen have recorded a case in England. Hagen has also drawn attention to a case in Boston.

Ætiology.—It is thought that the flies deposit the eggs near the meatus urinarius, and that the newly-born larvæ pass up into the urethra. Sleeping in the open is generally accused as the method of infection, but paralyzed persons become infected, especially those with urinary troubles. The larvæ which so far have been recognized are those of *Fannia canicularis* Linnæus, 1761, and *Fannia scalaris* Fabricius (p. 852).

Symptomatology.—Generally the larvæ are discovered accidentally when passing urine, when they may cause some slight obstruction.

Treatment.—This apparently is unnecessary, as the larvæ come away without causing harm.

VAGINAL MYIASIS.

Definition.—Vaginal myiasis is the invasion of the vagina by the larvæ of dipterous insects, especially those of the Muscidæ.

Historical.—This form of myiasis appears to be rare, but Cipriani, in 1902, came across a case which had a recto-vaginal fistula, and Castellani saw two cases in Ceylon, but the larvæ were not identified, except *Sarcophaga carnaria* Linnæus, 1758. In 1912 Pieter reported the presence of *Chrysomyia macellaria* Fabricius, 1794, in the vagina of a beggar-woman, and Low has seen a similar case in the West Indies.

Symptomatology.—There is a thick purulent discharge containing the larvæ, and some ulcerations deep in the walls of the vagina.

Treatment.—Vaginal douches with an antiseptic are recommended.

Prophylaxis.—Recto-vaginal fistulæ should be operated upon.

ORO-GASTRO-INTESTINAL MYIASIS.

Definition.—Intestinal myiasis is the invasion of the intestine by the larvæ of certain species of flies, but especially by those belonging to the genera *Sarcophaga* (p. 830), *Fannia* (p. 852), and *Aphiochæta* (p. 824).

History.—Many stray cases of myiasis—*e.g.*, Jenyns (1839)—have been reported from time to time, but these have been gathered together by Portschinsky in 1879 in the twelfth volume of the *Horæ Societis Entomologicæ Russicæ*, by Huber in 1899 in *Bibliographie der Klinischen Entomologie*, Heft 3 (Diptera), and by Calandruccio in the same year in the *Archives de Parasitologie*; by Pfeiffer in 1900 in his work *Fliegenlarvæ als gelegentliche Parasiten des Menschen*; in 1901 by Thébault in the *Archives de Parasitologie*; also by Wellman, and by Austen in an excellent paper read before the Society of Tropical Medicine and Hygiene of London in March, 1910. Cases are also referred to by Splendore (*Arch. de Parasitologie*, 1910), by Garrod, and by Soltau in the *Journal of Parasitology*, 1910. We have seen several cases in Ceylon and in the Balkans. Cases have been reported in England by Stephens (1905), Hewitt (1909), Cattle (1906), Garrod (1909), Soltau (1910), and Austen (1912).

Ætiology.—Intestinal myiasis may be produced by the larvæ of the following species:—

Sarcophagidæ:—
Sarcophaga carnaria Linnæus, 1758.
,, *hæmorrhoidalis* Fallen, 1810.
,, *hæmatodes* Joseph.
,, *affinis*.
,, *magnifica* Schiner, 1862.
,, *wohlfarti* Portschinky, 1875.
,, *latifrons* Meigen.
,, *ruralis* Fallen.
,, *meigeni* Schiner.
Cynomyia mortuorum Linnæus, 1761.

Anthomyidæ:—
Fannia canicularis Linnæus, 1761.
,, *incisurata* Lett.
,, *manicula* Meigen.
,, *saltatrix*.
,, *desjardensii*.
Hydrotæa meteorica Linnæus.

Muscidæ:—
Musca domestica Linnæus.
,, *corvina* Fabricius.
,, *nigra*.
Cyrtoneura stabulans Macquart.
Pollenia rudis Fabricius.
Calliphora vomitoria Linnæus, 1758.
,, *erythrocephala* Meigen.
,, *azurea*.
Lucilia cæsar Linnæus.
,, *regina* Macy.
Chrysomyia polita Linnæus.
Teichomyza fusca Macquart (?).

Tachinidæ:—
Tachina larvarum Meigen.

Micropezidæ:—
Calobata cibaria Meigen.

SYRPHIDÆ:—
Eristalis tenax Fabricius.
,, *arbustorum* Fabricius.
,, *dimidiatus*.
Helophilus pendulinus Meigen.

PHORIDÆ:—
Aphiochæta ferruginea Brunner.
Phora rufipes Meigen; synonym, *P. pallipes* Latreille.

THEREVIDÆ:—
Thereva nobilitata.

SEPSIDÆ:—
Piophila casei Linnæus.

DROSOPHILIDÆ:—
Drosophila funebris Meigen.
,, *melanogastra* Brunner.

ŒSTRIDÆ:—
Spilogaster divisa Meigen.
Gastrophilus pecorum.

Sometimes more than one species may be found in the same case.

Rarer forms of myiasis are those by larvæ of the Tipulidæ, by eggs and larvæ of the Culicidæ, and by the bots of *Gastrophilus equi*.

The eggs or larvæ of the above-mentioned flies enter the alimentary canal with the food, especially with vegetable food in an uncooked or partially cooked condition. Another method is for the fly to deposit its eggs on the nostrils and lips of children, from which they pass into the stomach and intestines, and a third method is entry of the larvæ into the rectum while using a privy. Intestinal myiasis is not uncommon in cattle, both in the Temperate Zone and in the tropics. There seems to be no doubt that the larvæ can live for a considerable time in the intestine, but the most marked example of this is *Aphiochæta ferruginea* Brun, which is believed to be capable of passing through its entire life-cycle in the human colon, because both newly hatched and fully grown larvæ were passed by a patient every two months for nearly a year, notwithstanding the fact that nothing was said to be eaten which could have contained either eggs or larvæ. It is stated that species of the Phoridæ have been found in corpses, and it has been stated that the living larvæ, pupæ, and imagines of species of *Conicera* were found in numbers in a corpse exhumed at La Fayette, Indiana, U.S.A., two years after burial.

If there is any truth in this statement, it proves that the life-cycle of these flies can be completed in a parasitic state, and would explain the possibility of a patient suffering from myiasis for twelve years, and during treatment passing 1,000 to 1,500 larvæ. Fenwick also reports cases in which it seemed probable that the whole life-cycle was completed in man. It is obvious that these statements require careful confirmation by other similar cases before they can be accepted without reservation.

Pathology.—The larvæ usually cause gastro-intestinal symptoms. Those of the Muscidæ may cause little or no disturbance, but those of the Œstridæ and Tipulidæ cause much disturbance.

Morbid Anatomy.—We are not acquainted with the details of any post-mortem examination in man, but in dogs the mucosa of the intestine is congested and marked by numerous small hæmorrhages, and it is thought that bacteria may enter the blood through these wounds.

Symptomatology.—After an incubation period varying from four to twelve days after the ingestion of the eggs, the patient, who has either felt quite well or has suffered from vague abdominal pains and anorexia, begins to feel ill with general malaise, headache, thirst, and faintness, and in children with rigors, convulsions, and even delirium. Vertigo may be felt, and generally there is some fever, which may last two to ten days or longer. Sometimes the continued fever and the diarrhœa renders the diagnosis of enteric fever probable. Pains vary from vague sensations to violent colic. Retching and vomiting may occur, and sometimes hæmatemesis, while dysenteric-like symptoms may also occur. When the larvæ attain maturity, they are sometimes violently evacuated.

Diagnosis.—The diagnosis can only be made by *repeated* examination of the motions and the discovery of the larva, the nature of which may be determined in the same way as in nasal myiasis (p. 1621). Care must be taken that the larvæ really come from the bowels, and are not contaminations of the fæces.

Prognosis.—This is good.

Treatment.—The bowels should be cleared with a dose of castor oil and then an anthelmintic—*e.g.*, Filix mas—should be administered. Thymol or santonin may also be used.

Prophylaxis.—All vegetables should be carefully washed and by preference cooked before being eaten, and fresh salads should be avoided.

Ovænya.

This word means maggots, and is applied, according to Wellman, by the natives in Angola to an alimentary canal myiasis associated with dysenteric symptoms and caused by *Fannia desjardensii* Macqu . It is easily treated by castor oil.

Muculo.

This is the African myiasis, concerning which the editors of the *Journal of Tropical Medicine and Hygiene* asked for information in 1907, but which so far has not been traced.

THE EXTERNAL OR DERMAL MYIASES.

These are the infections of the skin, whether wounded or not by dipterous larvæ. There are two varieties of this type—viz., traumatic dermal myiasis and subcutaneous myiasis.

Traumatic Dermal Myiasis.

Definition.—Traumatic dermal myiasis is the invasion of wounds or ulcers of the skin by the larvæ of dipterous insects, principally belonging to the Muscidæ and Sarcophagidæ.

Historical.—One of the earliest publications with references to this is Joseph in his 'Myiasis Externa Dermatosa,' published in Hamburg in 1800, but a large number of observations have been published since then.

Ætiology.—The larvæ which have been recognized so far are:—

Muscidæ (Subfamily: Muscinæ):—
  Chrysomyia macellaria Fabricius.
  Chrysomyia viridula Robineau-Desvoidy.
  Calliphora, sp. ?
  Lucilia argyrocephala Macquart.
  Lucilia, sp. ?
  Cordylobia anthropophaga.
  Musca putrida.

Sarcophagidæ :—
  Sarcophaga carnaria Linnæus, 1758.
    ,, *magnifica* Schiner, 1862.
    ,, *ruficornis.*
    ,, *chrysostoma* Wiedemann.
    ,, *plinthopegga* Wiedemann. (The adult is one of the 'yaws flies' of Dominica.)
    ,, sp. ?

Symptomatology.—The larvæ accentuate the putrid condition of the sores and the sufferings of the patient.

Treatment.—Antiseptic douches, syringing, with removal of the larvæ, and subsequent antiseptic dressing.

Prophylaxis.—The myiasis can, of course, be prevented by simply applying aseptic dressings to wounds.

Subcutaneous Myiasis.

Synonyms.—Cutaneous myiasis. *French*, Myase cutanée, Myase furonculeuse, Myase rampante sous-cutanée; *Italian*, Myasis cutanea; *German*, Myasis.

Definition.—Dermal myiasis is the invasion of the skin by the larvæ of species of the Œstridæ, especially by *Dermatobia cyaniventris* Macquart, 1843, and by those of the Muscidæ, especially *Cordylobia anthropophaga* Blanchard.

Remarks.—It is necessary to be careful to consider the zoological region when determining the species of the fly to which a maggot found in a case of dermal myiasis belongs, as it is unlikely that a species known to occur in Africa will be found in America, and *vice versa*. Further, it is desirable to determine definitely the nature of the fly causing the myiasis, and therefore this should be bred out as described in the opening sections of this chapter.

Ætiology.—The following larvæ are known to cause subcutaneous myiasis in man:—

Œstridæ :—
Hypoderma bovis de Geer.
Hypoderma lineata de Villiers.
Hypoderma diana Brauer.
Dermatobia cyaniventris Macquart, 1843; synonym, *D. hominis* (Linnæus junior, 1781).
Dermatobia (?) *keniæ* Kolb.
Œstrus (*Cephalomyia*) *ovis* Linnæus.

Muscidæ (Subfamily Calliphorinæ):—
Cordylobia anthropophaga E. Blanchard.
Cordylobia rodhaini.

The life-history of the œstridæ is curious, as will be discussed below. With reference to *Cordylobia anthropophaga*, by a mistake the cutaneous myiasis of Natal, Rhodesia, British Central Africa, Uganda, and the Sudan, was assigned to *Bengalia depressa*, while it should have been placed under this heading.

Varieties.—As geographical distribution is important from the point of view of the causal parasite, it appears to us to be convenient to utilize this and to divide the subcutaneous myiases into the American, the African, the Asian, and the European, while the last variety is not geographical, but pathological—viz., creeping eruption.

American Dermal Myiasis.

Synonym.—Neotropical dermal myiasis, Dermatobiasis.

Definition.—Dermal myiasis as seen in Tropical America is caused by the larva of *Dermatobia hominis* (Linnæus junior, 1781), better known as *Dermatobia cyaniventris* Macquart, 1843, and perhaps by other allied, but as yet unknown, forms.

Nomenclature.—The fly which causes this myiasis has a large number of scientific and popular names:—

Scientific Names.—*Dermatobia hominis* (Linnæus junior, 1781); *Œstrus hominis* Linnæus junior, 1781; *Œ. humanus* Humboldt and Boupland, 1805; *Cuterebra hominis* (Linnæus junior) Say, 1822; *Œstrus guildingii* Hope, 1837; *Dermatobia cyaniventris* Macquart, 1843; *Cuterebra noxialis* Gondot, 1845; *Dermatobia mexicana* Serna, 1896.

Popular Names.—*Brazil*, húra (boil), verme, berne or berme: *British Honduras*, beef worm, cormollote; *Colombia and Venezuela*, gusáno, husano (worm), gusáno de monte (forest worm), gusáno peludo (hirsute worm), gusáno macaco (macaw worm, because it attacks the macaw-headed Capuchin monkeys); *Costa Rica*, torcel; *Guatemala*, colmoyote; *Pungoa*, mirunta; *Mayan name*, suglacura.

Names Suggestive of Mosquito Carriage.—*Mexico*, moyocuil (flyworm), gusáno moyocuil (maggot flyworm); *Colombia, Venezuela, and Guatemala*, gusáno de zancudo (maggot of mosquito); *Dutch Guiana, Trinidad*, mosquito worm.

History.—In 1569 Friar Pedro Simon appears to have been the first to have drawn attention to this myiasis as seen along the banks of the Rio Magdalena and the low plains to the east of the Andes. He was followed in 1653 by Father Bernabé Cobo, who reported its occurrence in the Mexican lowlands in the coast district of Alvarado, in the state of Vera Cruz. In 1745 De la Condamine reported it from French Guiana, as did Arture in 1757. In 1781 Linnæus junior reported it from Peru and gave a brief mention of the fly, while in 1822 Say gave a description of the larva as received from South America. In 1835 Hope gave an account of the larva from under the skin of the head of a man from Trinidad. The specimen was deposited in the museum of the Royal College of Surgeons of England.

From that date scattered, but fairly numerous, references can be found—*e.g.*, Hill (1830), Guyon (1835), Gondot (1845), Coquerel (1859), Laboulbène and Davaine (1860), Bonnet (1870), Der Verteuil (1884), Ormerod (1886), etc.—until between 1890 and 1896 Blanchard published a résumé of known facts, then a series of admirable investigations upon the subject: and in 1915 Sambon again gathered together known facts, together with the history of the mosquito carriage of the eggs, and extended this with his own personal observations.

With reference to the mosquito carriage, it is remarkable to note that Father Cobo, in 1653, says that each wound produced by the common mosquito produces *within the flesh a spine-covered worm the size of a haricot bean or even larger.*

In 1911 Morales of Guatemala first described the transmission of the eggs as being due to a mosquito, and performed an experiment on a man, first noting the escape of the larva from the egg carried by a living mosquito when placed on the palm of the hand, then allowing this larva to wander about the forearm, and then scratching the skin and watching the larva burrow in, then noting the gradual development of the furuncle, and finally, when threatened with suppuration, removing the larva, transplanting it into the back of a rabbit, and watching its escape as a nymph. Also in 1911 Tovar of Maturin, in Venezuela, had noted this mosquito carriage, which was also studied by Blanchard in 1912, Rincones, Zepeda, and Surcouf in 1913, and Sambon in 1915.

Climatology.—The causal agent being a neotropical insect, the distribution of the disease is confined to Tropical America, in which it occurs in the lowlands along the coast and also in the valleys of the river, but it is absent in the hills and mountains. It begins near the southern borders of the United States, being found in Mexico, in Central America—*i.e.*, British and Spanish Honduras, Guatemala, Nicaragua, Costa Rica, and Panama: in South America —*i.e.*, Colombia, Venezuela, the Guianas, Brazil, and Peru; while it is known to occur among the West Indian Islands near South America—*e.g.*, Trinidad.

It requires a warm, moist climate, with surface water and forest vegetation.

Ætiology.—The cause of the disease is the invasion of the body by means of the larva of *Dermatobia hominis* (Linnæus junior, 1781).

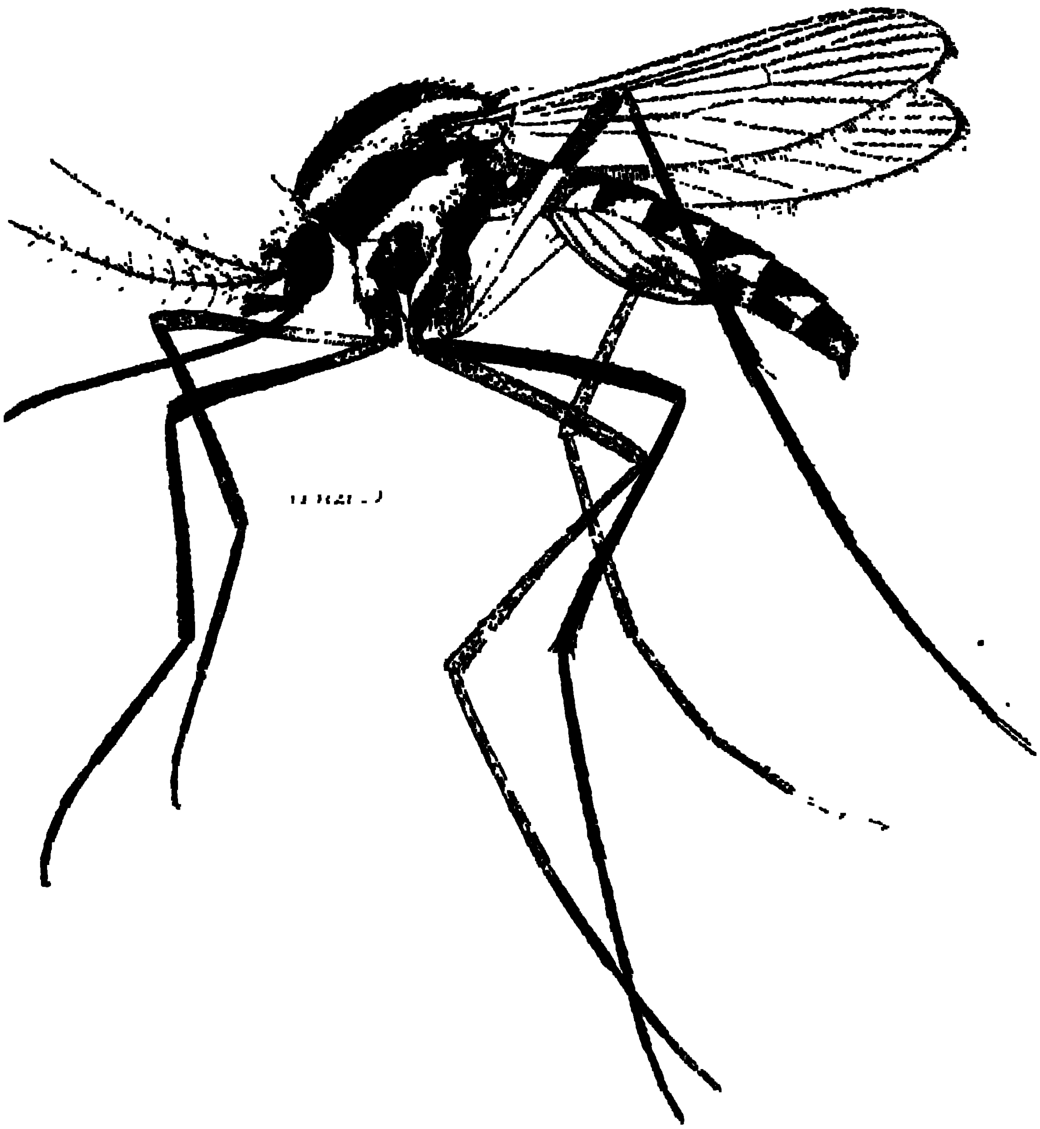

FIG. 724.—*Janthinsoma lutzi* THEOBALD, CARRYING 1 EGGS OF *Dermatobia hominis* LINNÆUS JUNIOR.

(After Sambon.)

On the evidence at present available it would seem that the fly seizes the female mosquito of the species *Janthinsoma lutzi* Theobald and attaches her eggs to the ventral aspect of the abdomen, but it has been suggested that it deposits the eggs upon foliage, and these accidentally reach the mosquito, which appears hardly probable.

When the mosquito feeds upon man or animals the little larva which has been held in position in the egg by its spines slips out and pierces the skin by means of the aperture made by the mosquito bite.

Pathology.—As it escapes from the egg, the larva possesses, in addition to the numerous spines on its first seven segments, a crown of large black rose thorn-shaped spines along the anterior border of the fifth, sixth, and seventh segments, while the last shows two posterior stigmata. When it has pierced the skin the spines on the fifth to seventh segment are shed (they are no longer required, as their function is to keep the larva in the egg-case), and the stigmata become three in number. What happens to the larva in the body is not known, but that it can wander under the skin is known, and its production of the warble and escape therefrom is also known.

Symptomatology.—*The incubation period* or time between the infection and the first appearance of the warble is unknown.

Appearance of the Warble.—Suddenly the patient feels a sharp pain in some region of the skin. It may last two to three minutes, and then pass away, but after a time it will return either in the morning or in the evening. These intermittent seizures will continue, and the pain will increase as the little rounded swelling which appears in the affected region increases in size. This swelling is the warble.

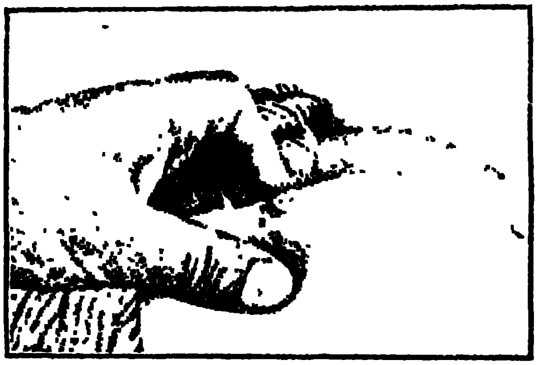

FIG. 725.—WARBLE CAUSED BY *Dermatobia hominis* (LINNÆUS JUNIOR) (After Sambon

The Warble Stage.—When fully developed the warble resembles a boil being some 2-3 centimetres in diameter and of a dark red or bluish-red colour. At the apex there is a more or less centrically placed small circular aperture which increases till it reaches a size of 3-6 millimetres. It is usually covered by a scab, which, if removed, shows a moving body with two small brownish-yellow spots. This is the posterior end of the larva. These warbles may be single or multiple, placed in close proximity or scattered, with usually only one larva to a warble, but sometimes with more and rarely as many as five larvæ to one warble. Warbles may exist in any part of the body, but are more painful in regions like the nose. Usually there are no constitutional symptoms, but there may be slight fever, and there may be swelling of the surrounding subcutaneous tissue, especially in the head, where the œdematous swelling may be limited by the adhesions of the fasciæ. When the warble is mature the larva may be seen actively moving up and down like a jack-in-the-box, appearing and disappearing from the aperture. In due course it gradually dilates the opening in the warble by means of its posterior end, and eventually escapes and, falling to the ground, crawls away and becomes a pupa.

Post-Warble Stage.—After a period varying from six weeks to six months the larva escapes and leaves behind an empty cavity, which is closed by granulation tissue and heals, leaving a hardly visible scar.

Complications.—Secondary bacterial infections may take place, giving rise to erysipelas, tetanus, lymphangitis, and enlargement of the lymphatic glands. If the larva dies an abscess is formed.

Diagnosis.—The cardinal points in the diagnosis are:—

1. The formation of boil-like swellings on the skin.
2. The presence of an aperture at the apex of these swellings.
3. The presence of the posterior end of a larva, with its stigmata in the opening.
4. The boils forming in the neotropical zoological region.

Treatment. The native places a tobacco-leaf over the aperture in the warble, or squirts tobacco-juice therein, and after twenty-four hours squeezes the larva out.

Tincture of iodine may be used in a similar manner or 1 in 20 carbolic lotion. When the larva has departed, wash the empty warble out with antiseptic lotion and dress aseptically.

African Dermal Myiasis.

The known form of African dermal myiasis is *tumbu disease*, caused by members of the Calliphorinæ subfamily of the Muscidæ.

TUMBU DISEASE.

Definition.— Tumbu disease is an African dermal myiasis caused by the larvæ of *Cordylobia anthropophaga* E. Blanchard and allied species living under the skin.

Historical.—It was reported from Senegal, where the larva is called ' ver de cayor ' by Berenger-Féraud, and later by E. Blanchard from Natal, when it was called the Natal worm, while the fly was named *Ochromyia anthropophaga*. A similar larva was found in the arm of Commander Lund in the Congo, and was long known as Lund's larva until it received the name *Cordylobia rodhaini* Gedoelst, 1905.

In 1901 it was reported that there was a maggot fly in Natal, limited to the coast, not extending inland, and not rising higher than 1,000 feet. It was also found about Delagoa Bay, in Rhodesia, British Central Africa, Uganda, and the Anglo-Egyptian Sudan. Unfortunately this fly was recognized as Walker's *Bengalia depressa*, when it was really the well-known *Cordylobia anthropophaga*, and the true Bengalia is altogether a different genus, probably an Auchmeromyia with an unknown life-history. It also occurs in late German East Africa, where it was called *Ochromyia anthropophaga* by Grünberg and *Cordylobia grünbergi* by Doenitz.

Austen has described a third species, *Cordylobia prægrandis*, in Nyasaland, Cape Colony, Transvaal, Natal, North-West Rhodesia, and late German East Africa, and contributed a valuable paper on the whole subject in 1908 to the *Journal of the Royal Army Medical Corps*: while Smith described the symptoms of the disease in the same journal.

In 1913 Rodhain, Pons, Vandenbranden, and Bequaert, demonstrated by experiment the method of infection: and Heckenroth and Blanchard recorded four cases due to *Cordylobia rodhaini* in French Equatorial Africa.

Climatology.—Tumbu seems to be widespread throughout tropical Africa, extending from Senegal in the north to Natal in the south, and from the west to the east coasts.

Ætiology.—The cause of the disease is the invasion of the subcutaneous tissues by the larva of *Cordylobia anthropophaga* and allied species. The method of infection, thanks to the labours of Smith in 1908, and Rodhain, Pons, Vandenbranden, and Bequaert in 1913, is fairly well known.

The eggs are apparently sometimes laid on the clothing, the fly, perhaps, being attracted by the odour, or perhaps at other times the egg is laid in dirt or fæcal matter on the floor, from which the larva wanders on to the human being, especially when using the latrine.

Having arrived on the skin of man or animals, it penetrates this by means of its buccal hooks, but seems to require a long time to do so, as one experiment took six hours. If this is really so, then there must be some ancillary process, as this is not natural.

Monkeys, goats, rabbits, dogs, and cats are also attacked.

Symptomatology.—During the attack slight pricking sensations may be noted. The parts most affected are the scrotum, thigh, and buttocks in Europeans, but the forearm, axilla (especially in natives), and the head also may be invaded. The infected area presents the appearance of a boil, in the central portion of which there is an opening, more or less clearly defined, which is marked by black matter (the excrement of the larva). In this hole the posterior end of the larva may be noted, and on pressing on it considerable pain is produced, probably due to the movements of the larva. Surrounding the central opening is an inflamed area about ¾ inch in diameter. The opening may, however, be obscured by dried-up discharge. Strong pressure easily expels the maggot, so that it is seldom allowed to grow old. In children and helpless persons it may attain its full size, and is then usually associated with suppuration, and when full grown is about 12 millimetres in length, of a yellowish-white colour, and bluntly pointed anteriorly, while it possesses twelve segments, on the posterior aspect of the last of which are the two posterior stigmatic plates, which are visible in the orifice of the swelling, appearing and disappearing after the manner of a jack-in-the-box.

Treatment.—The larva is easily expressed by strong pressure, and then the resulting hole can be cleansed with antiseptic solutions and the wound dressed aseptically.

Asian Dermal Myiasis.

Myiasis has not been sufficiently studied in Asia, though it is fairly common there. ***Sarcophaga ruficornis*** is reported as causing occasionally a very severe form of cutaneous myiasis, but beyond this much cannot be said.

European Dermal Myiasis.

The myiasis of Europe scarcely comes under the scope of tropical medicine, but it may be mentioned that dermal myiases are known to be caused by *Hypoderma bovis* de Geer, 1776 (p. 826): ***H. diana*** Brauer: *H. lineata* de Villers, 1789; *Gastrophilis* ***nasalis*** Linnæus, 1758: *G. hæmorrhoidalis* Leach, 1761: *G. veterinus;* and ***Lucilia sericata.***

Creeping Eruption.

Synonyms. Creeping disease, Larva migrans *Bulgarian*, Nova Bolest, Pulzasta Bolest, *German*, Hautmaulwarf, Kreechkrankheit, Hautkratzschorf.

History.—This disease was first described by A. Lee in 1875. Later on, Procke, Blanchard, Topsent, Fülleborn, and others have recorded several cases It is not rare in some parts of Europe, Africa, and Asia, and in South America. We have seen numerous cases in Ceylon. It is extremely rare in North America.

Ætiology and Pathology.—Larvæ of the genera *Gastrophilus, G. hæmorrhoidalis* and ***G. nasalis, Œstromyia satyrus***, *Hypoderma bovis, and H. lineata* have been found in several cases. In others no larva whatever was found. Looss states that the same clinical picture may be caused occasionally by Ancylostoma and Strongyloides (*Anguillula*) larvæ, or even by an inanimate object like a piece of horsehair. A larva has been found 2 millimetres from inflamed end, under a small dark spot.

Symotomatology.—The eruption is characterized by the presence of a narrow raised red line, ¼ to 1 inch broad. This line extends daily one or several inches, and is generally sinuous, but may be straight. While the advancing end progresses, the opposite end slowly fades away. The duration of the malady is long, generally several months, but occasionally two or three years. There is much pruritus.

Treatment.—Hypodermic injections of various disinfectants have been tried, with little success. Hutchins recommends a cocaine injection, followed by the injection of 1 or 2 drops of chloroform.

ALLIED CONDITIONS.

Allied to the myiases are infestations by the larvæ or imagines of the Lepidoptera, Coleoptera, Diplopoda, Chilopoda, and Dermoptera.

Scolechiasis.

Synonym.—Scholechiasis.

Definition.—Scolechiasis is the invasion of the body by the larvæ of the Lepidoptera.

History.—Originally the term 'scolechiasis' was used by Kirby and Spence for the invasion of the body by the larvæ of any insects, but Hope suggested that the term should be restricted as indicated, and invented new terms for other infestations.

Varieties.—Hope gives a list of seven cases, of which five were gastro-intestinal, one was rhinal, and one was not classified.

Gastro-Intestinal Scolechiasis.—This is due to *Pontia brassicæ* Linnæus, belonging to the Papilionidæ, and observed by Calderwood in Scotland. Two were due to *Crambus pinguinalis*, of the Noctuidæ, one being observed by Linnæus in Sweden and one by Church in England, and one was due to *Phryganea grandis*, observed by Church in England. The one without determination was found by Lister in England.

Rhinal Scolechiasis.—There is only one case caused by *Crambus pinguinalis*, and recorded by Kirby and Spence, on the authority of Fulvius Angelinus, as occurring in Ravenna.

Canthariasis.

Synonym.—Scolechiasis as used by us in the second edition.

Definition.—Canthariasis is the invasion of the body by the larvæ of the Coleoptera.

Remarks.—The term used above was introduced by Hope in 1840, when he recorded a number of cases of rhinal, gastro-intestinal, and urinary infestations.

RHINAL CANTHARIASIS.—This was due to *Tenebrio moletor* Linnæus, and was recorded by Tulpius and by Oswald Allen.

GASTRO-INTESTINAL CANTHARIASIS.—The genera recorded are numerous.

Carabidæ.—*Sphodrus leucophthalmus* by Paykull in Sweden, in 1797; *Dermestes lardarius* by Otto and Chichester, in 1807, in England; and *D. murinus* by Otto, also in England.

Staphylinidæ.—*Pæderus elongatus* Fabricius; *Oxyporus subterraneus* Fabricius; *Staphylinus splendens* Fabricius; *S. politus* Fabricius; *S. fuscipes* Fabricius; and *S. punctulatus* Fabricius by Paykull in Sweden, in 1796-1798.

Scarabæidæ.—*Geotrupes vernalis* by Van Brommell in Sweden, in 1720; *Melolontha*, sp. ?, by Leniaout, Depalse (1817 ?), and Desvoidy in France.

Tenebrionidæ.—*Tenebrio moletor* Linnæus by Forestus, in 1568, at Brielle; by Kellie in Scotland; by Pickells and by Thomson in Ireland; by Traill and others in England; by Acrel in Sweden, in 1796.

Blapidæ.—*Blaps mortisaga* Fabricius by Pickells, Thomson, and O'Brien in Ireland, in 1827; by Bateman and others in England.

Mordellidæ.—*Mordella*, sp. ?, by Rosen, in 1752, in Sweden.

Cantharidæ.—*Melæ proscarabæus* Fabricius by Germar in Silesia, in 1816.

Circulionidæ.—*Balaninus nucum* Fabricius by Henry, Astley Cooper, and others in England, in 1805-1809.

URINARY CANTHARIASIS.—*Tenebrio molitor* Linnæus is recorded by Tulpius as occurring in the bladder of a female aged fifty years; *Balaninus*, sp. ?, by Henry and Phillips in the urinary passages of a man aged sixty-two years, in Lancashire, in 1809. King in the Anglo-Egyptian Sudan has recorded a case where the larva depicted in Fig. 460, p. 870 was passed *per urethram.*

DERMAL CANTHARIASIS.—*Dyticus marginalis* Linnæus is recorded by Hope, in 1831, in England.

Diplopodiasis and Chilopodiasis.

Diplopodiasis occurs in the alimentary canal, and is caused by *Julus terrestris* Linnæus, *J. londinenensis*, and *Polydesmus complanatus.*

Chilopodiasis occurs in the rhinal passages, where *Geophilus carpophagus* Leach, *G. electricus* Linnæus, *G. cephalicus* Wood, *G. similis* Leach, *Lithobius forficatus* Linnæus, and *L. melanops* have been found, while *G. electricus* and *S. coleoptrata*, *Chætechelyne vesuviana*, *Himantarium gervaisi*, and *Stigmatogaster subterraneus* occur in the alimentary canal.

Dermapteriasis.

Dermapteriasis of the alimentary canal caused by *Forficula auricularia* has been reported by Griffin in 1830.

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CHAPTER LXVIII

POROCEPHALOSIS

Synonym—Definition—History—Climatology—Etiology—Pathology—Morbid anatomy—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—References.

Synonym.—Porocephaliasis.

Definition.—Porocephalosis is the invasion of the body by the larvæ of *Porocephalus armillatus* Wyman, 1848, and *P. moniliformis* Diesing, 1836, and possibly other forms, which become encysted in the liver and lungs, and ultimately develop into nymphæ, which may, by their wanderings, cause inflammation of organs and serous membranes.

History.—*P. armillatus* was first found in man by Pruner in 1846, and has since been studied by Bilharz, Fenger, Aitken, Giard, Broden and Rodhain, Dutton and Todd, and one of us. *P. moniliformis* has been met with in Asia, and by Salm in Java. Sambon thinks that Welch's Indian parasite may have been *P. najæ* Leuckart, 1860, or *P. crociduræ* Parona, 1890, found in Blyth's musk shrew *Crocidura fuliginosa*; and that Flint's case in America may have been an infection with *P. crotali* Humboldt, 1808, but for details with regard to these parasites, see pp. 734 and 736.

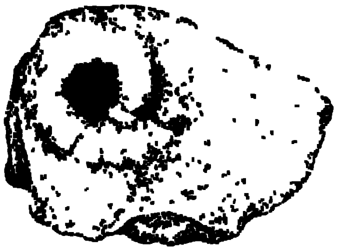

FIG. 726.—*Porocephalus armillatus* ENCYSTED IN LIVER.

(After Sambon from our West African case.)

Climatology. — *Porocephalus armillatus* is confined to Africa, being met with in negroes resident, or who have resided, therein. It has been reported from Egypt and various parts of the West Coast of Africa, but especially from the Congo.

With regard to *P. moniliformis*, it occurs in Java and the Philippine Islands. Welch described a peculiar parasite as occurring in the mucosa of the intestine of a man in India which he considered to be an *Echinorhynchus*, but which, judging from the drawing, might well be a *Porocephalus*.

Ætiology.—The adults of both *P. armillatus* and *P. moniliformis* live in the nasal cavities and lungs of pythons and snakes, and though the life-history is as yet unknown, it is quite possible that

Sambon's suggestion that the ova pass into the drinking-water, and so to man, may be correct. It is possible that the eggs hatch in the alimentary canal, and that the larvæ then pass into the organs.

Pathology.—The larvæ are found lying coiled in cysts in the liver and lungs. In due course these larvæ become nymphæ, which leave the cysts and wander through the body, appearing in the lungs and bronchi, causing bronchitis and broncho-pneumonia; in the peritoneal cavity, causing peritonitis; in the bowels, causing irritation. Perhaps they leave the body by the fæces; perhaps, also, by the sputum; but in any case they cause serious illness in, and death of, the victim.

Morbid Anatomy. In opening the abdomen, the nymphæ may be found quite free in the peritoneal cavity, and may crawl up the hands and arms of the pathologist. They may also be found in the lumen of the alimentary canal, in the mucosæ, and thickness of the wall of the bowel. The larvæ may be seen encysted in the liver and lungs.

In the cysts they lie in a curved position, with the ventral surface on the outer aspect of the curve. The lungs show signs of bronchitis and pneumonia, and the peritoneum is usually chronically inflamed, but not always.

Symptomatology.—The symptoms of the early stages of the disease are at present quite unknown, but the terminal symptoms are emaciation and weakness, associated with attacks of bronchitis, pleurisy, or other respiratory symptoms. There may be cavities in the lungs, and the sputum may be offensive and may contain the parasites, of which as many as 75 to 100 have been recorded as being expectorated by a single patient. The liver is usually considerably enlarged.

Diagnosis.- The disease has often been mistaken for phthisis; therefore any patient in the tropics suffering from the usual symptoms of phthisis associated with enlargement of the liver may be suspected, and the sputum and fæces carefully watched for the possible appearance of the parasites. When a parasite is found, it may not necessarily be either *P. armillatus* or *P. moniliformis*, but is more likely to be some form found in some animal which lives in the region where the patient resides or works.

Prognosis.—The disease is generally chronic. The prognosis is serious.

Treatment.—There is no known treatment.

Prophylaxis.—If the drinking-water is boiled or filtered, there ought to be no danger of infection.

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CHAPTER LXIX

LEPROSY

Synonyms—Definition—History—Climatology—Ætiology—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—References.

Synonyms.—Elephantiasis Græcorum. *French:* La Lèpre. *Italian:* Lebbra. *German:* Aussatz. *Norwegian:* Spedalskhed. *Arabic:* Djudsam.

Definition.—Leprosy is a chronic general disease, caused by the *Mycobacterium lepræ* Hansen, 1874, (usual term *Bacillus lepræ*), which produces characteristic lesions in the skin, mucosæ, and nerves. The method of infection is unknown.

History.—Even at the present time there is occasionally much difficulty with regard to the diagnosis of leprosy from allied diseases, and therefore in ancient times and in the Middle Ages syphilis and skin diseases without doubt were confused with it. Hence the history is not easy to write. Nevertheless, such a repulsive and striking disease must have been noticed by the ancients, and therefore it is possible that the references in the Ebers Papyrus, and in the English Bible, the Rig Veda, and ancient Japanese books, actually refer to what we call leprosy, together with other diseases. If this is so, leprosy is indeed ancient and widespread. Certain authorities, however, are of opinion that the Hebrew word Tsaraath, which the translators of the Bible have rendered as leprosy, does not refer to such disease. It is probable that the malady passed from Egypt to Greece, and later to Italy, by means of Pompey's troops, and that it was disseminated throughout Europe by the Roman legions, by traders, and later, perhaps, by the Crusaders returning from the East. In any case, leprosy gradually increased in Europe from the days of Pompey till, in the thirteenth century, it existed to such an extent as to move Church and State alike to combat its ravages. Stern measures were enforced, and the lepers were isolated in lazarettos. They were compelled to wear a special dress, to use a clapper when passing along the roads, to only indicate with a stick the articles they desired to buy in a market; while they were forbidden to drink from public fountains, to touch children, to speak to a healthy person in a loud voice, or to eat with any person other than a leper. Further, the Church performed the Burial Service over a person who was diagnosed to be a leper, and therefore officially he was dead. The result of this appears to have been beneficial, as the number of lepers diminished rapidly in the fourteenth and fifteenth centuries, since when the disease has almost disappeared from many parts of Europe.

But while abating in Europe, it appears to have been introduced into Madeira and the Canary Islands about the end of the fifteenth century, and perhaps also into America by the Spaniards. The infection of the West Indies would appear, however, to have been mainly due to the negro slaves brought from Africa about the middle of the sixteenth century, after which the disease became common. There is great doubt as to whether it did not exist in South America in ancient times, but no clear evidence is forthcoming at present.

In India, Japan, and probably China, leprosy is most ancient, while it is very common in South China. During recent years the Chinese have been moving about the world, and are accredited with introducing the disease into Kamschatka, the Sandwich Islands, Polynesia, Columbia, California, Australia, New Zealand, and also into Indo-China.

Though very common in North and Tropical Africa, it appears to have been unknown in South Africa until introduced in 1756 by the Dutch from Java, who carried it through Cape Colony and the Orange Free State into the Transvaal. It must, however, be stated that some people think it has existed for a long time in South Africa.

It is said that the numbers of lepers have markedly increased in South Africa since the advent of the East Indian troops in the middle of last century.

As regards medical literature, Hippocrates says but little about the disease, and perhaps really refers to psoriasis, while Aristotle defines it better. It is not, however, until the first century that Aretaeus of Cappadocia gives a clear description of the disease, and not till 1847 that the first modern clinical account by Danielssen and Boeck appeared. The pathology of the disease has been carefully studied by Virchow, Vandyke Carter, Leloir, Babès, Unna, Zambaco, Innes, Campana, De Amicis, Philipson, Mantegazza, and Bergmann. In 1871 Hansen discovered the bacillus, and in 1877 definitely associated it with the causation of leprous lesions, and it has subsequently been studied by Neisser in 1879, and many others.

Many attempts have been made to cultivate this bacillus, notably by the Indian Commission, van Houten and Rost, and more recently by Keebrowsky, Clegg, Bayon, and Duval. In 1903 Stephansky and Dean, and later Rabinowitsch and Tidswell, discovered a peculiar leprosy-like disease in rats, the lesions of which contain bacilli closely resembling Hansen's bacillus in appearance, and not capable of cultivation. A diphtheroid bacillus has, however, been cultivated by Dean from two cases, and is said by him to be capable of being agglutinated by human leprous serum. There is probably no connection between the human and the rat disease, though some authorities admit it. The condition has been recently investigated by Marchoux and Sorel, Bayon, and others.

The method of infection is at present unknown, though there are various theories, more or less ably defended, which will be mentioned later. Marchoux and Bourret consider that they have successfully inoculated a chimpanzee, and Nicolle and Blaizot have produced lesions resembling leprosy in lower monkeys. The condition of the eye has been much neglected until recent years, when the researches begun by Bull and Hansen as far back as 1873 have been extended by Grossman in 1906, de Silva in 1907, but most importantly by Borthen in 1899.

Deycke and Reschad inoculated the surface cream of sterilized unskimmed milk with material obtained from the under aspect of leprotic tubercles by throwing back a flap of skin. Incubated at 30° C., a growth forms in fourteen days, which is characterized by its bright orange tint. This organism they called *Streptothrix leproides*, and from this they obtain a neutral fat, 'nastin,' which is similar to a fat found in Hansen's bacillus, and this Deycke considered to be the agent which produced favourable symptoms when cultures of *Streptothrix leproides* were injected into patients. Later he noticed that these favourable conditions were associated with a leucocytosis, and therefore used nastin mixed with cinnamic acid, which is excreted as hippuric acid, the two acids being connected by benzoic acid as an intermediate product. He therefore used benzoyl chloride to extract the 'nastin,' and injected the 'benzoyl nastin' into patients, producing a reaction. Deycke believes that the nastin is only a carrier of the benzoyl chloride to the bacilli, which it deprives of their fat, and so allows the phagocytes to attack them. Four solutions were prepared: Nastin B 0, Nastin B 1, Nastin B 2, and K., this last being only benzoyl chloride, and being used to shorten and reduce the severity of the reaction if required. The others represent nastin in varying degrees of strength, Nastin B 2 containing an excess of nastin, while Nastin B 1 is that usually employed. Unfortunately no general success has followed this line of treatment.

Climatology.—At the present time there is but little leprosy in many parts of Europe, but it is still common in Iceland, while it is found in Spain, Italy, the Balkans, Turkey, Crete, and Cyprus. It is less frequent than formerly in Norway, Sweden, Greece, and some of the Mediterranean islands, rare in France and Germany, and almost extinct in Denmark, Belgium, Holland, Austria-Hungary, and England.

It is very common throughout the whole of Asia. In Ceylon there are numerous lepers, many of whom are treated in a leper asylum at Hendela, near Colombo, which is believed to be one of the best in the world.

In Australia the disease is known principally in Queensland and New South Wales, and also in Victoria; while in New Zealand it is known among the Maoris. It occurs in New Caledonia, Tahiti, and the Sandwich Islands.

It is spread sporadically over the United States, but is rare in Canada, while it is well known in Mexico and Central America, and common in the West Indies. In South America it appears to be common in Colombia, Venezuela, the Guianas, and Brazil, but whether it is rare or simply not recognized in other countries is unknown.

It appears to be spread all through Africa, but is certainly rare in West Africa, more common in Central and East Africa, and decidedly more common in North and in South Africa, where there is the celebrated Robbin Island Leper Asylum. There are people who believe Egypt to be the original home of the disease, from whence it spread to Asia and Europe.

Ætiology.—The disease is caused by Hansen's bacillus, which morphologically has the greatest resemblance to the tubercular bacillus and is stained by the same methods.

With regard to the cultivation of the bacillus there are three views:—

1. That it has never been cultivated.
2. That it can be cultivated as a streptothrix or nocardia.
3. That it can be cultivated as a bacillus.

1. *That it has never been cultivated.*—This is still the most generally accepted view.

2. *That it can be cultivated as a Streptothrix.*—This is the view held by Bordoni-Uffreduzzi, Babès, Rost, Kedrowsky, Shiga, Hewlett, Bayon, Johnston, and others. They maintain that Hansen's bacillus in cultures becomes a filamentary branching non-acid-resisting organism, which, when injected persistently into animals, produces the signs of leprosy. From these animals, they say, it can be recovered as an acid-resisting bacillus. The strain separated by Kedrowsky, and further investigated by Bayon, is the one which in our opinion is the most important with a view to further researches. The growth of the germ is slow, and the colonies coalesce into a whitish mass. The inoculation of cultures into monkeys, rats, and guinea-pigs, gives rise, according to Bayon, to leprosy-like lesions, with very little tissue proliferation, no caseation necrosis, no vascular sclerosis, and with presence of numerous acid-fast bacilli. Serological reactions, such as agglutination and complement fixation, are rather in favour of Bayon's theory. Moreover, the inoculation of an extract of the cultures induces in leprotic patients a reaction with fever, comparable to that induced in tubercular patients by tuberculin.

In 1915 Fraser and Fletcher were unable to confirm Kedrowsky and Bayon's results, and came to the conclusion that Kedrowsky's bacillus is not the leprosy bacillus.

3. *That it can be cultivated as a Bacillus.*—This is the view held by Clegg, Duval, and others. Clegg succeeded in cultivating his bacillus in symbiosis with an amœba. The cultures are chromogenic. The inoculation of this germ apparently does not produce leprotic lesions. Duval gives importance to a non-chromogenic always acid-fast bacillus he has isolated, which grows very slowly,

and only on special media. He states that in addition to this bacillus he has at times grown a polymorphic organism, sometimes diphtheroid, sometimes streptothrical, and of varying degrees of acid-fastness. He compares this type of germ to those isolated by Kedrowsky and Bayon, and is not inclined to give it any importance.

The bacilli, which, as will be shown later, exist practically all over the body wherever diseased tissue is found, leave it by the nasal secretion, the tears, the salivary secretion, the sputum, the milk, the semen, urethral and vaginal secretions, and by the fæces, and are cast off with the scales of skin or the discharge of disintegrating tubercles. Of all these, the secretion of the nose appears to be of great importance, for, as Sticker and van Houten showed, the bacilli are very commonly met with in that situation. The bacilli are reported to have been found in *Culex pungens* and *Clinocoris lectularius* by Goodhue, of the Molokai Leper Settlement. Finally, notwithstanding one or two observations, the bacillus has never been found in earth, dust, air, water, or food.

With regard to inoculations of leprotic tissues and nodules into animals, experiments have been negative in rabbits, guinea-pigs, dogs, cats, bats, pigs, and birds, even though some experiments were thought at the time to be successful. Nicolle produced a hard indolent swelling with a few lepra bacilli by injection of leprous tissue in a *Macacus* monkey. Marchoux and Bourret have made inoculation experiments in a chimpanzee with partial success. Stanziale has inoculated leprotic material in the cornea of rabbits, inducing certain lesions which he has been able to transmit, to a certain point, from animal to animal. In rats a peculiar skin disease, somewhat resembling leprosy, occurs spontaneously, as observed by Stephansky, Dean, and Rabinowitsch. This has been investigated by Marchoux and Sorel, who have come to the conclusion that it is generally transmitted by contact, and not by parasitic agencies. They have not succeeded in cultivating the bacillus, while Bayon has cultivated a streptothrix very similar to the Kedrowsky strain isolated from human lesions.

With regard to the experimental inoculation of human beings, the only case cited as successful is Arning's inoculation of a Sandwich Island criminal in the arm with a leprous tubercle. This man developed a neuritis of the ulnar and median nerves four weeks after the inoculation, a tubercle five months later, the full signs of leprosy two and a half years later, and died a leper six years after the inoculation. It is, however, to be noted that he lived in a leprous country, and that there was leprosy in his family—facts which decrease the importance of the experiment.

There can, however, be no real doubt that the disease is in some way spread from human being to human being. In support of this there are many well-known facts—*e.g.*, the case reported by Benson, where an Irishman, having acquired leprosy in the West Indies, returned to Ireland, and died from the effects of the disease in about eleven months. During this period his brother not merely lived with him, but slept in the same bed, and, after his death, wore his clothes. In about four to five years this brother showed all the typical signs of tubercular leprosy, though he had only once been out of Ireland, and then only to visit England. Another similar case may be quoted of a person who, acquiring leprosy in Tonkin, returned to Strasburg and lived with a nephew, who subsequently developed the disease. Turning to the evidence of history, there is the spread of leprosy throughout Europe, and, later, the rapid spread of the disease in the Sandwich Islands, where, though existing probably for many years, it increased from 1859, when it was hardly known, till in 1881 no less than 800 lepers were isolated, and it is said that no less than one-tenth of the population were affected Another instance is the case of New Caledonia, in which the disease, though now common, is believed to have been introduced for the first time in 1860, and Pine Island, which is said to have been infected from New Caledonia: or Mauritius, which was infected by a single leper, and from which, later, the island of Rodriguez was infected, also by a single leper.

As to individual cases of infection by residence among lepers, the most noted is that of Father Damien de Venster, who went from Belgium as a missionary to the Molokai Leper Asylum of the Sandwich Islands in 1873, and who was first recognized to be suffering from the disease in 1882, from which he died in 1889

Again, the prophylactic success of even partial isolation of lepers, as evinced in Europe in the thirteenth and fourteenth centuries, and to-day in Norway, Sweden, and Iceland, is in favour of the view that the disease passes from man to man. But it is not wise to hastily conclude that this transference is direct, for any of the above cases are easily explicable by the disease being conveyed by food or biting animals. The success of partial isolation might be simply to diminish the chance of infection by these means. Moreover, the fact that the attendants of the Hendela Leper Asylum of Ceylon have so far not been known to contract the disease is against the theory of direct contagion. Further, though there is evidence that married people may both suffer from the disease, there is no proof that sexual intercourse is a means of infection. Nor is there any evidence of heredity being a source of infection, for never has a child been born in a leprous condition, though it is said that 10 per cent. of the children of leprous mothers become sooner or later lepers themselves.

If the germs are not carried from one person to another by contact, sexual or germinal transmission, they might still be conveyed by air, dust, water, or food, and, indeed, all these theories have their supporters.

It does not appear likely that it is conveyed by air, otherwise it would surely be spread more commonly from patients to attendants in leper asylums. With regard to dust, it is quite true that, though some persons report the presence of a very few bacilli in earth taken from places frequented by lepers, the majority have failed to find them; and, again, what has been remarked with regard to air also applies to dust. The germs have never been found in the water of the most highly infected places.

Many articles of food have been suspected, especially fish, and more particularly salted fish—a view which Sir Jonathan Hutchinson has strongly advocated: but even he admits that it will not explain all cases, particularly its presence in people who have no chance of eating cured fish.

After excluding all these, there is still the possibility of the infection being carried by some blood-sucking insect. This subject has been most ably discussed by Nuttall, who points out that Linnæus and Rolander considered *Chlorops* (*Musca*) *lepræ* to be the active agent; while Corredor suspected flies in general: Sabrazés, insects; Joly, *Sarcoptes scabiei* and *Pediculi*; and Sommer, mosquitoes. Nuttall himself says that the possibility of such transmission cannot be denied. Goodhue has demonstrated the bacilli in *Culex pungens* and in *Clinocoris lectularius*; and Marchoux and Bourret have suggested that some Simuliidæ might be the carriers of the disease. Flies, lice, bugs, fleas, ticks, etc., have all been studied recently without any great success.

It might be thought that, direct inoculation having failed, the infection by means of insects would be unlikely. But that is not so, because it is well known that the passage of bacilli through another animal may markedly modify the virulence of the germ. On the other hand, a great many facts are in favour of the insect spread of the disease—*e.g.*, the infection in a family. The cases cited above as examples of contagion would be easily explicable by the action of an insect, as would the effect of isolation in preventing the disease. Moreover, the predisposing causes of dirt, poverty, etc., are also explicable on the same reasoning, especially the curious disappearance of the disease in the families of Norwegian peasants emigrating to America, where they became much cleaner in their habits. The difficulty of cultivating the germ on ordinary media is very suggestive of its being accustomed to live solely in animal tissues; while the abundance of the bacilli in the skin is also suggestive of that being the natural method of leaving the body. Everything in the history of the disease appears to us to favour its spread by animal agency.

Cases of infection by vaccination and variolization are on record. Natives of Ceylon generally state that the disease begins after a bite by a rat.

Pathology.—According to different theories, the bacillus enters the body via the skin, the nasal or respiratory mucosæ, the alimentary canal, or the generative organs.

The list is so comprehensive that it will be obvious that the real method of entry is entirely unknown. On arrival inside the body, the bacillus is ***supposed*** to come to rest inside a lymph space somewhere, and there to grow and form colonies, from whence it can be disseminated through the body, perhaps by the blood and the lymph streams. It must be remembered, however, that the nature of the initial lesions is quite unknown. So enormously do the bacilli multiply in the body that there are few diseases which show an equal infection.

The pathogenesis of the lesions is not very well known, and there are many points of dispute which so far have not been settled. The early stages have been most carefully studied by Unna in the neurolepride, in which there is at first a dilatation of the capillary vessels of the skin, on the walls of which the typical bacilli can be found. The organisms now pass into the wall of the vessel, and appear to irritate the connective-tissue cells of the vicinity, which, becoming plasma cells, surround the periphery of the vessel.

There is a dispute as to whether any diapedesis of the white cells takes place. Thus Thin and Neisser support the view of a diapedesis, to which, however, Unna is opposed. According to the former observers, the cells of the leproma contain not merely plasma cells, but also leucocytes and lymphocytes, while according to the latter they are entirely plasma cells and their derivatives, for Unna holds the view that the bacillus has but little attraction for the white cell. The organisms pass from the vessel wall into the lymph capillaries, in which they grow. These early stages have not been seen in the typical leproma, in which the bacilli from the first are met with in the lymphatics, in which they grow luxuriantly, causing the considerable dilatation which is a marked feature of the lesion.

Now occurs a phenomenon concerning which there is much difference of opinion, for either the plasma cells increase in size, and, becoming multinucleated, engulf the bacilli, forming in this way the typical 'lepra cells' of Virchow—a view supported also by Neisser and others—or the bacilli attack the plasma cells, destroy their cytoplasm, and so damage the nucleus that it becomes achromatic and breaks into several pieces, which remain surrounded by, or on the side of, a mass of bacilli embedded in mucus, thus giving rise to a false appearance of a giant cell or chorio-plaque enclosing bacilli, as asserted by Unna and others. Unna's staining method with Victoria blue and saffranin colours normal bacilli blue, and dead bacilli yellow.

The lesions show large cells—the 'lepra cells,' containing large masses of bacilli—but in addition to these cells there are also masses of bacilli embedded in mucus, and not enclosed in cells, which are the 'globi' of older writers, and which in fresh preparations appear as large, rounded, brownish masses. Bayon believes that the bunches of bacilli arise partially by the choking of the lymphatics by phagocytes swollen by the numbers of the bacilli which they have engulfed, and partially by the endothelium of the vessel wall also becoming distended with bacilli. The nuclei of these cells degenerate and are eliminated, while the remnants of the cells, together with the bacilli, form 'the globi,' and when these remnants disappear the bacilli are left free in the tissues. The hyaline coating of many bacilli may be a product of the protoplasm of these cells or may be secreted by the bacilli themselves. Sometimes typical giant cells, called 'Langhans' cells,' are seen. Marchoux and Bourret consider the so-called lepra cells to be undistinguishable from the large mononuclear leucocytes.

The bacilli do not invade the surface epithelium, nor the layer of the cutis directly below this; nor do they affect the sweat glands, nor the hair sheaths superficial to the opening of the sebaceous glands.

The typical leproma, therefore, shows superficially epithelium, normal in every respect, except that there are no interpapillary processes. Below the epithelium there is a layer of connective tissue, free from bacilli, under which lies the typical lesion, composed of lepra cells, plasma cells, and connective-tissue cells, separated by a very slight amount of fibrillar connective tissue, and containing vessels, whose walls are thickened by an infiltration of the adventitia, media, and intima to such an extent that at times the lumen may be obliterated, while the lymphatic spaces are dilated and filled with bacilli surrounded by mucus, forming the 'globi.' Beneath the lesion the connective tissue may be more or less normal.

The attacks of fever and the erysipelatous eruptions, which will be described under the Symptomatology, are explicable by the dissemination of the bacilli throughout the body by the blood stream, the bacilli being contained in the large mononuclear leucocytes, according to Marchoux and Bourret, and by the embolism of the capillaries of the skin by bacilli and white cells, which, however, are soon recovered from.

Lesions may remain stationary for years, and retrogression may take place as the result of treatment, or spontaneously, in which case the dead bacilli are absorbed, and sac-like spaces left, which rarely become sclerosed by connective tissue. If on a surface, the leproma may soften, break down, and ulcerate, thus disseminating the bacilli in the discharge.

The bacilli may also enter into the nerves and cause a hyperplasia of the connective tissue cells of the coats and the formation of typical leproma cells at first around the vasa nervorum, and later in the perineurium and endoneurium.

These cells press on the nerve fibres, causing a degeneration of the neurilemma, and later a disintegration of the arteries and a destruction of the nerve fibres, which finally results in the nerve being largely converted into connective tissue. In places where the nerve is apt to suffer from compression or other slight injuries, it becomes so thickened as to be easily palpable—a fact which Lie explains by saying that the bacilli which he found in the cutaneous nerves pass up the nerves and become located at spots liable to injury.

It is usually believed that the nerves only are affected, and that the paralyses, etc., are the results of disease of the peripheral nerves, but it has been shown that the bacilli attack the anterior cornua of the spinal cord, and therefore this may play a part in the production of the symptoms.

The bacilli may be carried by the blood stream all over the body, but show a selective affinity for certain organs, in which they develop the typical leprotic lesions. A certain number of leprotic subjects react to tuberculin injections, and give a positive Wassermann reaction.

Morbid Anatomy.—The skin lesions which may be found are the tubercles, which may or may not be ulcerated, and the pigmented and apigmented areas. On cutting into the leproma, it is seen to be situated usually in the cutis, and covered by the epidermis; but it may lie in the subcutaneous tissue, in which case it does not form a tubercle. It is yellowish-white in colour, firm in consistency, and if squeezed, usually a little clear fluid can be obtained. It will be noted that the sweat and sebaceous glands and the hair follicles are compressed and as a rule atrophied, while vesicles and pustules may occur on the surface, which may be ulcerated and covered with crusts. The macules consist of round-celled infiltration, with but few large cells, which are generally free from bacilli. In the spots which during life were anæsthetic, which are derived from the macules, the corium is largely converted into fibrous connective tissue, which has caused glands and hairs to atrophy and disappear.

The typical lepromatous infiltration may occur, not merely in the skin, but in the mucosæ of the tongue, pharynx, larynx, epiglottis, and in the submucosæ of the intestine.

The liver, which is usually enlarged, shows a leprous infiltration of the portal systems, while the spleen, which also may be enlarged, shows the same along the course of its vessels, particularly while they are in the septa, and a similar infiltration may be seen at times around the bronchi.

The ovaries and testes may show infiltrations and fibrosis of the interstitial tissue, which destroys the secretory elements, and causes the sterility which is usually so marked among lepers. The lymphatic glands are often enlarged, infiltrated, and full of bacilli, especially the femoral. Nephritis and leprous infiltration of the kidneys may be seen. The nerves most commonly affected are the palmar branch of the ulnar, the ulnar, the median, the peroneal, posterior tibial, and the great auricular. When exposed, the nerve is seen to show a fusiform, reddish-grey swelling, which, when examined, is found to consist of lepromatous tissue lying among the nerve fibres.

In the spinal cord there may be posterior sclerosis and meningitis, though it is doubtful whether these are really due to the disease or to some complication. The cells of the posterior cornu have been said to be atrophied, as well as those of the anterior cornu, in which Lie has found bacilli.

In the circulatory organs periarteritis and endarteritis are met with, while osteomyelitis, necrosis, caries, and absorption of the bones may be seen, and will be mentioned again later. Trophic changes in the joints and perforating ulcers are met with in the nerve form of the disease.

For a long time the presence of lepromata in the lung was disputed, but recently it has been proved that the lungs can become infected with leprotic lesions. The lesions of leprotic lungs are very similar to those of tubercular lungs, but are more solid, caseate less frequently, and are less prone to be destroyed. Some of the earliest signs are petechial haemorrhages, which upon microscopical examination show a diffuse, small, round-celled infiltration, with occasionally a giant cell, but without fibrosis, but with a slight cellular exfoliation in the surrounding alveoli and congestion of the bloodvessels and capillaries. In these areas there are numerous intracellular leprosy bacilli (Wise). In addition there may be an acute and at times caseating parenchymatous inflammation or chronic diffuse interstitial inflammation. These are distinguished from similar tubercular affections by inoculation into guinea-pigs with negative results.

Symptomatology.—The *incubation period* is entirely unknown, and must necessarily remain so until the method of infection and the date of the onset of the disease is discovered; hence the statements made by the different observers that it may last for a few weeks or months up to many years. The *method of invasion* is also quite unknown. Sticker suggests that it begins with nasal symptoms—blocking of the nose, epistaxis, and frontal headache; other observers with skin eruptions. The truth appears to be that, so far, the initial lesions and their symptoms, if any, have escaped notice.

Before the eruption appears there are, in many cases, attacks of fever of an intermittent or irregular character, with a marked feeling of general illness, associated with headache and pains in different parts of the body, peculiar sensations of cold, formication or numbness in various places, and, above all, of abnormal local or general perspirations. These attacks of leprotic fever, without any definite clinical signs of leprosy, may occur at intervals for years. This fever is probably due to the dissemination of the bacilli through the body, and may represent a septicæmic process due to the *Bacillus lepræ.*

After the general dissemination through the body, the bacilli appear to settle mainly in the skin or in the nerves, though, of course, there are many cases in which they settle in both. It is therefore convenient to distinguish the two varieties of the disease, first differentiated by Danielssen and Boeck-- viz., 'lepra tuberculosa,' or 'nodular leprosy,' and 'lepra maculo-anæsthetica,' or 'smooth leprosy' remembering that the division is artificial, and that numerous cases exist which show both forms.

TUBERCULAR LEPROSY.

After repeated attacks of fever the patient has a more severe one, during which an erythematous, diffuse, or macular eruption appears on the face and limbs. The fever subsides, and the maculæ may disappear or thicken and become tubercles, which are dermal lesions projecting from the skin or mucosæ, in addition to which there are subdermal infiltrations, which can be more easily felt than seen. If they disappear, it is only for the time, as new maculæ will appear with a new attack, and sooner or later the thickening will take place, and the nodules or tubercles, typical of the disease, will appear. Each outbreak of nodules is in some cases preceded by an attack of fever, with or without an erysipelatous-like eruption in the area to be affected, associated with enlargement of the lymphatic glands. In our experience, however, the fever may be absent in many cases.

The nodules may form all over the skin, but are most common on the face and limbs In the former situation they appear on the forehead, cheeks, alæ of the nose, lobules of the ears, lips, and chin, and as they increase in size, totally alter the appearance of the patient, defacing the natural facial lines, and forming new furrows between adjacent nodules; while at the same time, in many cases, the hair of the beard, moustache, and eyebrows drops out. These changes result in the countenance becoming like that of a satyr or, when the furrows are more marked, like that of a lion; hence the terms 'satyriasis' and 'leontiasis,' which the ancients applied to the disease.

Eye lesions are more commonly met with in this form of the disease, for Borthen, as the result of his investigations, concludes that only 8·08 per cent. of women and 1·67 per cent. of men suffering from tubercular leprosy escape without some form of disease of the eyes or their adnexa. Women are, however, less affected than men, but age shows no influence on the production of eye affections. In tubercular leprosy the eye is attacked by genuine leprotic lesions, and secondary infections are rare.

The supraciliary region, as has already been mentioned, is early attacked, and complete madarosis is not uncommon, and, later, paralysis of the frontalis muscle sets in. The eyelids are often attacked by diffuse or nodular lepromata, which may be merely extensions from the disease already in the supraciliary region, or may be quite distinct lesions. As a result of ulceration of these nodules, the eyelids may be destroyed.

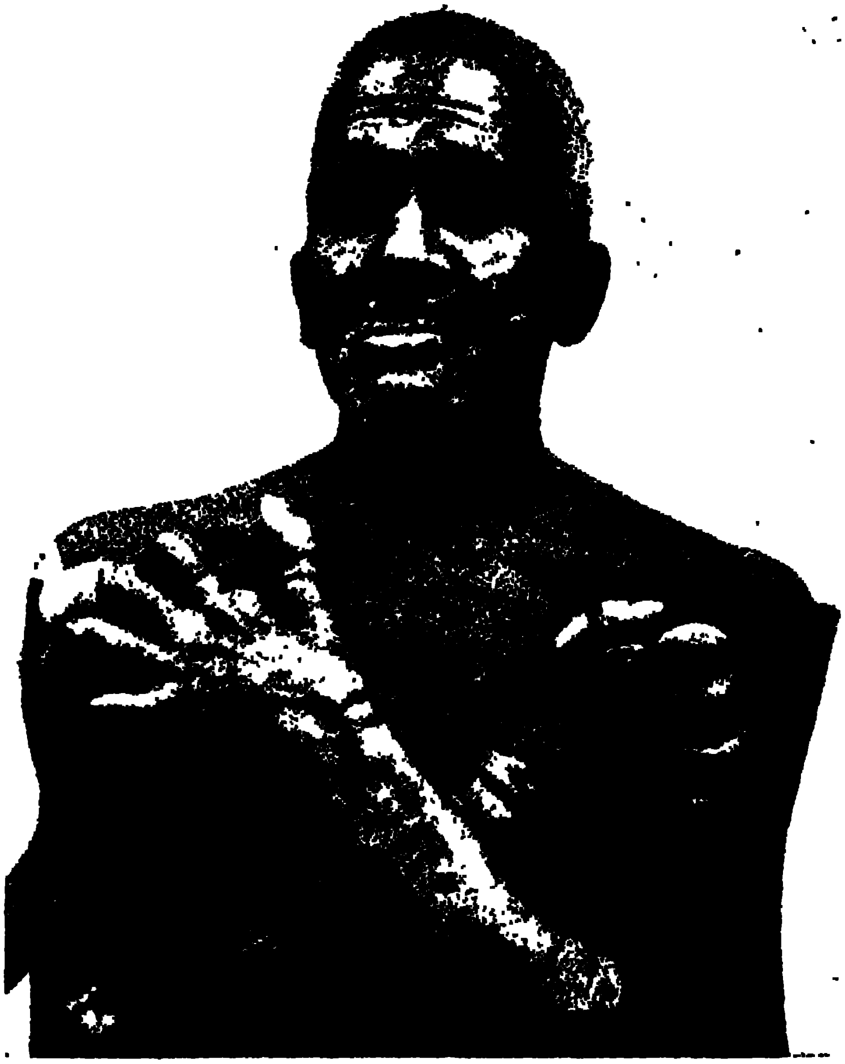

FIG. 727.—LEPROSY, SHOWING THE ERYSIPELATOUS-LIKE ERUPTION ON THE ARMS AND FACE.

The conjunctiva may be infiltrated, leading to hyperæmia, or, more rarely, anæmia, and producing lagophthalmos, ectropion, and, if cicatrization takes place, xerophthalmia.

The episclera is apt to become infiltrated along the external aspect of the corneo-sclerotic junction, resulting in white, grey, or yellow flattish masses, which spread round the cornea dorsally and ventrally, and are prone to invade its tissue in the form of a diffuse infiltration, which spreads from the outer side towards the pupil. More rarely small spots form on the cornea, giving rise to the 'keratitis punctata leprosa' of authors.

The disease may also spread to the uveal region, in the form of an infiltration, which causes an anterior or posterior iritis; or, more rarely, nodules may form in the ciliary body or near the canal of Fontana, giving rise to an irido-cyclitis or irido choroiditis.

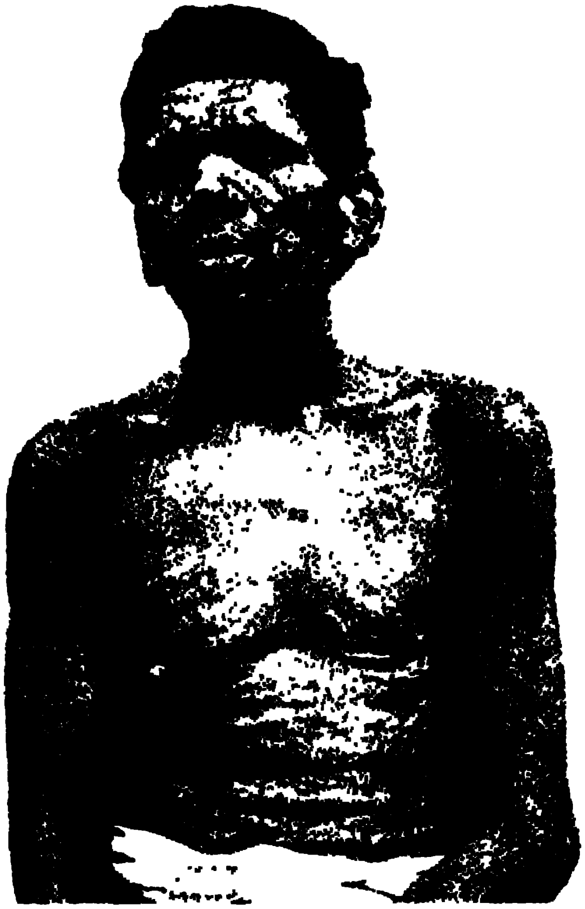

FIG. 728.—TYPICAL TUBERCULAR LEPROSY, SHOWING THE LEONINE EXPRESSION, THE THICKENED SUPERCILIARY RIDGES, AND THE MADAROSIS.

Lie has studied the pathology of these lesions, and has shown that it is rare for the optic nerve, the retina, the lens, and the vitreous humour to be affected.

The mucosæ of the nose may be attacked, with, first, blocking of the passage, and then, when the leproma extends down to the cartilage and ulcerates, falling-in or destruction of the nose, with much disfiguration of the countenance, resulting from the cicatrization which follows the ulceration. The tongue may also be affected, and show numerous tubercles, separated by furrows, or it may be simply infiltrated. The walls of the mouth and pharynx may become lepromatous, which causes mastication and deglutition to be rendered difficult, while the same condition in the larynx makes the voice raucous, and may impede respiration, especially if there is ulceration and cicatrization.

The skin of the hands, arms, and legs also shows numerous raised tubercles, which may ulcerate. The nipple is often infiltrated. The submaxillary, cervical, and femoral glands may be enlarged, and may suppurate. The testes often become fibrous, and menstruation becomes irregular and stops.

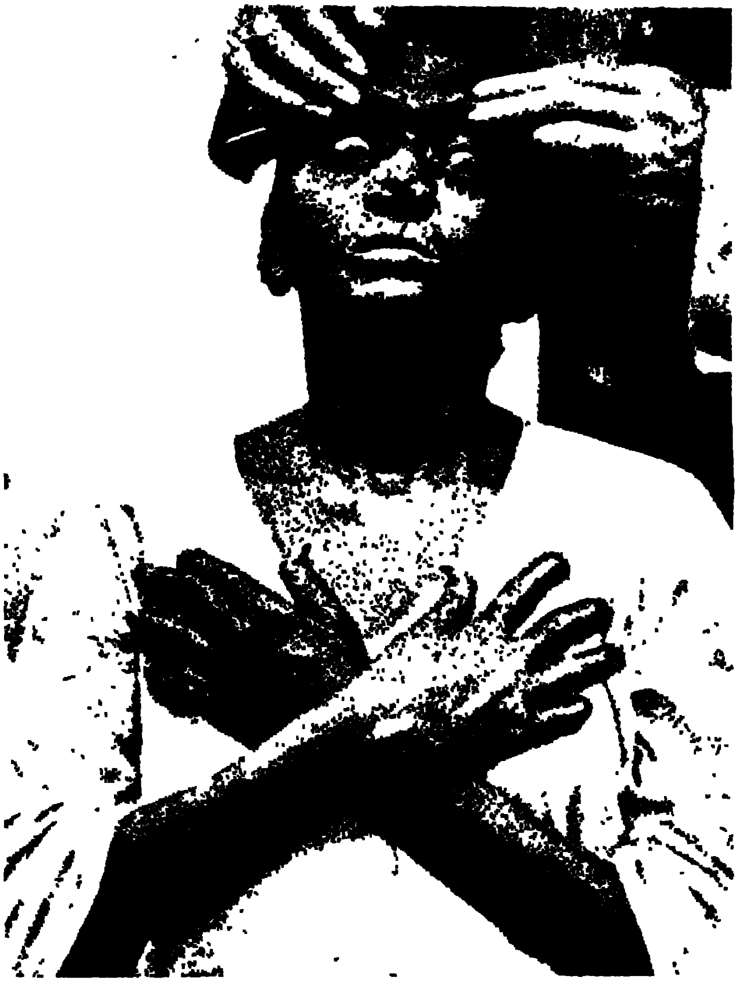

FIG. 729.—DIFFUSE INFILTRATION OF BOTH CORNEAS AND DEFORMITIES IN THE FINGERS OF THE RIGHT HAND.

Blood.—In the early stages the blood shows no changes, but later it shows a diminution in the erythrocytes and a lowering in the colour index. The red cells may show abnormalities in the form of poikilocytes, polychromatophilia, and basophilia. The number of leucocytes is generally normal, or, according to Bourret,[1] diminished; while this observer records an eosinophilia in all stages of the disease, which he says may at times be quite considerable. There may be leucocytosis during the febrile attack. Neutrophile myelocytes may also be observed. According to our researches the leucocytic formula is extremely variable, and is of no help in the

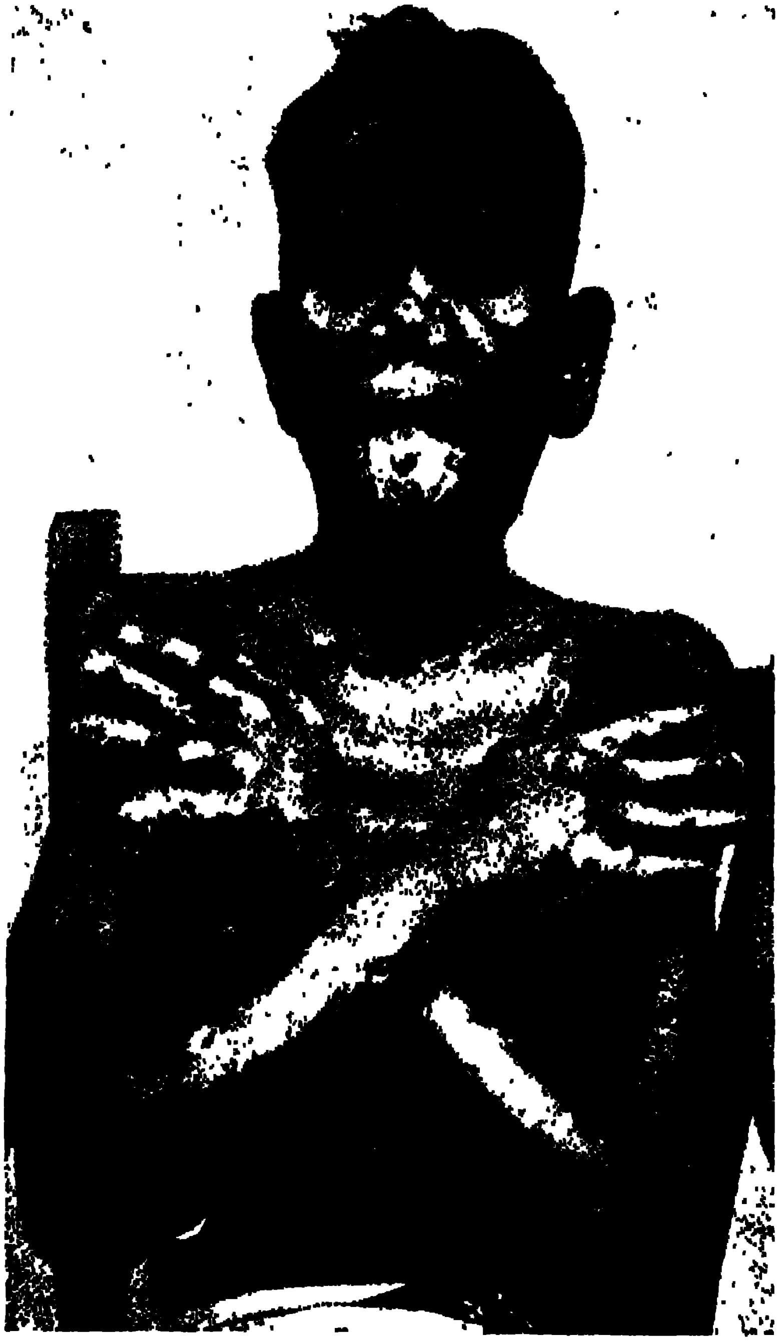

FIG. 730.—LEPROMA OF THE TONGUE.

special leucocytic index. Some authors state that they have found the specific bacillus in leucocytes, or, more rarely, free in the peripheral blood. Wassermann's reaction is, in our experience, at times present even in cases where there is no history of syphilis or yaws.

Urine.—There are not many observations upon the urine. The most marked feature is a great increase in the ethereal sulphates. Brinton, of Rio de Janeiro, has isolated two ptomaines from the urine, one allied to choline and the other to muscarine.

The nerves may become attacked, and the signs and symptoms of nerve leprosy be added to those of the tubercular, forming a variety of mixed leprosy.

The ulcerations generally become marked towards the end of the disease. If treated, they cicatrize and produce deformities: if left to themselves, they suppurate and produce amyloidosis, or, becoming phagedænic, cause gangrene of the fingers or toes, and septic poisoning.

Complications, in the form of phthisis and amyloidosis, appear, causing fever, cough, and expectoration, diarrhœa, and enlargement of liver and spleen.

Unfortunately, in the midst of disease of almost every organ of the body, the mind is quite clear; but the patients are most irritable, and it is not surprising that, under these circumstances, the patients of a leper asylum require considerable tact in management, and are often peevish and discontented, and that small rebellions occur.

MACULO-ANÆSTHETIC LEPROSY.

In this form of leprosy the infiltration takes place principally into the nerves, with the result that first the fibres are irritated, and later they become destroyed. The first stage is therefore one of irritation of the nerves with such symptoms as shooting-pains down certain nerves, especially the ulnar and the peroneal, accompanied with sensory disturbances, such as burning, numbness, formication, along with vasomotor disturbance—*e.g.*, flushings of the face, glossy skin—and motor disturbance, such as twitching of the muscles, particularly of the face.

Sooner or later a macular eruption appears, which is looked upon by some as due to a lepromatous infiltration of the skin, and by others as nervous in origin. This macular eruption may appear as flat red spots of various shapes and sizes, neither hyperæsthetic nor anæsthetic at first, which appear without fever or any general disturbance of the health. Other maculæ may appear which, instead of being red, are simply pigmented, while still others may be seen in which the pigmentation is less than usual. In any case the spots grow larger, the centres becoming pale, while the peripheries, which are usually raised, and occasionally marked with papules or vesicles, or covered with dry whitish scales, may coalesce with other spots, forming large areas.

The skin in the affected area becomes anæsthetic; the hairs fall out, and wrinkles and scales appear. After a time the areas cease to spread, the raised margin disappears, and the disease becomes quiescent.

Meanwhile the infiltration into the nerve trunks has proceeded to such an extent that a swelling can be easily felt in certain regions —as, for example, in the ulnar behind the internal condyle, in the great auricular over the sterno-mastoid, in the peroneal just below the head of the fibula, and in other nerves in suitable places if affected. With the destruction of the nerve fibres, the hyperæsthetic stage ceases and the anæsthetic stage of the disease begins.

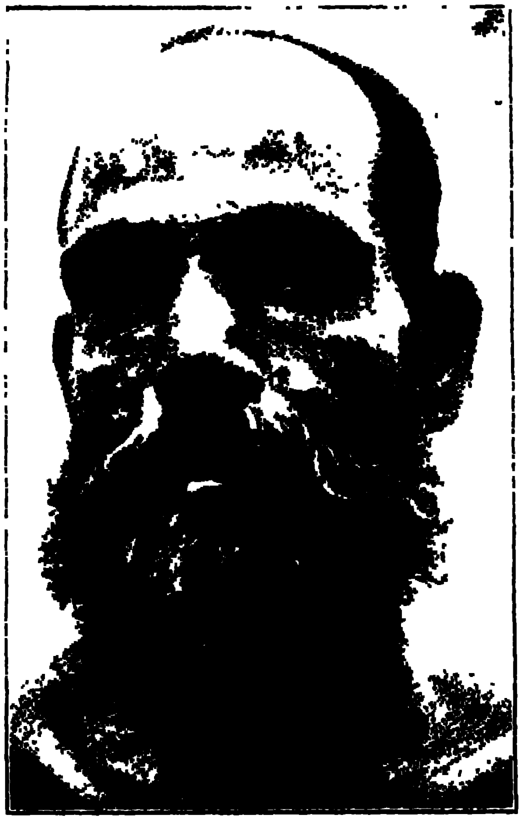

FIG. 731.—MACULO-ANÆSTHETIC LEPROSY: CIRCINATE TYPE.

This is to be noticed along the ulnar side of the hand, forearm, and arm, or on the inner side of the foot, first of all, and afterwards in other places. It may be segmental in arrangement, restricted to the distribution of a nerve, or in patches. At the same time the muscles may be found to be paralyzed, notably the interossei of the hands, but also those of the foot, if carefully looked for. The lower efferent neurones being affected, the symptoms resemble those of muscular atrophy of the Aran-Duchenne type, with the production of the main-en-griffe and the extension of the paralysis to the muscles of the forearm, and even at times, according to Jeanselme, to the deltoid. As a result of the paralysis of the muscles of the forearm the occurrence of dropped wrist is not uncommon.

In the lower limb the plantar muscles of the toes may be affected, while the spread of the paralysis to the peronei and extensors may result in a dropped foot with an internal twist. The reflexes are exaggerated at first, but when paralysis sets in they diminish, and when the muscles waste, the reaction of degeneration may be obtained electrically.

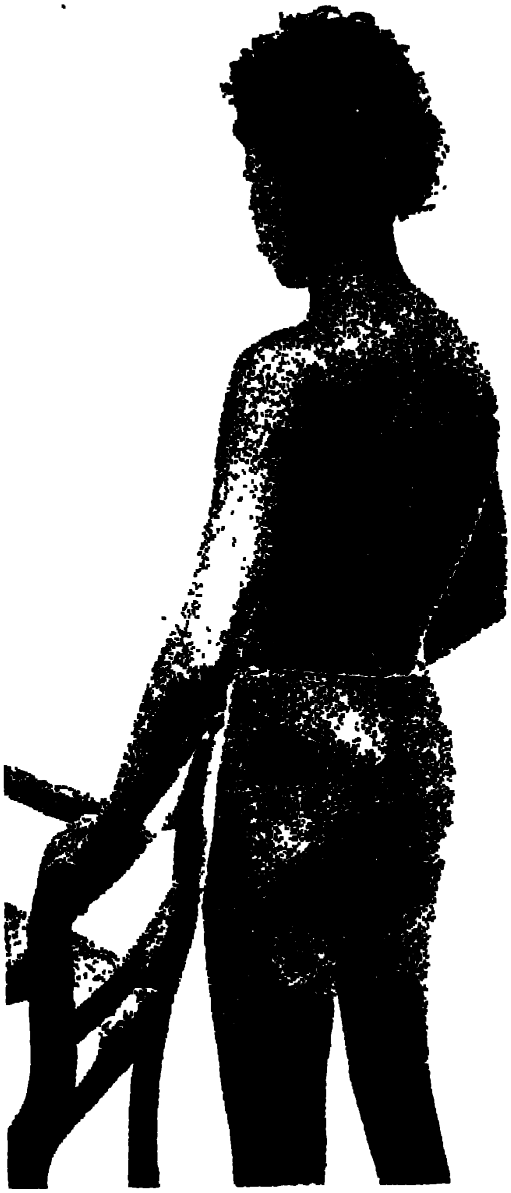

FIG 732.—MACULO-ANÆSTHETIC LEPROSY.

Trophic lesions may also appear in the form of whitlows in the fingers and necrosis of the phalanges, or, instead of this, a simple absorption of the bone of the phalanx or metacarpal, so that the nail may ultimately appear to spring from the metacarpal, the wrist, or even, it has been said, from the elbow. Similar trophic lesions may appear in the foot. Bullæ may appear on the hands or feet, and when broken may form ulcers. Injuries to anæsthetic areas may also result in ulcers, which may be of the perforating type. Fissures may form in the digits, hands, or feet, and, more rarely, dry gangrene may cause loss of the fingers or toes, or greater portions of the limbs, and, still more rarely, the bones of the fingers will soften and become osteomalacic. Trophic lesions of the elbow or knee, like Charcot's joints, have been recorded.

Jeanselme, Bourret, and one of us have studied the cerebrospinal fluid, and have found in a few cases a lymphocytosis, but more usually no cells or bacilli.

The eye is far less commonly affected than in the tubercular variety, Borthen's figures showing that in anæsthetic leprosy no less than 36·83 per cent. of the female cases and 26·80 per cent. of the male cases escape without eye complications. True leprotic lesions are much rarer, the eye being damaged by secondary infections brought about by the absence of the lachrymal secretion and the lagophthalmos. The forehead and supraciliary regions are often reddened and œdematous, but complete madarosis is rare; while paralysis of the frontalis, corrugator supercilii, and orbicularis palpebrarum cause lagophthalmos and ectropion; and as there is a diminution in the secretion of tears, xerophthalmia with posterior or total symblepharon, while desiccation and destruction of the cornea may result.

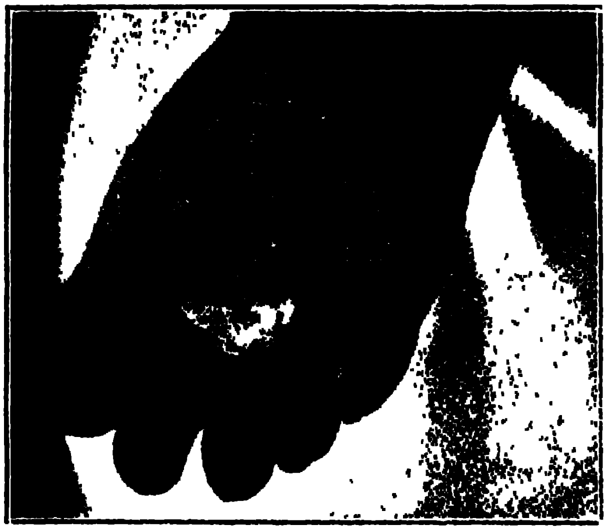

FIG. 733.—LEPROSY: ULCER OF THE FOOT.

Secondary infections may lead to keratitis, onyx, hypopyon, iritis, irido-cyclitis, and destruction of the eye.

Sterility is not so frequent in nerve as in tubercular leprosy. The skin may become infected at an early or late stage of nerve leprosy, thus forming one of the types of mixed leprosy.

Mixed Leprosy.

This term has been used to comprise those cases of tubercular leprosy which develop nerve symptoms, and those of maculo-anæsthetic leprosy which develop nodules, as well as those general cases in which both nerve and skin lesions advance hand in hand.

Paraleprosis.

Zambaco, Von Duhring, Glück, Leboeuf, and others have drawn attention to various phenomena indicating an attenuated infection in regions in which leprosy has long existed. These conditions are mostly nerve or trophic changes—*e.g.*, thickening of the ulnar nerve, the curving of the fingers, the loss of phalanges, the atrophy of the muscles of the hand or face, which are present in the children or grandchildren of lepers. Further, it is believed by some authors that syringomyelia and Morvan's disease may be modified forms of leprosy. Paraleprosis, however, requires further investigation.

Complications.—The important complications of leprosy are nephritis, phthisis, chronic enteritis, and dysentery. Amyloidosis occurs in the internal organs if there is much discharge from ulcerated surfaces. An interesting case of mixed infection—leprosy and syphilis—has been described by Frugoni.

Diagnosis.—The diagnosis of cases of the nodular type is generally easy, and may be readily confirmed bacteriologically by excision of a nodule and microscopical examination of a portion for Hansen's bacillus. The diagnosis of the maculo-anæsthetic cases presents greater difficulties, especially as in most cases the bacteriological examination of excised portions of the patches will give a negative result, though occasionally the examination of the blood taken from the patches or the surrounding zone may show a few mononuclear leucocytes containing bacilli. In these cases the diagnosis must be based on the presence of anæsthesia in the erythematous, non-pigmented, or hyperpigmented patches. Another valuable sign will be, in many cases, the palpable enlargement of the ulnar, peroneal, and other nerves. The search for the lepra bacillus in the nasal mucus is sometimes useful to clear the diagnosis. This method of diagnosis may be facilitated by administering a full dose (30 grains) of iodide of potassium, which often produces nasal catarrh. Sometimes this drug produces a general reaction accompanied by fever, and the appearance of fresh nodules. Leboeuf, acting on Marchoux's suggestion, has found Hansen's bacillus in the enlarged superficial lymphatic glands, and recommends the examination of the gland juice as a method of diagnosis. It is to be noted, however, that this examination will give a positive result much more frequently in nodular cases than in the macular type of the disease.

Chujo recommends drawing 5 c.c. of blood from the arm, diluting it with 200 c.c. of a 3 per cent. solution of acetic acid, avoiding contact with the air.

The microscopical examination would give more than 50 per cent. of positive results.

Some authors recommend the blistering of the skin, and examination of the liquid of the blebs for the presence of Hansen's bacillus. Thompson recommends for diagnostic purposes the injection of pilocarpine, with the view of discovering dry areas in the sweating skin.

Differential Diagnosis.– In countries where leprosy is endemic, other diseases are liable to be mistaken for it. One of the diseases most frequently mistaken, as has been pointed out by Powell and others, is framboesia, which may be recognized by the presence of the *Treponema pertenue* and the framboesiform appearance of the nodules. Leucodermic patches and morphoea are also occasionally mistaken for leprosy, but in such conditions there is no anaesthesia.

Prognosis.—The prognosis is not good. The probability of a permanent cure is slight, but the disease may last a long time. Four to twelve years is laid down for the mixed or tubercular leprosy, and longer for the maculo anaesthetic, and during that time a great deal can be done by appropriate treatment; and, indeed, the disease may be stopped for the time being, only, usually, to recur again. It has been shown by Lie that, even when all the skin eruptions have disappeared, and the patient is only troubled by anaesthesia, and the atrophy of the muscles, and may be thought to be cured, still the bacilli are present in the nerves and spinal cord.

Leboeuf from his recent investigations in New Caledonia has come to the conclusion that in a certain number of cases showing slight symptoms, an actual cure takes place.

Treatment.– So far no specific treatment has been found, though Carrasquilla attempted to prepare a serum by the injection of the blood of lepers into equines, and Abrahams and Hermann by inoculating the juice from lepromata into an animal. These sera have been found useless. Rost prepared a substance, which he called 'leprolin,' on the lines of tuberculin, but, unfortunately, the bacillus he was using was not the leprosy organism. Clegg's vaccine and Bayon's extract of Kedrowsky's strain have not been very successful. Tuberculin has been tried without success, and, in fact, very serious symptoms may follow its injection.

Chaulmoogra Oil.—As regards symptomatic treatment, there is no doubt as to the great value of Chaulmoogra oil, which is said to be obtained by cold expression from the seeds of some species of *Gynocardia* (*vide infra*), but may be adulterated with other oils, especially that of *Hydnocarpus wightiana*, or may be altered by being expressed when heated. It should be rubbed into the diseased patches, and also given internally in doses of 5 to 10 minims, working up gradually to 30 to 60 minims, in capsules, or in a pill with tragacanth and soap, or in an emulsion, or as Engel-antileprol capsules. To remove the after-taste a lime can be sucked. This treatment must be persisted in for a very long time, and should be combined with hot baths, and, in nerve cases, with doses of strychnine, $\frac{1}{60}$ grain three times a day, which may gradually be increased. After a length of time it is as well to make a slight break in the treatment, to prevent toleration, and therefore Unna's ointment of ichthyol, 5 per cent.; salicylic acid, 2 per cent.; and pyrogallol, 5 per cent., or some other ointment, may be temporarily substituted. But the Chaulmoogra oil must not be long discontinued, and must be persisted in for two years or longer if any good is to be obtained.

The oil may be given hypodermically, but is badly absorbed. To facilitate its absorption Heiser has successfully combined it with camphorated oil, and Mercado has combined the mixture with the resorcin formula of Unna. Heiser's present formula is—

Chaulmoogra oil	60 c.c.
Camphorated oil	60 ,,
Resorcin	grms. 4

Mix and dissolve with the aid of heat on a water bath and then filter.

The injections are made in the gluteal region, at weekly intervals, in ascending doses, one to five or ten cubic centimetres. During the treatment the patient takes a hot sodium bicarbonate bath (2 per cent.) every other day. The results are fairly satisfactory. *Sodium Gynocardate.*—Rogers recommends the intravenous injections of sodium gynocardate, which is supplied in sterile vials by Smith, Stanistreet and Co. in doses of $\frac{1}{10}$ grain and upwards. There is a definite reaction, local and general, after the injection. He also gives gynocardic acid and sodium gynocardate orally in 2 grain pills after meals, or by subcutaneous injection.

Neumann has advised the combination of salve and theonin with Chaulmoogra, given either by the mouth or hypodermically, but the advantages are doubtful, and Hollmann has recommended the use of eucalyptus oil in conjunction with opia leaves (*Jambos malaccensis*) or with Chaulmoogra oil.

Sources of Chaulmoogra Oil. According to Ghosh, true Chaulmoogra is *Taractogenes kurzii* from Burma and Assam; false Chaulmoogra is *Gynocardia odorata* from Sikkim, Assam, and Chittagong; other Chaulmoogras are *Asteriastigma macrocarpa*, *Hydnocarpus venenatus*, *H. wightianus*, *H. anthelminticus*. The oil known in Europe as Chaulmoogra is said never to come from *G. odorata*.

Cod-liver Oil and Sodium Morrhuate.—Cod-liver oil is occasionally beneficial. Rogers recommends an intramuscular injection (1 to 3 c.c.) every other day of a 3 per cent. solution of sodium morrhuate.

Other remedies are legion—*e.g.*, X rays have been well spoken of, but must be pushed to the extent of almost burning the patient. A 10-inch spark-coil with a bifocal tube, situate 7 to 10 inches from the lesion, has been used. Hypodermic injections of perchloride of mercury, as advocated by Crocker (0·01 gramme every other day), have been found satisfactory at times—a treatment which we recommend in cases at the very beginning of the disease.

Cashew nuts (Beauperthuy treatment) have been applied to the lepromata with the idea of local caustic action. Thyroid gland, salol, salicylates, arsenic, Gurjun oil, chlorate of potash, iodine, hypodermic injections of iodoform, have all been tried and found wanting.

Hypodermic injections of 'nastin' have been tried. This is a fatty principle extracted by Deycke from cultures of a streptothrix (*Streptothrix leproides*), which he found in the nodules of leprotic patients. The nastin is combined with benzoyl chloride, and made into ampoules with sterilized olive oil by Kolle and Company, of Biebrich, on the Rhine. Each ampoule contains from 0·0005 to 0·0002 gramme of nastin, which is to be injected once a week, and in the small doses produces no local reaction, but in the larger dose causes considerable local inflammation. Deycke's views as to the method of action are that the nastin attaches itself to the lepra bacillus, and then the benzoyl acts on the bacillus, damaging it by removal of its fat, when the normal fluids of the body complete its destruction.

Wise and Minett and others have reported unfavourably on this treatment, but recommend benzoyl chloride in petroleum oil as a valuable nasal spray or paint, as it renders the discharge from the nose free from bacilli.

Castellani and Woolley, and more recently Nicholls, have tried a vaccine prepared by triturating nodules rich in bacilli in salt solution or broth, then filtering through gauze, and finally heating to 60° C. for an hour.

Pasini has tried Finsen light, and Beurmann radium, with good results, and Luque, Moreno, and Padilla have obtained considerable improvement, and it is said cures, by treatment with decoctions of 20 to 60 grammes or 2 to 5 grammes of the powdered mangrove *Rhizophora mangle*, which, given in small doses at first, and gradually increased, are well stood, and produce a gradual improvement in the symptoms; and in the course of a year, it is said, cases may be cured. A. Bertarelli has obtained temporary good results by treating a patient with hypodermic injections of a solution of carbolic acid. Wellman and Rocamara have tried salvarsan, and claim good results. Maxwell has tried Williams' leprolin and Malegin Sprengler's I.K. Lepra with good results. Sugai recommends intravenous injections of a solution of potassium cuprocyanide.

Surgical treatment on the ordinary lines is required for ulcers, whitlows, etc. Eye lesions should be treated as though the disease was non-leprous, and should not be neglected. Grossmann thinks that leprous infiltration might be arrested by the production of cicatricial tissue, by a corneal or pericorneal incision.

With regard to other measures, lepers should be provided with plenty of fresh air and good food, and their quarters should be kept strictly clean. Care should also be taken that they are supplied with some form of light work and amusement, and the institution of rural colonies, provided they are well supervised, is to be recommended.

Prophylaxis.—Beyond isolation and antiseptic precautions after handling leprous people, nothing more can be done, as so little is known about the causation of the disease. The financial burden of isolating large numbers of lepers is very heavy. Hence the difficulty of carrying out this very necessary method of protection completely and efficiently.

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CHAPTER LXX

HISTOPLASMOSIS

Definition—History—Ætiology—Pathology—Morbid anatomy—Symptomatology—Treatment—References

Definition. Histoplasmosis is an acute specific infection caused by *Histoplasma capsulatum* Darling (*Cryptococcus capsulatus* Darling).

History.—This disease has been described by Darling, who also found the parasite, but being first discovered post mortem, the clinical signs are rather deficient. The first case was in a negro who, three months previously, had come from Martinique to the Canal zone of Panama.

Ætiology.—The disease is caused by the parasite *Histoplasma capsulatum* Darling, which was at first considered to be a protozoon, but is now believed to be a fungus (*Cryptococcus capsulatus* Darling, p. 1070).

Pathology.—The parasite infects epithelial and endothelial cells of the lungs, liver, and spleen. It also exists free in these organs. In the lungs it gives rise to pseudo-tubercles resembling miliary tubercles.

Morbid Anatomy. In the first case there were ecchymoses and small nodules beneath the visceral pleura of both lungs, which was studded throughout with pale grey hyaline and miliary tubercles, 2 to 3 millimetres in diameter, while the remainder of the organs were of a bright red colour. The peribronchial glands were full of soft caseated tubercles. The heart was small, but normal. The liver was enlarged, pale, and in a condition of slight atrophic cirrhosis. The spleen was enlarged to about three times its usual size, very firm, with distinct Malpighian bodies. The kidneys were slightly cirrhotic; the pancreas, bladder, bone-marrow, and brain were normal, and no tubercle bacilli could be found.

Microscopically the lung tubercles were found to consist of alveoli, the walls of which were broken and collapsed, and were filled with alveolar epithelial cells distended with parasites. In the liver the hepatic cells and the vascular endothelial cells were much infected with parasites. Some areas which stained badly were found to consist simply of the débris of cells with numerous parasites. The spleen showed intracellular and free parasites.

Symptomatology.—The symptoms closely resemble those of Indian kala-azar, there being irregular fever with enlargement of the spleen and liver, and severe anæmia with marked leucopenia.

Treatment.—Nothing is known as to the treatment or prophylaxis.

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CHAPTER LXXI

BERI-BERI AND EPIDEMIC DROPSY

Beri-beri—Infantile beri-beri—Epidemic dropsy—Potter's references.

BERI-BERI.

Synonyms.—Polyneuritis Endemica, Neuritis Multiplex Endemica, Hydrops Asthmaticus, Synclonus Beriberia, Myelopathia Tropica Scorbutica, Paraplegia Mephitica, Sero-phthisis Perniciosa Endemica, Panneuritis Endemica, Berbiers, Kakké (signifying a disease of the legs in Japan and China), Loempoe (Java), Kaki lem but, Hinchazon de los Negros y Chinos, Maladie des Sucreries (French Antilles), Hinchazon (Cuba), Inchaçao, or Perneiras (Brazil).

Etymology.—The word 'beri-beri' is said to be derived from the Sinhalese term, meaning 'cannot,' which is used as a phrase, which means 'I cannot,' employed in the sense that the person is too ill to do anything. There is another Sinhalese word which may equally be translated as 'cannot,' but this means that the person is unwilling to do something, not that he is too ill to do it. It is possible that the above interpretation of the word is correct, for Ceylon has long been in the hands of Europeans—*e.g.*, Portuguese, Dutch and English—and therefore a term used therein would be widespread. There is no doubt that the word covered a large number of diseases, from which a definite pathological entity has gradually been separated out. It is to be noted, however, that—at all events, at the present time—the disease does not exist endemically in Ceylon, where there are only imported cases.

Definition.—Beri-beri is an acute or chronic, endemic or epidemic, disease, of unknown causation, which is characterized by degeneration of many peripheral nerves, especially the vagi, the phrenics, and those of the limbs, associated with gastro-intestinal disturbance, cardiac disturbance, and œdema.

History.—According to Scheube, it is possible that the first mention of beri-beri is to be found in the accounts given by Strabo and Pio Cassius of a disease which attacked a Roman army in 24 B.C. in Arabia. Kakké is also mentioned in a Chinese pamphlet belonging to the second century of the present era, and is minutely described in another belonging to the seventh century, while it is recorded as occurring in Japan in the ninth century. In the tenth century a distinction was made between the atrophic, dry, or paralytic, and the hypertrophic, wet, or dropsical forms of the complaint.

In 1758-59 Bontius was the first European doctor to give an account of the disease, which he described under the term 'beri-beri.'

Later, Tulpius, a Dutch physician, also described the symptoms of the disease as seen in a person who had returned to Holland from the Indies. From that time the literature on beri-beri has grown until it has reached enormous proportions, but unfortunately there is no doubt that until recently several diseases, especially ankylostomiasis and epidemic dropsy, were confounded with it. Rogers in 1808, and later Davy, described the disease as 'beri-beria,' while the latter says that it is almost peculiar to Ceylon. There is little doubt that the condition described by Davy was in reality ankylostomiasis.

In 1847 Carter gave a description of the disease, indicating asthma as the principal feature, probably because of the cardiac dyspnœa. In 1873 Fayrer laid great stress on œdema as the important clinical feature. In 1877 Wernich defined the disease kakké in Japan, while van Meedervoort showed that it was the same disease as beri-beri. In 1886 Kynsey published an account of the anæmia or beri-beri of Ceylon, by which he really meant ankylostomiasis: hence the idea that beri-beri was due to *Ancylostoma duodenale*, and hence the large number of cases of so-called beri-beri in Ceylon years ago.

The scientific and clinical study of the disease has been largely due to the work of Oudenhoven, Da Sylva Lima, Overbeck de Rieyer, Baelz, Scheube, Pekelhäring and Winckler, Hamilton Wright, Jataki, Braddon, Fraser and Stanton. The workers on the ætiology of the disease are so numerous that this part of the history is best treated in the section on the causation.

Beri-beri is in certain regions a most serious disease. Thus Braddon says that in the Straits Settlements and Malaya, where the population is only 1,250,000, no less than 150,000 cases of the disease, with 30,000 deaths, have occurred in Government hospitals and infirmaries in the last twenty years: but he says that only one-third of the deaths of Chinese took place in those hospitals, and therefore the total deaths in that period would be about 100,000. It is also a great element in inefficiency, for it is reckoned that 33 per cent. of the sailors of the Japanese Navy prior to 1884 were continuously disabled by it. In 1904-05 it is said that 24 per cent. of the entire sick and wounded in the Japanese armies—*i.e.*, about 85,000 men—were also disabled by it. It is obvious, therefore, that the disease is of great medical and economic interest, for its incidence particularly falls upon the labourer, the sailor, the soldier, and the prisoners in the gaols, and hence hampers both the employer of labour and the Government. Braddon estimates the cost of the disease to the Government of Malaya as £10,000 per annum in direct hospital charges only.

Much work has been done by Eijkman, Vordeman, Fraser, Stanton, Funk, and many other observers, with the result that the consensus of opinion at the present time is that beri-beri is a *deficiency disease*—*i.e.*, is caused by the deficiency of some essential substance in the dietary (*vide* Chapter IV., p. 109).

In 1913 Cooper, and in 1917 Chick and Hume, studied the subject of vitamines, the two latter especially dealing with beri-beri vitamine.

Climatology.—The endemic centre of beri-beri appears to be Eastern Asia, Japan, China, the Philippine Islands, Indo-China, Java, and Malaya. It is also said to occur in Brazil and, according to Plehn, in Réunion, Mauritius, Nossi-bé, Zanzibar, Cape Colony, Senegal, Angola, the Congo Free State, and the Cameroons. We have met with the disease on the Gold Coast in Chinese miners, but have not noted it in the native population, though it may possibly exist. Isolated epidemics, sporadic or imported cases, occur in England, Ireland, and other parts of Europe, the United States, Canada, and in Ceylon. In the last-named place it is now almost entirely absent, and, indeed, it is possible that many of the cases reported years ago may have been ankylostomiasis or some other disease. Imported cases from India and China are frequently met with in Colombo, owing to its possessing a large harbour where numerous vessels, with Chinese and Indian crews, call.

It is believed that the Bihimbo disease of the Chaka district of Uganda is beri-beri. The disease known in that country as munhiyo, and believed at one time to be beri-beri, has been demonstrated to be Malta fever. In the tropics it is said to occur more often in the cool wet months.

Ætiology.—The causation of beri-beri is at the present time believed to be due to the deficiency of some essential substance in the food, but as may be imagined in such a widespread and fatal disorder, the investigators have been many, and hence the theories are legion. In order to comprehend the present state of the question, it is necessary very briefly to review a few of these theories, which will be best done by following a method of classification.

A. Physical Cause.—The older writers, like Davy, considered that it was brought about by some unusual state of the atmosphere, but they said, honestly, that this was merely a cloak for their ignorance of the true cause.

B. Chemical Causes.—The chemical causes which have been advanced are:—

1. Arsenical poisoning (Ross).
2. Oxalate poisoning (Treutlein).
3. Carbon dioxide poisoning (Ashmead).
4. Food poisoning:—
   (*a*) Ichthyotoxismus (Grimm and Miura).
   (*b*) Sitotoxismus (Eijkman, Vorderman, Yamagiwa, Van Dieren); rice (Gelpke, Braddon); lathyrism (Le Roy de Méricourt).
5. Some deficiency in the food:—
   (*a*) Deficient nitrogenous complex (vitamine) (Eijkman Fraser, and Stanton).
   (*b*) Deficient nitrogen (Takaki).
   (*c*) Deficient fat (Brémaud and Laurent).
   (*d*) Deficient vegetables, together with an infection (Fales).
   (*e*) Deficient phosphorus.
   (*f*) Deficient cholesterin (Chrisostem)
6. An intoxication from a germ living outside the body (Manson).
7. An intoxication or an auto-intoxication (Duerck).

1. **Arsenical Poisoning.**—R. Ross, in 1900 and subsequent years, drew attention to the similarity between beri-beri and the arsenical poisoning which at that time was prevalent throughout Lancashire, being brought about through the agency of arsenical beer. He further supported this by finding arsenic in the hair in recent, but not in old, cases of the disease in Penang, and woke up a controversy as to whether arsenic existed in normal hair or not. But apart from the obvious reasons against this theory as an explanation for such a widespread disease, Herzog has definitely shown that no arsenic could be found in the hair of ten cases of different types of the disease. There is no doubt that cases of chronic arsenical poisoning do occur in the tropics, as we have seen, particularly in Europeans who have had to live for a long time on tinned food, but these cases are not beri-beri.

2. **Oxalate Poisoning.**—The oxalate theory is based upon the fact that Maurer and Treutlein were able to produce a condition resembling beri-beri in fowls by giving them oxalic acid in their food. The latter observer considered that the acid removed the calcium salts from the body of these animals, and caused thereby a degeneration of the peripheral nerves and heart muscle, and considered that this was proved by curing them by the administration of calcium salts. Further, he showed that there was an excessive excretion of calcium in the urine of beri-beri patients. But polyneuritis has been produced in fowls by Eijkman by feeding them with cooked rice, and it is possible that neither oxalic acid nor rice, but an infection, was the cause of the disease, which may, of course, be quite different from true beri-beri.

3. **Carbon Dioxide Poisoning.**—Ashmead believes that the disease is caused by the excessive inhalation of carbon dioxide, but outbreaks occur without any overcrowding, as we have seen ourselves.

4. **Food Poisoning.**—(*a*) *Ichthyotoxismus.*—Grimm considers the ingestion of raw fish to be the cause of the disease, and Miura the consumption of species of the Scombridæ; but Wright has shown that in the gaol at Kwala Lumpur, the disease infected forty-nine prisoners when no fish had been given for eight months.

(*b*) *Sitotoxismus.*—Rice poisoning at present is the favourite theory, and has had many supporters. Thus Eijkman and Vorderman consider that it is due to eating rice without husk, which is the natural protection. Gelpke considers that it is due to stale or badly-kept rice. Yamagiwa considers it due to rice improperly stored and preserved, as it occurs even when this rice is well boiled. Braddon, who is often wrongly quoted, ascribes the disease to the ingestion of a *poison* found in the rice, which is the result of the specific product of some organism—epiphyte or parasite—but he does not believe that the disease is due to the ingestion of the organism. Contrary to Eijkman and Vorderman, Braddon looks upon the husk as the dangerous element, as it is in this that the germ grows.

But the disease has been observed, according to Scheube, who quotes Fiebig and Voorthuis, in Brazil, the Moluccas and Lingga, where the people live on sago, fish, and game, and where the attacked Europeans had never eaten rice.

Travers details an interesting observation on this point concerning an epidemic of beri-beri in the Pudoh Gaol of Kwala Lumpur, in August, 1895, when some of the cases were transferred to the Old Gaol, one and a half miles distant, on October 1, 1895, because the mortality in the Pudoh Gaol was extremely high; and on October 25, 1805, sixty prisoners, showing no signs of the disease, and apparently in good health, were similarly transferred. From October 1 to December 14, 1895, all food supplied to the healthy prisoners in the Old Gaol, as well as to the beri-beri patients transferred from the Pudoh Gaol, was cooked in the Pudoh Gaol with the food for the other prisoners who were suffering from the disease.

This food was carried to the Old Gaol twice daily, and the diet was exactly the same in both gaols, the rice being taken out of the same bag and cooked in the same steamer. Further, it appears from Braddon's remarks that in 1895 a new scale of ordinary diets, with an increased amount of rice, was allowed, fresh fish was replaced by salted, and beans were omitted, and

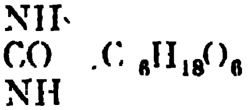
Braddon considers that it was this increase of the rice that increased the poison and made people ill; but this ought to apply to both places.

Moreover, Braddon considers deductions adverse to rice in the above experiment to be fallacious, for he holds that the length of period of incarceration of the above prisoners is an important factor; for the liability to acquire the disease, he says, increases with and varies directly according to the length of the time served in prison, which must be more than six months. He points out that it is not stated how many long-sentence prisoners were sent to the Old Gaol, which he thinks may not have been more than two or three; and concerning these, he says, there is no proof that any of them were kept for the period necessary to acquire the disease by rice intoxication. He therefore concludes that Travers' experience affords no ground for opposing the theory that beri-beri is incurred through the consumption of certain sorts of rice.

5. SOME DEFICIENCY IN THE FOOD—(a) *Deficiency of Certain Nitrogenous Complexes.* There is a growing tendency to consider that certain diseases—*e.g.*, beri-beri polyneuritis of birds, epidemic dropsy, scurvy, experimental scurvy, infantile scurvy, and ship beri-beri—are diseases due to the deficiency in some essential substance in the food. These diseases Funk classifies together as 'deficiency disease,' and characterizes them by certain general symptoms—*e.g.*, (1) Cachexia, with great loss of weight; (2) marked nervous symptoms, generally of the nature of peripheral neuritis. He divides these diseases into two groups—the beri-beri group comprising beri-beri, polyneuritis in birds, and epidemic dropsy; and the scurvy group.

With regard to beri-beri, as already pointed out, Braddon drew attention to the importance of rice as an ætiological factor. Eijkman in 1897 had shown that it could be prevented and cured by the use of hand-milled rice. Prisoners fed upon red rice escaped, and those on white rice were very prone to take the disease. Fraser and Stanton showed that members of gangs of coolies, who had previously remained quite healthy, developed beri-beri when fed on white rice, while other members fed on brown rice remained healthy. Strong and Crowell observed that in eight out of seventeen prisoners fed on white rice, symptoms of beri-beri appeared in from 61 to 75 days. The difference between these two forms of rice is that the white rice is deprived of its subpericarpal layers (*vide* pp. 104 and 105) by the process of milling.

These layers contain a substance called by Funk beri-beri vitamine, which is probably a base belonging to the pyramidine group, and has the formula—



$$\left.\begin{matrix}NH\\CO\\NH\end{matrix}\right.\,.C_6H_{18}O_6$$

and not $C_{17}H_{18}O_4N(HNO_3)$, as previously stated. This substance is soluble in water, alcohol, and acidulated alcohol, is dialyzable, and can be destroyed by heating to 130° C. It is present in the proportion of 0·1 gramme to the kilogramme of rice. According to Funk, this substance is essential for the metabolism of nervous tissue; and if it is not present in the dietary, must be supplied by the animal body, and if this fails, the nervous tissues begin to break down, and as a result the signs and symptoms of beri-beri appear.

Fraser and Stanton believe that the phosphorus content of the rice is a good index as to whether it is harmless or harmful. A safe rice yields more than 0·4 per cent. of phosphorus pentoxide, while a dangerous rice yields less than this figure. Chamberlain and Vedder have suggested that potassium should be used instead of phosphorus for standardization purposes.

With regard to these findings there is an almost unanimous support from all sides, but the Philippine investigators, while believing that their studies support the polished rice theory, bring forward the curious fact that beri-beri began to diminish among their Native Scouts during the last half year of 1910 without any decrease in the general incidence of the disease in the islands, and *four months before the use of under-milled rice was introduced into the dietary*. They consider that the reduction was either due to unknown causes acting coincidentally with a reduction in the amount of rice in the dietary, together with the addition of a legume, or was due directly to these dietetic changes.

Eijkman, Braddon, Fraser, Stanton, Vedder, and Chamberlain have done sufficient work to make imperative the use of brown rice cooked in ordinary vessels, and the exclusion of the white rice as a staple article of food.

Edie, Evans, Moore, Simpson, and Webster have separated an antineuritic base called 'torulin'– $N(CH_3)_2C_4H_7O_2(HNO_3)$– from yeast, and Thomson and Simpson have noted rapid recovery of patients placed on a full diet, and given 1 ounce of yeast and 200 grammes of katjangido-beans daily.

Heiser reports that after being present for five years in the Culion Leper Colony in the Philippines, beri-beri disappeared in nine months on a dietary of unpolished rice.

In 1917 Chick and Hume showed that in order to keep a man in health there must be (*a*) a suitably proportioned supply of protein, fat, carbohydrate, salts, and water; (*b*) an adequate amount of vitamines; and that these two factors could not replace one another. The vitamines of importance in beri-beri they call 'antineuritic or anti-beri-beri,' as the first term covers the polyneuritis in fowls. Neither vitamine has yet been isolated in a pure condition. Pigeons deprived of anti-beri-beri vitamine develop acute polyneuritis in fifteen to twenty-five days. The principal source of this vitamine is the seeds of cereals and pulses. In the former it is mainly deposited in the germ or embryo of the grain and to a less extent in the grain. It is also found in eggs and yeast. It can withstand drying and also temperatures of 100° C., but is destroyed at 120° C. The deduction is that, in order to prevent beri-beri, bread and biscuit should be made from the germ-containing or wholemeal flour. Antineuritic vitamines cannot be expected to survive in tinned or sterilized foods; hence the necessity in armies to supply vitamine from other sources.

The deficiency theory in some form is at the present time accepted all over the world, but there are still some observers who think that there may be more than one form of disease concealed under the name beri-beri.

The following objections have been raised against the food theory:—

(1) Beri-beri may occur in people who do not feed on rice. We have seen an epidemic among officers on a man-of-war.
(2) The geographical distribution. In populations eating the same kind of rice some suffer from beri-beri and others do not.
(3) Tamil coolies in Ceylon do not get beri-beri, though they suffer from this disease in the Straits Settlements. In both countries they are mostly supplied with the same kind of rice (Rangoon rice).
(4) People recovered from beri-beri go back to their usual rice diet without again suffering from the disease. Thus in the Malay States the mortality is only 20 per cent.; therefore 80 per cent. of sufferers recover. Do these people change their diet?

Fraga, having failed to produce beri-beri in prisoners fed on polished rice, believes that dietary deficiency acts merely as a predisposing cause.

(*b*) *Deficient Nitrogen.*—Previous to 1884, 33 per cent. of the sailors in the Japanese Navy were disabled owing to beri-beri.

In 1883 the *Ryujo*, a Japanese warship, went on a voyage of 271 days to New Zealand and South America, and developed 160 cases of the disease out of a crew of 350 men. Takaki investigated this outbreak, and came to the conclusion that there was too little nitrogen in the diet, the nutritive value of which was: Proteids, 109·29 grammes; fats, 15·8 grammes; carbohydrates, 622·32 grammes. He therefore changed the diet to: proteids, 196 grammes; fats, 43 grammes; and carbohydrates, 775 grammes; and on this dietary the warship *Tsukuba* was sent the same cruise, taking 287 days, and only suffered from sixteen cases of the disease. Takaki attributed the success to the increased nitrogen, a portion of the rice being replaced by corn or bread; but Fales has pointed out that fresh vegetables were increased from 215 grammes to 450 grammes, and that therefore nitrogen alone may not have been the cause of the decrease of the disease. This dietary was applied to the Japanese Army and Navy, and beri-beri decreased enormously. But Baelz has pointed out that this decrease was associated with a great improvement in general hygiene and that it also took place in barracks in which the food had not been changed. A similar decrease in the Dutch-Indian Navy, associated with a better diet, was attributed by some to the improved hygiene rather than to the diet.

(*c*) *Deficient Fat.*—Brémaud and Laurent believe that the disease is due to too little fat in the food, and consider that an epidemic at Chandabun, in Siam, was stopped by causing fat to be more freely consumed by the healthy. This theory, however, has found but little support.

(*d*) *Deficient Vegetables, together with an Infection.*—Fales, from a study of an outbreak of an epidemic of beri-beri in the Bilibid Prison, in Manila, came to the conclusion that the lack of fresh vegetables conduced powerfully to both beri-beri and scurvy.

In November, 1901, there were two cases of the disease, and no deaths, in that gaol. The food was then changed to a ration consisting of 97·17 grammes of proteids, 17·24 grammes of fats, 491·04 grammes of carbohydrates, and 26·52 grammes of salts. In this diet there were 85·05 grammes of potatoes, and 453·60 grammes of rice. Put into other figures, this diet consisted of: Nitrogen, 172·1 grammes; carbon, 4,166·5 grammes; hydrogen, 61·9 grammes; sulphur, 13·2 grammes; salts, 140·2 grammes—the proportion of nitrogen to carbon being as 1 to 24·2. Whereas, calculating the weight of Filipinos at 125 pounds, it was estimated that proteids ought, according to Voigt's diet, to have been at least 94 grammes, fats 45 grammes, and carbohydrates 400 grammes; or, according to Moleschott's diet, nitrogen 256 grammes; carbon, 3,789 grammes; hydrogen, 143 grammes, sulphur, 23 grammes; salts, 172 grammes—*i.e.*, N : C :: 1 : 0·15.

The epidemic of beri-beri now began: December, 1901, 52 cases and 2 deaths; January, 1902, 169 and 12; February, 1,087 and 16; March, 576 and 15; April, 327 and 15; May, 310 and 19; June, 451 and 17; July, 233 and 33; August, 571 and 24; September, 522 and 31.

On October 20 the diet was again changed, and this time proteids were 101·71 grammes; fats, 19·37 grammes; carbohydrates, 395·73 grammes; salts, 29·13 grammes; including 119·07 grammes of potatoes and 255·15 grammes of rice. Nitrogen was 209·8 grammes; carbon, 3,816·2 grammes; hydrogen, 70·4 grammes; sulphur, 17·2 grammes; and salts, 185 grammes—N : C :: 1 : 13·4.

In October there were 579 cases and 34 deaths; November, 476 and 8; December, 89 and 3; half January, 1903, 4 cases and no deaths.

Along with the beri-beri there was an epidemic of scurvy, and Fales was of the opinion that both diseases were led up to by a deficiency of vegetables, the essential principle of which he believes to be potassium carbonate, of which rice contains only 0·01 grain per ounce, while potatoes contain 1·875 grains. Hence, according to Fales, the disappearance of the disease when a sufficiency of vegetables, especially potatoes, was given. But he says this deficiency was only a predisposing cause, which enables the micro-organism, whatever it is, which is the true cause of the disease, to flourish and produce the symptoms. In other words, the people get run down by a bad diet, and are ready for any disease, so that this does not clear up the ætiology.

Recently Ingram has drawn attention to an outbreak in the 81st Pioneers and the 2nd Battalion of the King's Own Scottish Borderers, at Aden, in which he could find no clear evidence that beri-beri was due to diet alone, whether insufficient proteids or excessive rice, or bad rice, but he considered a diet rich in proteids good as a preventative. He could only find one thing in common in the two regiments—viz., both brought the disease with them—but was unable to find any source of infection, parasitic or otherwise.

(*e*) *Deficient Phosphorus.*—Schaumann and [illegible] have maintained that deficient organically combined [illegible]rus in the u[illegible]ed rice is the ætiological factor.

(*f*) *Deficient Cholesterin.*—Ch[illegible] has treated [illegible]s with injections of cerebrin with good results, and with 5 p[illegible]ent. cho[illegible]rin in olive oil with better results.

6. An Intoxication from a Germ living Outside the Body.—Manson brought forward the hypothesis that a germ may live in the soil, the house, or the ship occupied by the human being, under certain conditions of temperature and moisture, and may grow and produce some kind of toxin which, being inhaled or swallowed, or otherwise introduced, causes the disease. Moreover, this germ may be carried by men from place to place.

He supports this theory by pointing out—(1) that when patients are removed from an endemic spot they at once begin to rec[illegible] (2) he quotes Hirota's observation that fifty-two infants nursed by beri-beric mothers showed signs of the disease, and did not improve wh[illegible] treated medicinally, but rapidly improved, if th[illegible] had not advanced too far, when taken from these mothers and placed on artificial food or given to a healthy wet-nurse. Further, Herzog says that, according to Dr. Albert, similar cases are not very infrequent in the Philippine Islands, but the removal of the child from the mother is most difficult, as the people do not understand the necessity.

Manson rightly points out that these children must have been poisoned with some chemical substance, and not infected with a germ. But, of course, the germ causing the toxin might be in the mother's body.

Again, Manson points out that the disease clings to ships, in which it appears year after year when the tropics are reached. There is also evidence that the cause, whatever it is, clings to rooms for a short time.

7. An Intoxication or an Auto-Intoxication.—Duerck is convinced from the study of the pathology that the cause of the disease is a toxæmia, and points out that substances formed in the body by process of auto-

intoxication may produce peripheral neuritis, but the epidemics of the disease are quite against a theory of auto-intoxication.

C. Parasitic Causes.—A great many observers are in favour of a parasitic cause for the disease, without committing themselves as to whether it is animal or vegetal. Among these may be mentioned Sambon, who considers that the specific agent lives in the patient's body. Scheube considers that it is an infectious, but not a contagious, disease, and says that the analogy with malaria is in some respects striking, and that it is spread by mechanical transmission of the disease by human intercourse in some way or another. This is quite true, because there are numerous instances of disease being imported by human beings into a fresh place and spreading, but the curious point is that it generally sticks to one race.

Thus, in Malaya it is a common disease among imported Chinese, and hardly known among the natives. In the Bilibid Prison, mentioned above, the prisoners included Filipinos, Spaniards, Chinese, Japanese, Indians, American negroes, Americans, and Europeans, but the disease fell most severely on the Filipinos, the Chinese being almost exempt, only one or two contracting the disease, while the Americans were immune. Van der Scheer suggested that perhaps insects, such as cockroaches, might be the spreaders of the disease, but Durham's investigations are contrary to this. It would seem as though the causal agent was spread by some parasite, for Daniels has carefully considered the question of infection, and does not find any evidence in favour of it being conveyed by the excreta of persons suffering from the disease, especially the

Further, he points out that infection by air and water can be excluded, as in Kwala Lumpur all races drink the same water, but only Chinese are attacked, even though they drink little unl [illegible] water: and the immunity of prison officials from the disease while [illegible] pidemic rages among the prisoners excludes air. Disinfection appears, from Durham's results on Christmas Island, to be useless. As regards parasites Durham and Daniels are both against mosquitoes as being the cause—and, indeed, this is hardly likely—and also against bugs.

On the other hand, there appears to be some evidence in favour of *Pediculus capitis*, which is apt to cling to one race, and this is, according to Daniels, a plausible theory in explaining the racial selection of the disease. Experiments on an orang outang with pediculi from a beri beri case were negative, the lice rapidly disappearing. Daniels could not exclude fomites as a carrier of the disease in his observations. Only one observer, Taylor, is said to have produced the disease in animals by the inoculation of the blood from patients.

Having thus briefly considered the general question of contagium vivum, and its method of entry into the body, it is necessary to review the various organisms which have been held to be the cause of the disease.

They may be classified into:—

ANIMAL PARASITES:—

(*a*) *Protozoa.*

1. Plasmodium in the blood (Glogner).
2. Protozoon in the urine (Hewlett and Korte).
3. Hæmatozoa in the blood (Fajardo and Voorthuis).

(*b*) *Nemathelminthes.*

1. Some form of *Trichinella* (Gelpke).
2. *Trichuris trichiura* (Erni and Kynsey).
3. *Ancylostoma duodenale* (Erni and Kynsey).

VEGETAL PARASITES—FUNGI:—

(*a*) *Coccaceæ.*

1. Cocci in the alimentary canal, etc. (Dangerfield).
2. Diplococcus in the urine (Tsuzuki).
3. Diplococcus from the blood and urine or organs post mortem (Okata and Kokubo).
4. Four kinds of cocci (Musso and Morelli).

(*b*) *Coccus and Bacillus.*

Pleomorphic organism obtained by Pekelharing and Winckler from the blood.
Bacilli and cocci by Lacerda.

(*c*) *Bacilli.*

1. Bacillus by Taylor.
2. Bacillus by Rost.
3. Bacillus by Ogata.
4. Three kinds of bacilli by Nepveu.
5. Bacillus by Eecke.

Toxins from a bacillus in the alimentary canal (Hamilton Wright).

(*d*) *Fungi higher than Bacteria.*

Mouldy rice (Hose).

Protozoa.—Glogner's parasites were similar to malarial parasites, but were distinguished therefrom by being found only in splenic blood, by being always extracorpuscular, and by increasing by gemmation. They were more pigmented than malarial parasites. Scheube thinks that Glogner's cases were complications of beri-beri with malaria.

Hewlett and Korté centrifugalized the urine of beri-beri cases, and found small retractile spherical bodies, 2 to 3 μ in diameter, with a thick capsule and hyaline contents; others 20 μ in diameter, with a cytoplasm studded with retractile granules, and containing a single nucleus; and others 30 μ, with a thick capsule, an oval nucleus, and a rounded nucleolus. They further described the congestion of the glomerular vessels and hæmorrhages into the tubules of the kidney. Further, they saw a somewhat similar disease in monkeys, the urine of which contained highly refracted cells. They conclude that the above are either peculiar degenerate cells or protozoa, and suggest that the disease is a protozoan infection, and that the causal agent is eliminated by the urine. Fijordo and Voorthuis separately describe hæmatozoa, partly free and partly in the red cells, which are similar to, but not identical with, the malarial parasites. Their organisms do not agree with one another, nor do they correspond to Glogner's.

Nemathelminthes.—Gelpke suggested that the disease might be due to a *Trichinella* in fish, but he has withdrawn this. *Trichuris* and *Ancylostoma* need not seriously be considered, as this idea arose from a misunderstanding.

Fungi.—Pekelharing and Winckler's bacillus has also been found by Hunter, and experimental inoculations by both sets of observers produced degenerations of the nerves. But it must be admitted with regard to bacteria that competent observers have found the blood sterile time after time.

Hamilton Wright's bacillus, which occurs in the alimentary canal, has been found by Dudgeon to be non-pathogenic for monkeys, and not to be agglutinated by the blood of beri-beri patients. Stanley's experiments on animals with mouldy rice have been negative. Finally, attention may be drawn to the researches of Holst, Nocht, and the Norwegian Ship Beri-Beri Committee, which indicate that the so-called ship beri-beri is not beri-beri, as the symptoms are shortness of breath and weak heart, with weakness and dropsy of the lower limbs, but not paralysis of the limbs—*i.e.*, the degeneration of the nerves is not an essential phenomenon.

Chalmers and Archibald separately have found fungi in the organs of cases of beri-beri occurring at different times in British troops in Khartoum. We feel that more than one disease is included under the term beri-beri. One of these diseases is a ***deficiency disease***, but the others await discovery.

Predisposing Causes.—The disease can occur in all races, and at all ages, and in both sexes, but it is apt to cling particularly to one race in a country—*e.g.*, the Chinese in Malaya, the Filipinos in the

Philippine gaol outbreak. This racial incidence is most marked. Thus, Braddon says that of the Chinese immigrants into the Straits and Malaya, it may be reckoned that of every 1,000 living, 120 suffer and 16 die of the disease. The Malayas are said to suffer but little, if at all. In the Bilibid Prison in Manila, on the other hand, according to Fales, the Filipinos suffered most severely, the Chinese were almost exempt, only one or two contracting the disease, while the Americans were entirely free.

With regard to age, it is most commonly met with in young adults between fifteen and thirty years, but it has also been noted in babies at the breast and in old men. It is more commonly met with in men than in women.

Occupation has been carefully investigated by Hunter and Koch in Hong-Kong, and they conclude that the disease is universally present throughout the community, but especially affects the working classes, while the professions, the merchants, and the leisured classes are practically, but not entirely, exempt. Other predisposing causes are disturbance of the soil and a high atmospheric temperature.

Important Features. The peculiar features of the disease are that, though it generally occurs among rice-eating peoples, yet at times it occurs in other communities, as in the British regiment, in whose ration there was but a small quantity of rice, which was cured Rangoon rice. Finally, if observers are to be trusted, there are places where beri-beri occurs and rice is not eaten.

Pathology. As the cause of the disease is unknown, but little can be said as to the pathology, but Mott and Halliburton have performed an experiment which throws much light on the disease. They injected blood taken from an acute case of beri-beri into a cat, and found a fall of blood-pressure, with dilatation of the vessels of the stomach, intestines, and liver, as well as general venous engorgement, and they also noted dilatation of the right side of the heart, and microscopical hæmorrhages into the liver. This would clearly indicate that a poison capable of producing great vasomotor changes was circulating in the blood of beri-beri patients. In addition to the engorgements found in the cat, the human being suffers from congestion of the pharynx, and degeneration of the cardiac, muscular, and sensory nerves. The œdema is probably due to the vasomotor disturbance.

Durham considers that the urine indicates a serious diminution of the metabolism.

Morbid Anatomy.—The morbid anatomy and histopathology have been studied by numerous observers, among whom the investigations of Wright, Duerck, and Scheube must be especially mentioned. In acute cases there is always some œdema, but at times this may be excessive, and the veins of the neck are swollen. Hypostasis is always well marked, but may be excessive, especially about the face. There is often froth at the mouth. In chronic cases the body is pale, and may be swollen with dropsy or emaciated.

In the former the post-mortem rigidity develops quickly, and is well marked. In the latter, however, it is not so marked. On cutting into the body the subcutaneous tissues are usually œdematous, and the veins are filled with dark fluid blood. There is a varying quantity of serous fluid in the abdomen, the chest, and the pericardium, and there may be petechial hæmorrhages under the visceral pleura and pericardium in acute, but not in chronic, cases. The throat and tonsils are generally congested in acute cases, but they may be normal; the larynx may be congested or normal. The mucosa of the trachea and bronchi may be œdematous, with the lumen full of fluid. The lungs may be congested and œdematous, and may contain little air.

The right side of the heart is always greatly dilated in acute cases, and is also hypertrophied in older cases, but it is rare for the left ventricle to be hypertrophied, though it may be dilated to a moderate extent. The myocardium generally shows fatty degeneration, the striation is often absent, and segmentation and vacuolation of the fibres, with an increase of the interstitial tissue, can also be seen, and there is a round-celled infiltration beneath both endo- and epi-cardium in acute cases. (These changes are said by Scheube to be like those found in rabbits after section of both vagi.)

According to Wright, the entire nervous system of the heart is damaged in acute cases, the cells of the bulbar nuclei and the nucleus ambiguus on both sides being swollen, with excentrically placed nuclei and a disappearance of Nissl's bodies in the processes, and to a less extent at the periphery. These changes may also be seen in the first and second pair of the thoracic ganglia, and in the intrinsic ganglionic cells of the heart, while the vagal nerve-endings show rounded droplets of altered myelin (neurokeratin?), especially near the nodes. In chronic cases only the vagi may show degeneration, the ganglia in the heart being normal.

In acute cases the stomach and duodenum are markedly affected, the mucosa being hyperæmic, with more or less marked hæmorrhagic extravasations, and even at times effusion of blood into the lumen of the viscus. This inflammation may extend to the ileum, or very rarely even to the cæcum, but usually the small and large intestines show nothing abnormal, for the acute irritation is located to the pylorus and the duodenum.

Microscopically there is an acute congestion with round-celled infiltration, with, according to Herzog, a very large number of eosinophile cells and necrosis of the glandular epithelium. The cells of Auerbach and Meissner's plexuses are degenerate, and the nerve fibres in the stomach and duodenum also show signs of degeneration. In chronic beri-beri these gastro-duodenal signs are absent.

In an acute case the lymphatic glands near the stomach and duodenum are enlarged and congested. The liver is generally enlarged and congested, and at times in a nutmeg-like condition, and, according to Hewlett and Korté, there may be extensive hæmorrhagic patches. Scheube and Plehn draw attention to a round-celled infiltration of the interlobular connective tissue, which the latter calls a beri-beric interstitial hepatitis. The cells show fatty degeneration, cloudy swelling, and at times necrosis. The spleen may show some cyanosis, and be slightly enlarged and indurated, but usually it is normal. The wall of the gall-bladder may be œdematous at times; the pancreas is normal. The suprarenals may be pigmented and congested with vacuolated cells. The kidneys are usually swollen and hyperæmic, and there may be hæmorrhages into the glomeruli, tubules, and pelvis, together with cloudy swelling and cellular infiltration. The ureters and bladder are usually normal.

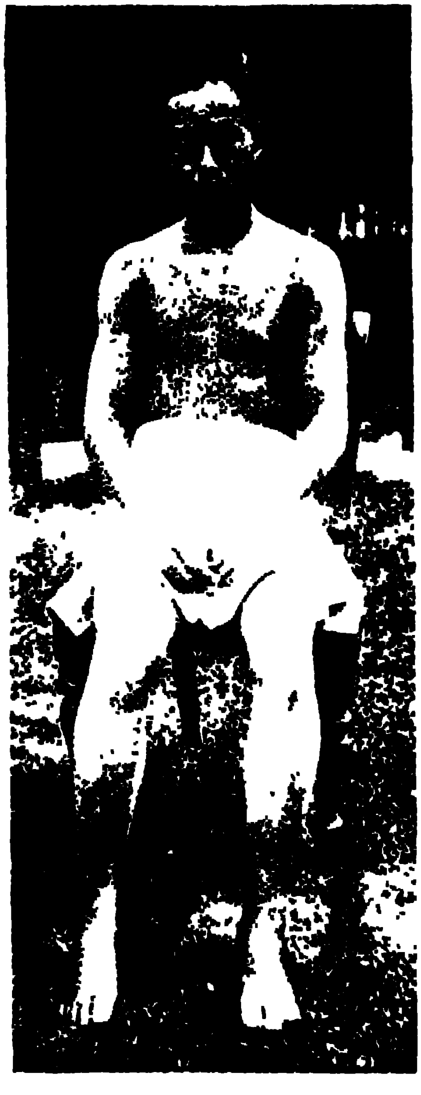


FIG. 734.—BERI-BERI: DROPSICAL OR HYPERTROPHIC FORM

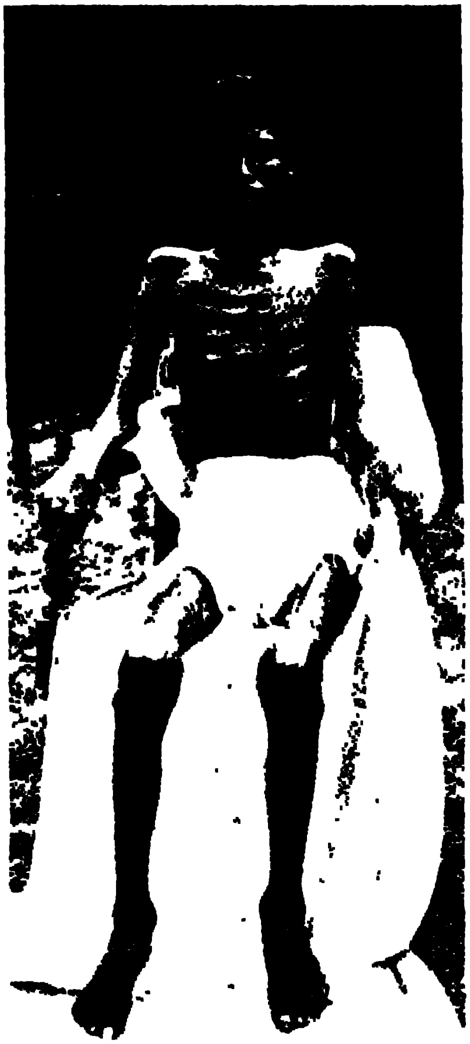


FIG. 735.—BERI-BERI: DRY OR ATROPHIC FORM

The nervous system is markedly affected. The meninges of the brain may be hyperæmic, and there may be some hyperæmia of the brain substance itself, and increase of fluid in the ventricles, but the microscope shows nothing abnormal except in the bulb, where, according to Wright, there are the changes already mentioned in the vagal nucleus. Kustermann also describes acute degeneration of the vagal ganglia at the base of the fourth ventricle.

The spinal cord is usually normal. Hamilton Wright and others have described degeneration of the cells of the posterior spinal ganglia and anterior cornua of the lumbar cord, together with atrophy of Goll's column, in which histologically there is a thickening of the glia tissue and a complete disappearance of the nerve fibres, with the presence of many granular cells.

The peripheral nerves are usually normal to the naked eye, but may be injected and hæmorrhagic. Scheube and Baelz first showed that these nerves were degenerated, the muscular branches of the nerves of the limbs being most affected, but even the fine sensory cutaneous branches were also attacked. The changes in the autonomic nervous system do not appear to have been closely studied, though several observers have recorded changes in the ganglia, and in the cardiac and other plexuses.

The degeneration of the nerve fibres has been carefully studied by Scheube, Baelz, Hamilton Wright, and Duerck. The neurokeratin network becomes irregular, and its meshes wider, while its rods disappear. The medullary sheath becomes vacuolated, and its inner boundary ill-defined. In other places the neurokeratin network condenses into small rosary-like masses or larger lumps, somewhat regularly arranged. Later the medullary sheath breaks up into spherical or elongated masses separated by clear intervals. The axone undergoes first chemical changes, and then appears like a wavy cord, or as a series of comma-like segments, or twisted up into a coil. Finally, both axone and medullary sheath disappear, while Schwann's sheath collapses, and so the nerve fibres become lost in the connective tissue of the endoneurium. Along with these changes there is a cellular infiltration of the perineurium, especially of the perivascular spaces, and also of the endoneurium. These cells are said to be like a similar infiltration met with in traumatic lesions of nerves, and to resemble the granule cells of the central nervous system. When fully degenerated, the nerve may consist simply of connective tissue. Regeneration has not been observed, but must occur—at all events, to some extent—in cases which recover.

The muscles show atrophied and normal fibres side by side. The diseased fibre first loses its striation, and becomes oval or round in transverse section. A colloid degeneration occurs, with proliferation of the nuclei of the sarcolemma. The fibre now appears of a homogeneous grey colour, and is very brittle. As it atrophies the connective tissue of the muscle increases in amount. The bone-marrow is said to be normal.

Symptomatology.—As the cause of the disease is unknown, and the invasion is insidious, the incubation period is also unknown. Hamilton Wright places it at some ten to fifteen days.

The disease is insidious in its onset, and is characterized by gastro-intestinal, cardiac, and nervous symptoms. For purposes of description three types may be recognized-- viz., (1) the acute pernicious form; (2) the typical form; (3) the rudimentary form.

1. **Acute Pernicious Form.**--The acute pernicious form may exhibit itself in several ways. The most acute is when the person, without previous illness, suddenly dies, and the autopsy reveals that he has died of beri-beri.

The more usual history is that the patient feels a disinclination for food, followed in a short time by a sensation of depression or pain in the epigastrium, and nausea. Tenderness is evinced if pressure is made over the pylorus or duodenum, while the throat is seen to be congested. The temperature is usually normal, though slight febrile rises have been recorded. Soon the heart symptoms, characteristic of the attack, appear in the form of a sensation of oppression over the heart, throbbing vessels in the neck, epigastric pulsation, cardiac palpitation, and dyspnœa, while the slightest exertion increases the pulse-rate markedly. The right side of the heart dilates, and hæmic murmurs are heard. As a result of this cardiac disturbance the urine diminishes and dropsy appears, but this varies from being trivial to fairly considerable, with effusion into the pericardium, pleura, and peritoneum.

There may early be found patches of anæsthesia or hyperæsthesia, particularly in the course of the anterior tibial and musculo-cutaneous nerves. Paralysis now appears, and may be slight, or may be so extensive as to prevent all voluntary movements, and at the same time the anæsthesia may increase considerably.

Sooner or later the cardiac symptoms become worse: the pericardial distress becomes agony, the lungs become engorged, and the unhappy individual, unable to obtain proper aeration of his blood, gasps for breath with open mouth and expanded nostrils, while the pupils dilate. His face becomes cyanosed, his extremities cold, and he becomes unconscious, and shortly dies of cardiac failure. During this dying agony the mind is clear almost to the last. The duration of such an attack is from twelve hours to a few days.

2. **The Typical Form.**---The typical form of the disease begins insidiously with malaise, lassitude, loss of appetite, dull pain in the stomach, tenderness on pressure over the pylorus and duodenum, headache, difficulty of breathing and palpitation, often some œdema along the shin, exaggerated knee-jerks, and a sensation of heaviness in the limbs, especially in the legs. Sooner or later a difficulty in walking sets in, and the knee-jerk diminishes and disappears, or the patient may suddenly find himself on wakening in the morning unable to raise himself. If he is capable of walking, the gait is peculiar, somewhat resembling that of locomotor ataxia, but generally being more of the 'high-stepping' type, the foot being raised with difficulty from the ground, brought forward with a jerk, and lowered abruptly. He walks with a support, and

often with the legs wide apart, in order to give stability to his locomotion. He cannot stand long with closed eyes, and complains that he feels as though he were walking on something soft. In addition he suffers from cramp, and his calves are very tender, and sensations of pins and needles, burning, etc., may be felt. It will be noticed that the anterior tibial and the peroneal muscles are mostly affected, and that often there is a tendency for the foot to assume the equino-varus position, and that ankle-drop is often seen.

The forearms may also be paralyzed, and wrist-drop, with great loss of power in the grip, may be noted. As the paralysis proceeds the muscles waste, and electrical excitation is much altered. Miura's rule is that if the foot can be flexed on the ankle, the excitation is only diminished; if only the toes can be dorsally flexed, there is a partial reaction of degeneration; but if no dorsal movement is capable of being made, then the reaction of degeneration will be fully developed. The paralysis spreads to the muscles of the calf, the muscles of the thigh, and the gluteal region, and to those of the hand and arm; then to the abdomen, the diaphragm, the intercostals, and the larynx, and, in rare cases, to the intra- and extra-ocular muscles.

Fletcher has drawn attention to jongkok, or squatting test The person places both hands on the top of the head, and slowly squats down on his heels, and then rises up again. In beri-beri this cannot be performed.

Associated with the paralysis there is at first hyperæsthesia especially in the calf muscles; paræsthesia, as already mentioned; and partial anæsthesia, which may be characterized by saying that the patient feels as though he were touched through some protecting cloth. There is also loss of sense of heat, and cold, and pain. This anæsthesia varies much in site and extent. Usually it begins about the feet and wrist, and moves upwards over the legs, thighs, forearms, and arms, and down into the fingers. It is this numbness of the fingers which incapacitates the patient from doing many simple actions. There is said to be a peculiar ring of anæsthesia around the mouth. The areas of loss of sensation do not correspond with segmental or nerve areas, but are remarkably patchy. The nerves of the affected regions may be tender.

The heart is also markedly affected, being dilated, especially the right side, with a diffuse apex-beat, a spacing of the sounds, so that the intervals may be nearly equal; while systolic murmurs may be heard, and reduplication of the second sound is common, particularly over the pulmonary area. Palpitation and epigastric pulsation are common, as is pulsation of the carotids and veins of the neck. The pulse is usually much increased in frequency and low in tension. The great danger of the disease is death from sudden cardiac failure.

The *blood* does not show much abnormality beyond a certain amount of anæmia. The differential leucocyte count contains about

58 per cent. of polymorphonuclears, 36 per cent. of lymphocytes, 4 per cent. of mononuclear leucocytes, and 2 per cent. of eosinophiles.

The *cerebro-spinal fluid* is generally normal. Lumbar puncture rarely shows, in our experience, any alteration of pressure, although a few authors have noted an increase.

The *urine* may be much diminished when there is œdema, but when this is passing off there is a large increase in the quantity. The total solids are said to be below normal, urea and chlorides being diminished, phosphates and indican being increased, and albuminuria being rare.

Dropsy may or may not be present, but some œdema, most marked anteriorly in the legs, is a practically constant symptom. It usually begins along the shin in the form of a rather solid œdema. It may spread over the legs into the scrotum, on to the abdominal wall, and into the face and arms, and is characterized by being at times in peculiar localized patches, and if it takes place in the muscles, gives rise to an appearance like pseudo-hypertrophic paralysis. Along with the cutaneous œdema there is often exudation into the peritoneal, pleural, and pericardial cavities.

When the dropsy is marked there may be a great diminution of the urine. This dropsical condition is often improperly considered to form a separate variety of the disease, and is called the 'wet,' 'hypertrophic,' or 'dropsical' form, while another variety, called 'dry' or 'atrophic' beri-beri, is mentioned by many authors, the two forms being merely the early and late stages of the disease.

The tongue is usually clean; the throat may be slightly congested; digestion is fair, but a large meal will increase the præcordial or epigastric distress. Vomiting is a bad sign. The bowels are often constipated, the temperature normal or subnormal. The urine may be diminished, increased, or normal in quantity, according to the presence, the passing off, or the absence of œdema.

The larynx may be paralyzed partially or completely, and the voice rendered raucous or lost. The lungs may be œdematous.

In this condition the patient may remain, at times better, at times worse, for weeks and months, and may proceed slowly to recovery, with, of course, deformities if paralysis remains, or may die suddenly of cardiac failure when sitting up or getting out of bed, or from some complication.

3. **Rudimentary Form.**—There is a rudimentary, abortive, or ambulatory form in which the symptoms are so slight that perhaps the sufferer does not seek medical advice, but in whom there may be first increase and then diminution of the knee-jerks, patches of anæsthesia, some muscular weakness, some gastric catarrh, and general malaise. Repeated attacks may occur.

Complications.—Whenever fever develops in a beri-beri patient there is sure to be a complication. The most common are tuberculosis, dysentery, and malaria.

Sequelæ.—Many authors do not believe in sequelæ to beri-beri, but certainly there may be the contraction left after the paralysis and anæmia, and attacks of palpitation may occur.

Diagnosis.—The principal positive signs on which to base the diagnosis are: (1) Loss of knee-jerks; (2) patches of anæsthesia, and occasionally hyperæsthesia, on the legs; (3) pain on pressing the calf muscles; (4) œdema along the shin; (5) absence of marked albuminuria; and (6) the absence of fever.

Suspicious early signs in endemic areas are loss of appetite and a desire for lighter food, together with tenderness over the pylorus and duodenum, with exaggerated knee-jerks.

Several diseases have to be distinguished from beri-beri: first of all the different kinds of *peripheral neuritis* e.g., alcoholic neuritis, by the history and the general tremulousness; arsenical neuritis, by the abdominal pains and the diarrhœa; lead paralysis, by the colic and the blue line of the gums.

Secondly, *dropsies* due to heart disease are recognized by the murmurs and the history of rheumatic fever, or other infectious disease; kidney disease, by an examination of the urine; ankylostomiasis, by the ova being found in the fæces; epidemic dropsy, by the fever and the absence of anæsthesia and paralysis; malarial cachexia, by the enlargement of the spleen, and perhaps the parasites in the blood; and kala-azar, by the enlarged spleen and liver.

Thirdly, certain *diseases of the spinal cord*; myelitis, by the loss of control over the bladder and rectum; locomotor ataxy, by the Argyll-Robertson pupil; pellagra, by the skin eruptions.

Fourthly, *certain intoxications*, such as ergotism by the gangrene and the history, and lathyrism by the absence of tender muscles.

Prognosis.—The acute pernicious form is always fatal, the rudimentary never. The general mortality varies in different countries, as follows:—

	Per Cent.
Sumatra	60 to 70
Hong Ko	18·6
Malaya	10·7
	2 to 6
	2·5 to 3·

But it apparently depends upon many things, of which the most important is the avoidance of sudden cardiac failure. If the patient is treated carefully in bed the danger is much diminished, but if he is allowed to sit up and move about the danger is great. Complications are most unfavourable.

An attack does not confer an immunity. On the contrary, it rather predisposes to another attack.

Observers who believe in the infectious nature of the malady are generally of opinion that there are no relapses, but that reinfections, even shortly after an attack, are common.

Treatment.—The treatment is essentially symptomatic, the patient being placed in bed, and care being taken to avoid anything which is likely to bring on cardiac failure. Especial care is required if the patient gets up or moves about. A cardiac tonic, in the form of strophanthus or digitalis, is advisable, and amyl nitrite, nitroglycerine, or trinitrin should be placed at hand, in order that they may be used at once if a sudden cardiac attack takes place. If the attack is severe, with great embarrassment of the right heart, it has been advised to perform venesection, and remove some eight ounces of blood. Oxygen is useful during the attacks of dyspnœa. For the paralysis strychnine should be administered, and the muscles massaged to prevent atrophy and cramps. Electrical excitation is also good.

If possible, the patient should at once be removed from the place in which he is supposed to have acquired the disease.

Braddon strongly recommends atropine either as the alkaloid in hypodermic injections of $\frac{1}{150}$ to $\frac{1}{50}$ grain, according to the urgency of the symptoms, or in the form of the tincture of belladonna. He considers that the atropine is specially useful in cases of dyspnœa due to cardiac failure and pulmonary embarrassment, while he gives a mixture of tincture of belladonna $\frac{1}{2}$ drachm, tincture of scilla $\frac{1}{2}$ drachm, and citrate of potash $\frac{1}{2}$ drachm, in 4 ounces of water three times a day for three or more days.

With regard to after-treatment, any deformity, such as club-foot, must be rectified, as described in works on orthopædic surgery. Fraser and Stanton have prepared a remedial agent on the lines indicated by their researches, and this should be tried when available. Only harmless rice—*i.e.*, brown rice with more than 0·4 per cent. of phosphorus pentoxide—should be given to the patients, and care should be taken that it is cooked in ordinary pots, and not under pressure. Thomson and Simpson recommend a full diet with 1 ounce of yeast and 200 grammes of katjangido-beans daily. Chamberlain and Vedder recommend that 5 c.c. of an extract of rice polishings be given daily to infants suffering from beri-beri, and this is administered in 20-drop doses every two hours. The patient must be placed upon a good nourishing diet, with plenty of proteid and good vegetables, and rice should be eliminated from this diet. Careful nursing is necessary because of the danger of cardiac failure, and good hygiene is also necessary.

Prophylaxis. Rice should be avoided as a staple article of diet, but if it has to be used it should be in the form of the Indian, country rice, or paddy, variously described as the cured, stale, unpolished, or parboiled rice. Great care should be taken with the cooking, for a good rice can be converted into a harmful rice by cooking, which should always be performed in ordinary pots, and never under pressure by steam. With regard to the different kinds of rice, Schüffner and Kuenen find that Rangoon rice contains 0·42 to 0·46 per cent. of P_2O_5, while Siam and Java rice is much lower. They maintain that there should be a rice reform, and that a minimum legal limit of 0·5 per cent. P_2O_5 for dry rice should be imposed, or, failing this, the substitution of other foods, to make up the deficient ingredient, and a strict control of cured rice—*i.e.*, white rice. Pregnant and nursing women especially should have a liberal diet and harmless rice.

A good nourishing diet is most important.

Good hygienic surroundings—*i.e.*, good ventilation, the avoidance of overcrowding, plenty of sunshine, and exercise in the open air—may be mentioned.

It is as well to thoroughly disinfect with Clayton gas or sulphur and formalin any room in which beri-beri patients have been living, or any infected house or ship.

SHIP BERI-BERI.

Synonym.—Norwegian Beri-beri. Some authorities consider ship or Norwegian beri-beri to be a separate entity from tropical beri-beri, and believe it to be a deficiency disease taking an intermediate position between true beri-beri and scurvy. Clinically, however, the condition is identical with tropical beri-beri, and runs the same course.

INFANTILE BERI-BERI.

Synonyms. *Philippines:* Taon, taol suba.

Infants nursed by mothers suffering from beri-beri, and living on a defective dietary in the Philippine Islands, suffer from œdema, dyspepsia, and cyanosis, and often die suddenly. Post-mortem investigations show degenerations in the vagi, phrenics, intercostals, and anterior tibial nerves, but not so extensive as in adults. Chamberlain, Vedder, Andrews, and others conclude that this is an infantile beri-beri due to some deficiency in the mother's milk, and find that it causes 56 per cent. of the infantile mortality in the Philippines.

EPIDEMIC DROPSY.

Synonym.—Acute anæmic dropsy.

Definition.—Epidemic dropsy is an acute infectious disease of unknown cause, characterized by fever, dropsy, an erythematous eruption, and sometimes cardiac symptoms, but without paralysis or anæsthesia.

History.—In 1876-77 there was a great famine in Southern India, during which a dropsical disease, at the time called 'beri-beri,' was noted. It is possible that this dropsical disease was conveyed in some way from Madras to Calcutta, for in 1877 there was an outbreak of epidemic dropsy for the first recorded time in that city. It appeared when the rains were over, and extended through the cold season into 1878, disappearing when the warm weather commenced in April. It recurred again, and followed the same course in the cold season of 1878 and 1879, and it disappeared in the warm weather of 1880, reappearing this time in the warm weather of 1881. It only attacked natives of India, but it spread from

Calcutta to Shillong, Dacca, and South Sylhet, and to Mauritius, by means of labourers passing through that town. Mauritius became infected in 1878, and was clear of the disease in 1879.

No further accounts of the complaint appeared until 1901, when it was again recognized in Calcutta and Madras. In 1902 it occurred in the Barisal Gaol in Bengal, and in 1907 it occurred in Assam and the two Bengals. It is probable that during the intervening years it has really been present in some part of India, but has been called 'beri-beri.' Greig has come to the conclusion that it is a deficiency disease.

Climatology.—The disease is met with in India and Mauritius, and generally in the cold season. Recently cases of this condition have been reported by Leporini from Cirenaica.

Ætiology.—The causation of the disease is unknown, but there are various theories—*e.g.*, (1) that it is beri-beri; (2) that it is a post-dysenteric anæmia or hydræmia; (3) that it is due to nitrogen starvation; (4) that it is due to eating Burma rice, the action of which is explained in various ways; (5) that it is dál poisoning; (6) that it is a special bacterial disease conveyed from person to person by the bed-bug.

This latter is Delany's theory, and is supported by the fact that the disease is epidemic, and spreads apparently by the agency of human beings, but not from man to man; that it begins with an initial fever, and has a rash, and that there is a local house infection; and, finally, by its sudden disappearance and reappearance. Other theories are that it is a ptomaine poisoning, or a bacillus in fish, or a rust or fungus on rice.

Pathology.—No remarks can be made on this part of the subject.

Morbid Anatomy.—There is subcutaneous œdema and fluid in the peritoneal and pleural cavities. The mouth and pharynx are œdematous, and the œsophagus may be ulcerated. The stomach is very congested, and may show hæmorrhagic patches, and the jejunum is congested, as are the mesenteric glands and the liver. The pancreas is normal. The aryepiglottidean folds and the lungs are œdematous and congested. The kidney is congested, and may show cloudy swelling, but the bladder is normal. The spleen is shrunken; the pericardium may be normal, but the heart is dilated.

Symptomatology.—Generally there are no distinct prodromata: occasionally the onset of the disease is preceded by diarrhœa.

Epidemic dropsy begins with an attack of fever without any initial rigor, the temperature rising to 99° to 104° F., and continuing of low type with remissions and, later, intermissions for a variable period of time, sometimes as long as a month. Associated with the fever, and, indeed, the most constant and characteristic symptom, is the dropsy, which, beginning in the feet and legs, may spread up the thighs to the abdomen, and even to the hands, arms, and face.

There is distinct anæmia after the disease has lasted a little time. Rogers records a count of 3,090,000 erythrocytes per cubic centimetre, and a hæmoglobin count of 54 to 65 per cent. The colour index is said by other observers to be about normal, and the proportion of white to red cells to vary from 1 to 430 at the invasion, to 1 to 384 in the course, to 1 to 615 at the end. Leucocytes are apparently always increased in number, but only slightly. The differential count is:—

	Per Cent
Polymorphonuclears	60·2
Lymphocytes	21·4
Mononuclears	11·7
Eosinophiles	6·7

No animal or vegetal parasites have been discovered in blood which is sterile.

The condition of the urine is described as very variable, but there is no albumen and no casts are to be found.

Effusions into the peritoneal and pleural cavities may take place. The alimentary canal is early irritated, and vomiting and diarrhœa are common occurrences. A rash appears early on the extremities in the dropsical areas; it is usually erythematous or 'measly,' but vesicles and hæmorrhages may be seen. Anæmia, as remarked, is progressive during the disease, and there may be cardiac dilatation with hæmic murmurs. In severe cases there may be cough and dyspnœa, due to œdema into the lungs. Recovery is the rule, but death may occur from cardiac or pulmonary complications.

Sequelæ.—The only sequela so far observed is cardiac weakness.

Diagnosis.—Epidemic dropsy shows the following characteristic signs: dropsy, slight fever, diarrhœa, rash, anæmia, and no albuminuria.

Its diagnosis from *beri-beri* is based upon the presence of fever, the persistence in some cases of the knee-jerk, the lack of paralysis, of painful muscles, and of anaesthesia. Some authorities maintain, however, that in epidemic dropsy there is no fever and no rash, and is indistinguishable from beri-beri.

Prognosis. The prognosis is favourable except in the aged, the case mortality being only 2 to 8 per cent.

Treatment. Rest in bed and the administration of calcium chloride, or iron and strophanthus, are the only remedies usually required. High temperatures should be treated by diaphoretics, quinine, and sponging.

Prophylaxis. Segregation and disinfection are recommended, but no rational prophylaxis can be advised so long as the cause remains unknown.

POTTER'S DISEASE.

In 1913 Potter in Jamaica described a disease which began with numbness, tingling cramps, loss of power, loss of hearing, and defective vision, without skin or mental symptoms, œdema or cardiac symptoms. Both sexes are attacked, generally after puberty and in rural districts. Whole families may be attacked.

WAR ZONE ŒDEMA.

In soldiers, prisoners of war, and refugees, having a very scanty and unsuitable diet an œdematous condition of the legs and feet is far from rare. It is a deficiency condition more closely related to scurvy than true beri-beri. It should be differentiated by blood examinations from a clinically similar condition due to malaria.

TROPICAL ŒDEMA.

Some years ago we called attention in Ceylon to an œdematous condition of the legs, seen especialy in new-comers and tourists in the hot season The whole leg from below the knee is affected, but if the person wears boots tightly laced, the foot and ankle do not show any œdema. There is no anæsthesia, the knee-jerks are normal, and the general condition is good. The condition is not related in any way to beri-beri or scurvy and is not influenced by a change of diet. It disappears rapidly on going to the hills. The same condition has been recently recorded by Marshall from the Red Sea and Bagdad

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CHAPTER LXXII

TROPICAL POISONINGS

General Remarks—Ackee poisoning—Onyalai—References.

GENERAL REMARKS.

We have already defined a poison and discussed criminal poisoning, accidental poisoning, stimulant and sedative poisoning, and the poisons used in trial by ordeal in Chapter X. (p 161), in which we gave a brief outline of the symptoms produced by a number of these poisons, as well as some few remarks with regard to treatment.

There, however, remains one form of accidental poisoning, to which we have already referred on p. 173, to which special reference may be made here, and that is *ackee poisoning*, which was long known as the *vomiting sickness of Jamaica*, and was included in the clinical part of the last edition.

This particular variety of poisoning might also be looked upon as a form of vegetal food poisoning, a subject which is considered in Chapter XIII., p. 193.

Other forms of poisoning, such as arrow poisons, animal poisons, trade poisons, can be found in Chapters XI. (p. 180), and XII. (p. 187).

ACKEE POISONING.

Synonym.—The vomiting sickness of Jamaica.

Definition.—An acute and often fatal illness, occurring mostly in children and to a less extent in adults in Jamaica, characterized by sudden onset, persistent vomiting, causing in fatal cases collapse, and brought about by eating the unsound fruit of the ackee tree, *Blighia sapida* Koenig, or drinking the water in which such fruit has been cooked.

History.—For many years the term 'vomiting sickness' was applied to any disease associated with this symptom, but as various diseases became differentiated and better diagnoses were made, it became evident to Turton in 1904 and to Kerr in 1905 that there was a definite disease in Jamaica to which the term could be applied.

This disease only appeared in the cooler months, and was associated with vomiting and convulsions, and a death-rate of 80 per cent. to 90 per cent., the end coming in a few hours.

In 1906 Branch considered it to be a syndrome, and mentioned the ackee, without, however, being definite as to its causal effect.

In 1912 Potter, after considering cerebro-spinal meningitis, ptomaine poisoning, ackee poisoning, and cassava poisoning, came to the conclusion that it was a phase of yellow fever.

In 1913 Scott suggested that it might be fulminating cerebr[illegible] spinal meningitis, and in the same year Seidelin opposed the yell[illegible] fever and the meningitis views and believed it to be a l[illegible] disease.

In 1915 Scott, as a result of an investigation into an outbreak at Montego Bay, found that in the majority of cases *ackees* formed part of the last meal taken in health, and that they could not be excluded in a single case. Persons taking soup or pot-water made with ackees developed symptoms in two hours, and death nearly always resulted.

The ackee is the fruit or aril of *Blighia sapida* Koenig, belonging to the natural order Sapindaceæ, and, being a native of West Africa, is merely an introduced plant in Jamaica.

Only unsound ackees cause the symptoms, and an ackee is unsound (1) when it is unopened; (2) when it is picked from a decayed, bruised, or broken branch; (3) when it has been forced open; (4) when it has a soft spot.

In 1917 Scott confirmed this view as to the causal effect of the ackee, and by his experiments upon animals demonstrated the nature of vomiting sickness.

Climatology.—So far the disease is only known in Jamaica, but it must be remembered that the tree is a native of West Africa. We, however, do not know whether the fruit is used as a food in this country, and, at all events, up to the present no one has reported the poisoning from that part of the world.

Ætiology.—Vomiting sickness is caused by eating the *unsound* fruit of *Blighia sapida* Koenig, the ackee plant, or taking the soup or 'pot-water' made with this fruit. These latter are the more severe cases, because the poison appears to be extracted by boiling with water. Alcoholic extract of unsound ackees is not poisonous. The watery extract, on the other hand, when administered to cats and dogs, produced the same symptoms and mortality rate as in man, and after death the same post-mortem signs were found. Herbivorous animals are unaffected. The poisoning takes place in the months from November to April, which corresponds with the *ackee season.* Several members of a family are taken ill at one and the same time, as would be expected from a food poisoning. It also occurs among near neighbours in the settlement, and is rare in white children and East Indians, being confined to the children of the indigenous population. There is no indication that sex plays any part in the ætiology, which must be looked upon as an acute poisoning. A case of known ackee poisoning occurring in man showed the same symptoms, cause, and post-mortem changes as cases of vomiting sickness, and as the experimental animals.

Morbid Anatomy.—There is a general hyperæmia, with a tendency to hæmorrhages in various organs. The mucous membrane of the stomach and the bowels is congested, while the lumen of these organs may contain a dark slimy substance. There is fatty degeneration in the liver and kidneys, and in the former case this change is said to be more acute than in phosphorus poisoning. Microscopically necrobiotic changes are found in the cells of the liver, kidneys, and pancreas.

Pathology.—The illness comes on suddenly in a person who has previously been in perfect health, and is characterized by primary or gastric vomiting, followed by a few hours of temporary cerebral vomiting, which is rapidly followed by convulsions, coma, and death, the average duration of the illness being twelve and a half hours.

The poison appears to be an irritant to the stomach, and to cause vomiting, which may rid the body of it, when the patient rapidly recovers; but if it remains in the system it acts upon the nervous system, causing the cerebral vomiting, convulsions, and coma, which, apparently, always end in death.

Symptomatology.—Somewhere about midnight a child wakes up and complains of pain in its stomach, in a little time vomits its last meal, and after this feels better. In certain cases no further symptoms occur, and there is a rapid recovery.

More usually, however, after a period of temporary relief the vomiting commences again, and may be accompanied by fever, while the vomit consists of frothy mucus. These symptoms continue until the child passes into a state of collapse, with cold sweats, a weak and rapid pulse, and irregular respirations.

These symptoms invariably lead to death, which is preceded by convulsions.

Variety.—In rare cases there is no vomiting, and only the cerebral symptoms, drowsiness, convulsions, and coma, leading to death. This is the so-called 'vomiting sickness without vomiting.'

Diagnosis.—The cardinal points in the diagnosis are:—Its endemicity; its seasonal prevalence; its sudden onset in members of one family or in neighbours; in native children without regard to sex; the quick complete recovery of some cases, while others, after showing cerebral symptoms, end fatally; and finally the evidence of having partaken of a meal containing ackees or their extracts. It can be diagnosed from *yellow fever* by the absence of the black vomit, and from *cerebro-spinal meningitis* by an absence of Koenig's sign and of the meningococcus.

Prognosis.—This is very bad, as some 80 to 90 per cent. of the patients die. If recovery is to take place, it is rapid and complete.

Treatment.—No specific treatment is known.

Prophylaxis.—Instruct the people not to use unsound ackees. This has been done, with the result that in 1916 there were only three deaths from vomiting sickness in Jamaica.

ONYALAI.

Synonyms.—Edyuo (Bukoba); Kafindo (Congo).

Definition.—An acute disease of unknown causation, characterized by the appearance of bullæ containing blood on the surface of the body, the tongue, soft palate, or buccal mucous membrane.

History.—The disease was discovered by Yale Massey in Angola in 1904, and fully described by Wellman later in the same year in Portuguese West Africa, and by Feldman, in 1905, in East Africa, where it is called 'edyuo' by the natives of Bukoba. Mense (1906) thinks that the 'kafindo' disease of the Unyamwezi people of the Congo is the same disease. Hæmorrhagic bullæ in the mouth, but without general symptoms, have been described by Maxwell in Changpo, South China, as being due to the accidental introduction into the mouth of a kind of spider's web.

Ætiology.—This is unknown, but Mense thinks it may be some kind of poisoning, perhaps with some species of the Euphorbiaceæ. Wellman considers that it is not a manifestation of malaria; nor is it a vegetal poisoning, nor a snake-poisoning, though the bite of *Bitis arietans*, the puff-adder, simulates some cases closely. Neither trypanosomes nor bacteria were found. It is not a purpura hæmorrhagica, nor Henoch's purpura, nor Schönlein's disease.

Symptoms.—The onset is sudden, and is accompanied by lassitude and a dazed appearance. Sometimes the parotids are tender, and the eyes may be somewhat reddened, and in about 66 per cent. of cases there is a slight rise of temperature. Numbness and pain in various parts of the body may be noted.

The appetite is poor: bullæ may be seen on the tongue and in the mouth and pharynx, while they also occur in the œsophagus, stomach, and bowels. The tongue is swollen and painful. Vomiting of blood is not rare, and bloody diarrhœa may take place. Hæmaturia has been noted, and cerebral hæmorrhage, with the usual signs, has been seen. It is believed that hæmorrhage into the pancreas, liver, and spleen, may take place in some cases. Bullæ may also appear in the skin, ranging from the size of a split pea to several inches in diameter. The typical bullæ, whether on a mucosa or in the skin, extend deeply, involving the submucosa or the corium, and are crossed by fibrous trabeculæ, in the meshes of which lies partially coagulated blood, which appears dark through the skin or mucosa. The red corpuscles are not disintegrated, and can be seen by the microscope.

The disease is said to have a tendency to recur two or three times.

Diagnosis.—The diagnosis from snake-bite may be effected only by the history, as the bullæ may not be visible on the skin or mucosa. Malaria can be excluded by the blood examination. Schönlein's disease, or peliosis, is diagnosed by the rash, painful swelling of the joints, and the purpuric eruption. Henoch's purpura is met with generally in children, and has joint symptoms as well as a rash.

Prognosis.—Wellman reports three deaths in fourteen cases, and says that the malignancy varies in different seasons and districts.

Treatment.—Wellman thinks that arsenic in full doses is the best treatment. He says the natives use empirically ***Geigera wellmani*** Hutch and ***Albizzia anthelmintica*** A. Broga. Massey recommends large doses of bicarbonate of soda and cod-liver oil.

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CHAPTER LXXIII

PELLAGRA

Synonyms — Etymology — Definition — History — Climatology — Ætiology — Pathology — Morbid anatomy — Histopathology — Symptomatology — Diagnosis — Prognosis — Treatment — Prophylaxis — References.

Synonyms.—*Italian*: Umor Salso, Scottatura di Sole, Malattia della Miseria, Mal del Sole, Malattia della Insolazione di Primavera, Risipola Lombarda, Mal della Spienza, Mal del Padrone, Jettatura di Sole, Cattivo Male, Mal della Vipera, Calore del Fegato, Salso, Pelandria, Pellarella, Pellarina, Psychoneurosis Maïdica, Mal Rosso, Maïdismus, Lepra Italica Maïdica, Scorbuto Montano, Scorbuto Alpino, Elephantiasis Italica. *Spanish*: Mal de la Rosa, Mal d'Asturias, Mal del Hígado, Calor del Higado, Escamadura del Hígado, Flema Salada. *French*: Maladie de la Teste, La Gale de Sainte Ignace, Mal de Saint Amans, Mal des Saintes Mains, Mal de Sainte Rose, Mauvais Dartre. *German*: Der Lombardische Aussatz. *Roumanian*: Buba Tranjilor, Rana Tranjilor, Parleala, Jupuiala. *Greek*: Graeci Elephantiasis. *Egyptian*: Inshup, Qushuf, Golar, Lahooh. *South America*: Chichismo.

Etymology.—The name 'pellagra' is an Italian word, possibly coined by the peasants from two words—*pelle*, meaning 'skin,' and *agra*, meaning 'rough'—though other possible origins are also given. It was introduced into medical literature by Frapolli in 1771 in his work, 'Animadversiones in Morbum Vulgo Pelagram,' when he spelt it with only one *l* instead of with two.

Definition.—Pellagra is an endemic disease, usually of long duration and of unknown causation, which is characterized by cutaneous, gastro-intestinal, and nervous symptoms, which undergo exacerbations at recurrent intervals, usually in the spring or autumn.

History.—When it is considered that pellagra has been overlooked in quite recent years in America, Scotland, and England, and probably in many other parts of the world, it will not be thought to be astonishing that ancient literature is silent as to its existence in Europe, but the absence of these references by no means proves that the disease itself was not present. Strambio finds that some of the symptoms mentioned in Hippocrates may be those of pellagra, and says that his description of 'Sollicitudo' indicates a disease resembling the mental condition found in pellagra during an acute exacerbation. We have searched through Hippocrates, and have been unable to find anything which to our mind bears any resemblance to pellagra. The peculiar symptoms from which St. Francis of Assisi, who lived in a district which to this day is pellagrous, suffered, markedly resemble pellagra, as he had an eruption upon his hands and feet, associated with an extraordinary mental condition; but though these speculations are interesting, they are far too uncertain to be of any use in determining the interesting point as to whether pellagra existed in Europe before the introduction of maize by Columbus. In 1578 the disease seems to have been known in Milan as 'pellarella,' but was confounded with eczema, leprosy, erysipelas, and scurvy, and no real importance can be attached to a simple name unaccompanied by any description of the disease to which it was applied. A slightly more definite reference is found in 1713 in Ramazzini's work, 'De Morbis Artificium Diatriba,' under the heading 'Agricolæ,' where he says: 'Easdem ob causas, iis persæpe contingunt dolores colici et affecto Hippocondriaca quam ipsi appellant, il mal del Padrone.'

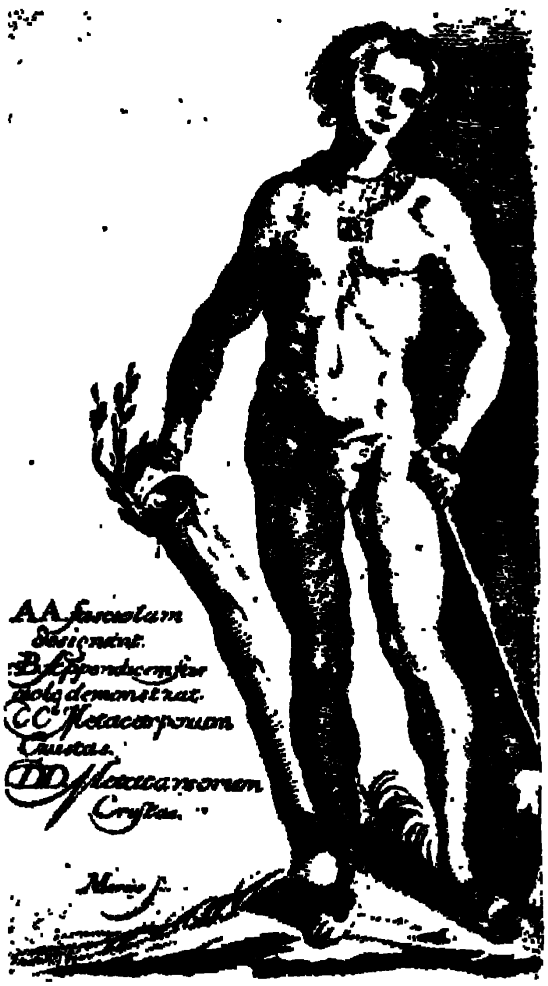

FIG. 736.—MAL DE LA ROSA. (After Casal.)

The recognition that the cutaneous, gastro-intestinal, and mental symptoms exhibited by the sufferers constituted a clinical entity was first made by Gaspar Casal on March 26, 1735, but, unfortunately, was not published until 1762, when his work, 'Historia Natural y Médica del Principado de Asturias Sequida de la Descripcion de la Enfermedad conocida por el Vulgo con il Nombre de Mal de la Rosa,' appeared. Casal gave a representation of the disease (Fig. 736), showing the eruption around the neck and down the front of the chest (called Casal's necklace), and on the dorsa of the hands and feet. With Sambon one of us has visited the Oviedo district of the Asturias in North Spain, where Casal first recognized pellagra, and find that, as regards the cases along the River Nero the disease exists as it did in his days. On December 2, 1740, a learned monk named Feijóo wrote to Casal stating that 'Mal de la Rosa' existed in his native country, Galicia. Before Casal's publication appeared the celebrated Thiéry visited Madrid, where he met Casal, and was shown cases of pellagra, and afterwards he observed one case himself. On his return to Paris he wrote a paper entitled, 'Description d'une Maladie appellée Mal de la Rose aux Asturies,' which was published in the second volume of Vandermonde's journal called 'Recueil Périodique d'Observations de Médecine, de Chirurgie, et de Pharmacie,' in May, 1755. It is pleasing to record that not merely did Thiéry give a most excellent description of the clinical signs of pellagra, but he also gave full credit to Casal for his, as yet unpublished, great discovery.

These publications of Casal and Thiéry laid the foundations of the modern knowledge of pellagra. We will now turn to the various countries, and study, very briefly, the history of the disease therein.

Italy.—Early in the eighteenth century the disease appears to be well known to the medical men of Cremona and Cremasco, as well as to Antonio Terzaghi at Sesto Calende on Lago Maggiore, and to Francesco Zanetti, who recognized it in 1769 at Canobis, also on Lago Maggiore. It will thus be seen that pellagra, hinted at in 1578 in Milan, written about by Ramazzini in 1713, had become a disease well known to the general practitioner and peasantry, and only required an historian to become recognized by the medical profession. This historian was found in Francesco Frapolli, one of the physicians in the large hospital in Milan, who in 1771 published his work, 'Animadversiones in Morbum Vulgo Pelagram,' in which for the first time the word 'pellagra' (spelt with a single *l*) was used. This work, followed by those of a number of authors, drew more attention to the disease, with the result that the Patriotic Society of Milan offered a prize for the best essay on the subject, while the Kaiser Joseph founded a special hospital for pellagrins, and placed it under the charge of Gaetano Strambio, whose justly celebrated work, 'De Pellagra,' appeared in three volumes during the years 1786-1789. In 1787 two young Dutch doctors, Jensen and Hollenhagen, and a young Frenchman, Levacher de la Feutrie, visited Italy to study pellagra, concerning which they published reports on their return to Holland and France. In 1799 Chevalier gave an account of Jensen's work in the *London Medical Review and Magazine*. In this way the knowledge of the disease called pellagra started and spread.

In the meanwhile a disease called 'Scorbuto Alpino' had been definitely recognized by Giuseppe Antonio Pujati in 1740 in Feltre, to the north of Venice, and the same disease was found later by Antonio Gaetano Pujati, the son of Giuseppe Antonio Pujati, and Nascimbeni in the Venetian Friuli, and this disease found its historian in Odoardi, a pupil of the older Pujati, who in 1776 published his work, 'Di Una Specie Particolare di Scorbuto,' in which an account of Professor Pujati's discoveries was given. In this way the knowledge of the disease 'Scorbuto Alpino' was started, so that in Italy at this time there were described two separate diseases under different names, and found in different regions; and it was not till Fanzago in 1789 published his work, 'Memoria sopra la Pellagra del Territorio Padovano,' that these two diseases were recognized to be one and the same. After this date the literature concerning pellagra increased considerably, but no work of great importance appeared until 1810, when Marzari published his book, 'Saggio Medico-Politico sulla Pellagra e Scorbuto,' in which he laid stress upon 'maize' as the principal ætiological factor in the disease—a view which had previously been mentioned, but not so forcibly, by Casal and others. The importance of this work is that, ever since its publication, the maize theory in some form has been generally adopted in Italy. Marzari was of the opinion that it was the deficiency of the gluten in the maize which was the main agent of the disease, but he also suspected toxicity. From Marzari's time there are very numerous publications, among which may be mentioned those by Henry Holland in 1817 on the pellagra of Lombardy, published in the Medico-Chirurgical Transactions, and by Zecchinelli in 1818.

Balardini in 1845, in his work entitled 'Della Pellagra, del Grano turco quale Causa Precipua di quella Malattia e dei Mezzi per Arrestarla,' promulgated the view that the causation was a fungus growing in the maize, which fungoid growth was called 'Verderame,' and was thought to be due to *Sporisorium maidis*. This publication was of the greatest importance, as it afforded an explanation as to why the disease should attack some people and not others, and thus gave the maize theory greater importance. This subject was further studied by Costallat and others, who produced symptoms in chickens by feeding them on maize containing verderame, which were said to resemble those of pellagra.

In 1872 Lombroso began to study pellagra, and continued to do so till he died in 1909. He believed that the disease was an intoxication produced by the toxins manufactured by organisms, harmless in themselves, and growing on maize. More recently a view has been promulgated that the disease is due to good maize, which in certain people produces the symptoms of the disease, and in others does not. Such, briefly, was the condition when Sambon in 1905 began his work, which he has continued up to the present time. This work, which is mainly epidemiological, has thoroughly shaken, if not completely destroyed, the maize theory, and has brought forward many facts which support strongly a parasitic theory of the causation of the disease as well as a probability of the infection being spread by one of the biting flies.

Spain.—The discovery of the disease by Casal in 1735 in the Oviedo district of the Asturias has already been mentioned, as well as the fact that Feijóo had recognized it in Galicia. The next publication is by an Englishman, called Townsend, entitled 'A Journey through Spain,' and published in three volumes in London in 1791. In the second volume, on p. 10, there is a short clear account of 'Mal de Rosa.' This is the earliest known account of pellagra in English. In 1820 Eximeno made an inquiry into the disease, and came to the conclusion that 'Mal del Hígado,' 'Mal de la Rosa,' and pellagra were one and the same disease. In 1835 Mendez Alvaro recognized pellagra in the malady called 'Flema Salada,' and in 1847 Henriquez showed that 'Mal de Monte' was the same disease. In 1849 Roussel visited Spain, and recognized that the disease in France and that in Spain were the same clinical entity. Since that date many excellent works have been published in Spain on pellagra, notably by Calmarza and Roël, while of late the disease has been carefully studied by Huiteras, Pittaluga, and the physicians of Oviedo.

The maize theory of the ætiology of pellagra has never gained credence in Spain, and hence the term 'Spanish pellagra,' or a pellagra not due to maize, has been used by some Zeists as a medical synonym for a hoax.

Portugal. —Pellagra is known to exist in Portugal, but we are in the same condition as older writers, in that we can give no history of its recognition or spread.

France.—We have already noted Thiéry's publication in 1755, and the fact that in 1787 a young Frenchman, Levacher de la Feutrie, proceeded to Italy to study the disease, concerning which he subsequently published accounts in 1802 and 1806: but it was Hameau in 1818 who first recognized the disease in France as occurring around Teste-de-Buch, in the Plain of Arcachon. Hameau was not acquainted with the literature which had sprung up concerning pellagra, and his observations were in reality a rediscovery of the disease. In 1829 he read an excellent dissertation on the subject before the Society of Medicine of Bordeaux, under the title 'Description d'une Maladie Nouvelle.' It would appear that he considered it to be an infection in some way acquired from sheep. In all he observed no less than seventy-six cases.

There is, however, evidence in favour of the suggestion that pellagra had long existed in France, and this is to be found in the fact that the peasants used to call the disease 'Mal de Saint Amans,' because there was a statue to St. Amans in Bascons which was always moist, and this moisture was used by the pellagrins as an application to their eruption. According to Roussel, there was another curious custom followed by the peasants of the Landes, which was to visit a certain statue in which the Christus was represented with red hands. The priest was wont to apply an ointment to these hands, from which the sufferers removed a little of the ointment and applied it to their own inflamed hands, feet, face, etc. From this interesting ceremony the disease was called the 'Mal des Saintes-Mains.' Other popular names, such as 'Mal d'Arouse' and 'Mal de Sainte-Rosa,' tend to show that the common people were well acquainted with the disorder. Sambon has also informed us that some of Napoleon's soldiers became affected by pellagra during the campaigns in Italy, and certainly cases are recorded in the Hôtel Dieu and in the Hôpital Saint-Louis, while Jourdan published a paper on the disease in 1819.

Brière de Boismont in 1830 drew attention to the fact that pellagra occurred around Paris, and in 1847 Ardusset showed that the 'Maladie de la Teste' of Hameau was pellagra. In 1843 Marchand, after investigations extending from 1836 to 1842, emphasized the fact that pellagra was essentially a disease of *the country*, and not of the town. In 1845 appeared Roussel's account of his researches in France and Spain, to which reference has already been made. In 1865 Billod published his account of asylum pellagra as a pseudo-pellagra - that is to say, a pellagra not due to maize. Sambon and one of us have investigated the pellagra of the Landes, where the disease has greatly diminished, and this appears to be associated with a diminution in the malaria of the same region, which appears to be due in part, at least, to the improved cultivation of the soil, the drainage of swamps, etc., and the stocking of the waters with fish.

Austria. The disease was first noticed in the Tyrol, where it is still very prevalent, and where it is being ably studied by Merk, Weiss, and others. In 1794 Nicolas and Jambon reported its presence near Vienna.

Hungary and Roumania. In 1840 Lachaise drew attention to an epidemic of pellagra in Roumania, in 1856 Julius Theodori reported its presence in the Danube provinces, while in 1862 Bouchard pointed out that Sigmund said that the Hungarian pellagra existed solely in the vast plains bordering the Rivers Danube and Theiss —*i.e.*, in the Alföld - which were often covered by inundations. It is interesting to note that these rivers have been regulated, and that the disease is said to have considerably abated there. Be that as it may, there is to our personal knowledge a considerable amount of pellagra in Transylvania, where it has been studied by Hollander, Kaiser, and others, and in Roumania, where Babès says there are more than 200,000 cases.

Macedonia. Cases of pellagra have been observed by us in Macedonia.

The British Islands. Though reported as long ago as 1860 by Brown, and again in 1909 by Cranston Low in Scotland, no attention has been seriously paid to the disease until recently, when Sambon and one of us, searching through the British Islands, came across cases in both Scotland and England, and it appears probable that more definite information with regard to the spread of pellagra in these islands will soon be forthcoming. The interest with regard to these cases is that while it is impossible to mathematically exclude all possibility that a patient had never tasted a grain of maize, still it would be straining the maize hypothesis to an unjustifiable extent to try to make it apply to all of these cases. It is interesting to note that pellagra has been found as far north as the Shetland Islands. Of late years quite a number of cases of pellagra have been reported in the British Isles.

Iceland.—We have no information as to the presence of pellagra in Iceland, with the sole exception of a statement by Holland that he had seen cases in Iceland resembling the pellagra which he had observed in Italy.

Africa.—Though first noticed in Egypt by Pruner in 1847 under the term 'leproses,' its recognition therein is principally due to Sandwith, who found it in 1893, and to Keatinge and Warnock, who have not merely kept that knowledge alive, but have added considerably to the study of the disease. There is, however, still a tendency to consider pellagra a part of the syndrome of ankylostomiasis. More recently pellagra has been recognized in other parts of Africa, and it is possible that it will eventually be found to be widespread in that continent.

America.—Notwithstanding careful inquiries, Wood has failed to discover any evidence of the existence of pellagra among the North American Indians during the eighteenth century, but he has found some evidence of cases in the early years of the nineteenth century. In 1864 Gray and Tyler first definitely reported cases in them, but though at times recognized, the disease was not generally admitted to be present until 1907, when Searcy reported eighty-eight cases, of which fifty-seven were fatal. From that date the works of Babcock, Lavinder, Siler, Roberts, Niles, Wood, and many others, have made the disease well known. In the meanwhile, pellagra has been recognized in the West Indies, Mexico, and other parts of America.

Asia and Oceania.—During recent years pellagra has been recognized in India, the Straits Settlements, the Philippine Islands, and the Sandwich Islands.

Summary.—The above history of pellagra demonstrates the ease with which the disease may be overlooked, even when abundantly present, by well-trained and most competent observers. It also impresses us with the fact that pellagra should be looked for in every country, without any preconceived idea as to its ætiology.

Climatology.—It appears probable that before many years have passed, pellagra will be found to be prevalent all over the world. At present it is known to exist in:—

Europe.—Scotland, England, France, Spain, Portugal, Italy. Austria (including the Tyrol, Bosnia, and Herzegovina), Hungary, Roumania, Russia, Serbia, Macedonia, Bulgaria, Greece, and Turkey. Cases have been reported as far north as the Shetland Islands.

Africa.—Algeria, Tunisia, Egypt, Central Africa, Rhodesia, and South Africa.

Asia.—Asia Minor, Persia, India, and the Straits Settlements.

Oceania.—Sandwich Islands.

America.—United States, Mexico, West Indies, Brazil, Columbia, and the Argentine.

The feature of the last few years with regard to the climatology has been the recognition of pellagra as an endemic disease in Scotland, England, and the United States. Mere geographical distribution *per se* is not so important as an epidemiological inquiry into the actual localities in which the disease occurs. Pellagra is essentially a disease of long duration, and patients are capable of moving far from the place in which the first symptoms appeared, and, again, the first symptoms often appear in early childhood and reappear after some years' interval, when the patient may be living in quite a different district from that in which he resided during his younger years. It is therefore necessary to prepare and study spot maps showing where the patients were first attacked by the signs and symptoms of the disease, and this is being done at the present time by Sambon, whose results will be awaited with interest. In general it may be stated that inquiries of this nature show that by far the larger number of cases occur in country districts, and not in towns, and that the densest localization is in houses near or alongside certain streams. In fact, study the localization in what country you will, as we have done in France, Spain, Italy, Austria, Hungary, Roumania, and Egypt, it is impossible not to be impressed with the relationship between pellagra and water. Generally the water is moving, and often it is moving rapidly, but this last does not appear to be absolutely necessary. As a rule, the nearer the dwellings are to such water, the greater the number of cases. Cases do, however, occur at a distance from water, but inquiry will often demonstrate that the affected people work near or have been in some way connected with a stream. Cases do occur in towns, but they are relatively few, and careful inquiry will usually elicit a perhaps almost forgotten fact that the disease really began after some visit to the country. Inquiries, however, must be made with care, otherwise wrong impressions may be obtained. One of the most interesting cases

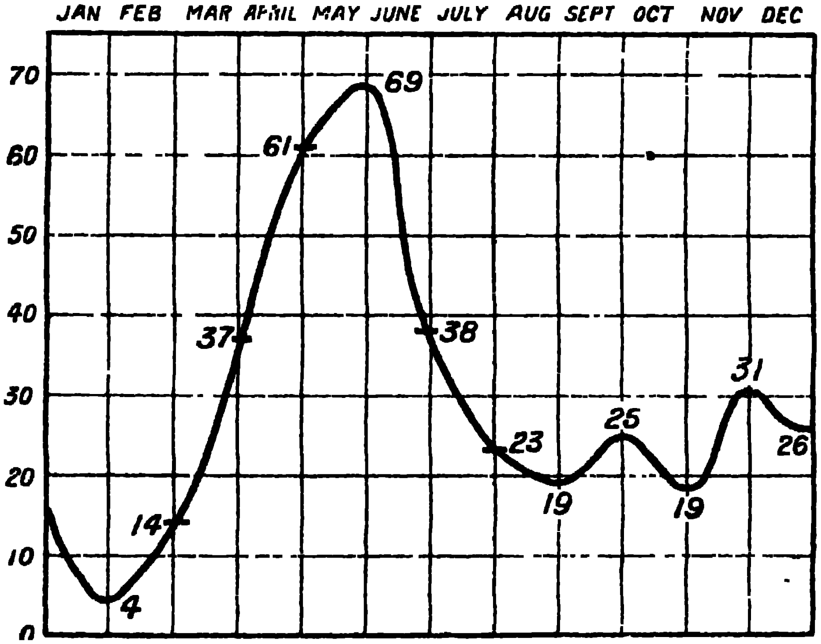

FIG. 737.—SEASONAL VARIATION IN THE ADMISSIONS FOR SIX YEARS OF PELLAGRA CASES INTO THE KASR-EL-AINY HOSPITAL, CAIRO.

(Specially prepared by Keatinge and Stiven.)

which we have met with was that of a young boy who was supposed never to have left a large town, and yet was suffering from pellagra. Careful inquiry elicited the fact that he was in the habit of going for a day or so every year to stay with some relatives who lived in a pellagrous area, and the time of the year chosen for this visit was one in which acute cases occurred. In a locality pellagra usually occurs among the poor, especially among field labourers; but it may also occur among the rich and among persons who habitually work indoors; it is, however, usually not difficult to trace a relationship between the commencement of the disease and a visit or residence in some pellagrous area, and very often, again, a relationship to water.

With regard to seasons, there is a universal consensus of opinion that most attacks appear in the spring or early summer (in Egypt with the Khamseen), after which there is a diminution in the cases, and although attacks may begin in the summer, they are not common. In the autumn, however, there is a definite, though secondary increase in the number of cases, which decrease almost to nil in the winter. These statements are well borne out by the curve of pellagra admissions into the Kasr-el Ainy Hospital, Cairo, for the years 1900-1911 inclusive. This curve, for which we are indebted to the kindness of Dr. Keatinge, was most carefully prepared by Dr. Stiven, and demonstrates the incidence of pellagra as seen in that hospital.

Pellagra may occur in hilly or even mountainous regions, where it is often very common as, for example, the Tyrol--but can equally occur on the flat alluvial deposit of rivers-- as, for example, the delta of the Nile. It would appear that pellagra extends from near the Equator to the Shetland Islands in the north, and to South Africa in the south, and that it encircles the world in an easterly or westerly direction. In our experience the one important factor to be certain that pellagra is endemic in a region is to find it in very young children born in the region from which they have never stirred.

To summarize, pellagra has a world-wide distribution. It occurs in hills and plains. The cases are densest near moving fresh water, and usually begin in spring or autumn.

Ætiology.- The causation of pellagra is at the present time *unknown*, so that we are compelled to consider possibilities instead of facts- a point which we desire the reader to bear in mind while perusing the remarks we are about to offer for his consideration.

The extraordinary theories which we have found still in existence among medical men in the various pellagrous regions which we have visited are:--

1. That it is not a disease, but merely dirt, and can be cured by turpentine, soap, and water. This theory of course applies only to the quiescent stage of a very chronic case, and is easily excluded by a little knowledge of the disease.

2. That it is not a disease *per se*, but merely a series of stray symptoms, and that no one has studied the cases from the commencement of the disease

to its fatal termination. A study of merely Hameau's writings, excluding all the modern Italian, Roumanian, and American literature on the subject, would, we think, satisfy any unbiassed person that this view is untenable.

3. That it is not a disease *per se*, but merely symptoms of some other well-known disorder. The disease which it is most commonly said to belong to is ankylostomiasis, but most of our readers will themselves have treated many cases of ankylostomiasis without meeting with the symptoms of pellagra, and many will be acquainted with pellagrins who show no signs of ankylostomiasis.

The above can be easily dismissed, and would not have been mentioned if we had not personally met with believers in all of them. With regard to the more likely theories, we must discuss the following:—

I. The deficiency theory.
II. The maize theory.
III. The parasite theory.

I. The Deficiency Theory. —In Chapter IV., p. 94, we have briefly traced the evolution of foods and the effects of a low protein dietary, as well as the effects of certain nitrogenous complexes on man, and therefore need not recapitulate what we have written on those pages. Arguing upon the theory of the causation of beri-beri by the absence of a nitrogenous complex, some people have asked whether pellagra may not be due to the lack of some nitrogenous complex in the food; and, further, it has been suggested, or rather hinted, that this might explain, not merely the maize theory of pellagra, but those cases in which no maize has been eaten, but in which the diet has been largely oatmeal or rice. Thus, Nightingale in his paper on Zeism, which appears to us to be pellagra, finds that when steam-milled mealie bread alone was supplied to the prisoners in the Victoria Gaol in Rhodesia the disease broke out, and when this was stopped, and meat, vegetables, and rice were substituted, the epidemic ceased; and when hand-milled rapoko (maize) was obtained, the effect, in Nightingale's words, was 'immediate and almost magical,' as the patients began quickly to recover. In this rapoko the husk was not eliminated by the hand-milling. The parallel between this and beri-beri is obvious. In our opinion there is one great flaw in this theory, and this is that pellagra may occur in people provided with an excellent dietary. To this it might be replied that some peculiarity of the individual's body destroyed the necessary vitamine, but this argument is, to our minds, rather strained. Modern work tends at the moment to support this theory as being the true course of the disease, but there are many difficulties, and it cannot be said to be proven.

II. The Maize Theory. —Much of a most convincing nature, if left unanalyzed, can be written in support of the maize theory in general. It can be pointed out that maize (*Zea mais* Linnæus) was originally a native of America, where it has been found in its ancient form of small grains in the graves of the Incas, and that it was introduced by Columbus or his followers into Europe, where it did not grow well in certain countries, like the British Islands, which, therefore, remained free from the disease until the nineteenth century, when importation of maize took place in greater quantities than heretofore, but where now there is plenty of maize sold as pop-corn for children, and it may possibly be made into bread, cakes, scones, porridge, etc., while whisky is often partially made from the same grain. On the other hand, it grew well in Spain, Italy, and France, and that its introduction into a country has always been followed by the appearance of pellagra in that country, and quotations supporting maize can be drawn even from the writings of its most vigorous opponent, Sambon, who states:—'From authentic documents of the time we learn that "melica," or "fromentone"' —*i.e.*, maize —'was grown in Cremona in the sixteenth century, and . . . in 1556 a Cremona nobleman offered the Duke of Florence ten *staia* of the new cereal.' When this statement that there is plenty of maize in Cremona in 1556 is compared with the statement that pellagra was well known in Cremona about 1700 to peasants and medical men alike, a Zeist would maintain that, allowing for the disease being so liable to be overlooked, this was a remarkable coincidence. Another epidemiological fact which, taken by itself, would strongly support the maize theory is the well-known fact that in the delta of the Nile there is plenty of pellagra and plenty of maize, but as the Nile is ascended the maize diminishes, millet being used instead, and the incidence of pellagra also diminishes and at present it is said to be unknown south of Assouan, which statement must be received with caution, as pellagra has so often been reported absent from places where it is now known: and, moreover, pellagra is known to exist in Central Africa. In Columbia pellagra is said to be found only in people who regularly take a drink made from fermented maize. This drink is called 'chicha' and the malady 'chichismo.' The Zeist states that pellagra is found wherever maize is used, at all events, as an important article of food. As a matter of fact, maize, either growing or imported, is found all over the world, and pellagra would appear also to be found all over the world.

Against the maize theory there are the facts that tend to demonstrate that persons who are alleged never to have tasted maize have suffered from pellagra: moreover, relapses have occurred after three, five, and even fifteen years' residence in gaols or asylums in which maize is not merely not allowed to be used as an article of diet, but care is taken, by inspection and by periodical chemical and microscopical examination, to exclude it. A Zeist would answer to these objections that there was some fallacy, and that nothing short of being the victim yourself would make it reasonably certain that maize was not consumed, and even then it might have been eaten unwittingly; and, further, that all safeguards designed to prevent food sophistications in institutions break down.

Notwithstanding this, some of the Scotch cases appear to exclude the possibility of maize being an ætiological factor, and prophylactic work on this basis has been so far a failure, for, although the disease has diminished in certain regions for a time, it has later returned with considerable vigour. With regard to the presence of pellagra in Europe before the introduction of maize there is no trustworthy evidence, and the possible occurrence of the disease in the celebrated St. Francis of Assisi is only an interesting speculation.

After carefully considering all the facts in support of the maize theory, and comparing them with those against, we have come to the opinion that the maize theory, *in general*, is so far based upon insufficient foundations. It is, however, necessary to lay before the reader the various phases of this theory, which may be classified as follows:—

1. Photodynamic theory.
2. Deficiency.
3. Toxicity.
4. Infectivity.

1. *Photodynamic Theory.*—The special promoter of this theory is Raubitschek, whose work has tended to show that an exclusive maize diet, good or bad, proves deleterious to white mice and guinea-pigs if these animals are exposed to sunlight. He also suggests that an exclusive diet of other cereals, such as rice, millet, or wheat, might, under similar circumstances, produce the same phenomena. This theory maintains that photodynamic substances are introduced by the cereals into the blood, and these, under the influence of sunlight, become toxins, and thus cause inflammation of the skin and other symptoms resembling to some extent pellagra. Moreover, Raubitschek maintains that he has cured mice suffering from fagopyrism by keeping them in darkness, even though the diet was unaltered, and, further, that he has obtained favourable results by excluding light from the skin of pellagrins by means of darkened rooms, red windows, ointments, bandages, etc. Hirschfelder has searched for this fluorescent (photodynamic) substance in the blood serum of five patients suffering from severe pellagra, and found that there was no difference in the fluorescence between their serum and that of healthy persons. Moreover, fagopyrism only occurs in white animals, and not in black; whereas pellagra can occur in the jet black negro, which appears to us to be a strong objection.

2. *Deficiency.*—This theory has been mentioned above with regard to the absence of nitrogenous complexes, and it only remains to add that protein deficiency has also been brought forward as a possible explanation of the action of maize in producing pellagra, but has no sound foundation. Moreover, many people live on rice and potato, which have lower nitrogen ratios than maize.

3. *Toxicity.*—Volpino, Mariani, Bordoni, and Alpago-Novello, have made investigations with regard to inoculating maize extracts into patients, obtaining several general reactions. These experiments support the latest view, which is really only the revival

of an older view, that normal maize in certain individuals may produce pellagra, or, in other words, that there is an individual susceptibility to maize. This subject has been recently carefully investigated by Rondoni in human beings. He procured his maize from the domestic store of certain pellagrins, and having tested his cases for tuberculosis by von Pirquet's test, administered extracts of the maize by intramuscular injections to thirty-three pellagrins and thirty non-pellagrins. He did not find any violent reaction, as described by other writers, but he found that recent cases of pellagra and convalescents reacted more definitely than non-pellagrins, showing slight fever, headache, malaise, excitability, and sleeplessness, and considered that this increased sensibility might be regarded as an anaphylactic reaction to some undefined factor in the maize extract. If this anaphylactic theory held, then any person who for a few weeks ate a quantity of maize at any time of the year should develop acute pellagra. The Illinois Commission attempted anaphylactic tests by von Pirquet's method, substituting maize extracts for tuberculin, and the result was negative.

A second theory states that pellagra is due to toxins produced during the spring by the germination of the maize. The objection to this is that some cases start in the autumn.

The third theory asserts that poisons are generated in the bowel from the grain (Neusser) by the aid of the *Bacillus coli communis* (De Giaxa). This latter theory of De Giaxa is supported by experiments, for he produced the symptoms in animals inoculated by the toxin produced by growing the *B. coli communis* in maize media.

Numerous observers have reported poisons in fermenting maize. Thus, Lombroso in 1871 obtained two alkaloids, one like conium and the other like strychnine, but the symptoms produced by these on men and animals were not like those of pellagra. Others have reported tetanic or narcotic poisons, etc., but, on the other hand, Monselice failed to obtain any such poisons in damaged grain from pellagrous districts.

4. *Infectivity.*—At the present time the popular belief is that the disease is caused by maize damaged by being cultivated and harvested under unfavourable circumstances, and stored in such a damp condition that it becomes mouldy. This has been supported by Hirsch, who points out that a bad maize harvest is followed by an increase in the cases of the disease. The theories as to the substance in the damaged maize which causes the disease are manifold, and may be classed into (*a*) fungi, (*b*) bacteria, (*c*) chemical substances.

(*a*) *Fungi.*—Monti and Tirelli showed that fungi were commonly found in maize, those most usually met with being ***Penicillium glaucum***, *Rhyzopus nigricans*, *Mucor racemosus*, and species of ***Aspergillus*** and *Saccharomyces*. The special fungus, ***Sporisorium maidis***, described by Ballardini in 1845 as the cause of the disease, is probably only ***Penicillium glaucum*** or ***Mucor racemosus***, the former being held by some writers to be the causative agent, but its effects on men and animals are quite different from pellagra. *Aspergillus fumigatus* and *Aspergillus flavescens* (or *A. varians*) have been obtained by Ceni in pure cultures from the lungs, pleura, and pericardium of pellagra cadavers, but the symptoms of the disease are quite different from aspergillosis. Later, Ceni and Fossati have stated that the real cause of the disease is the toxin from the fungi.

(*b*) *Bacteria.*—Monti and Tirelli showed that many bacilli grow in maize—*e.g.*, *Bacillus solanacearum*, and another like *B. subtilis*—and it has been shown by Paltauf that the so-called *B. maidis* of Majocchi and Cuboni is only the common potato bacillus. Another bacillus, called *B. pellagræ*, is stated by Carrarioli to produce toxins, which, when injected into animals, produce the typical symptoms of the disease.

Tizzoni has described a bacillus found in the cerebro-spinal fluid of pellagra patients and on maize, but this bacillus will be considered at greater length below.

The maize theory is therefore by no means proved, and in fact is, in our opinion, very doubtful.

Parasitic Theory.—The parasitic theory of the origin of pellagra, which is supported, to a certain extent, by our own observations and by the Illinois Commission, who conclude that it is a disease due to infection with some living organism, may be classified into:—

A. *Vegetal parasite.*
  Tizzoni's streptobacillus.

B. *Animal parasites.*
  Alessandrini's theory, 1910.
  Long's theory, 1910.
  Perroncito's theory, 1910.
  Babès' theory, 1911.
  Sambon's theory, 1905.

TIZZONI'S STREPTOBACILLUS.—This is really a part of the maize theory, as Tizzoni has found the bacillus on maize; but it is also a genuine parasitic theory, because he has also found it in the blood, cerebro-spinal fluid, and organs of pellagrins after death. He has found it in both acute and chronic pellagra; it is a non-spore-bearer, and resists temperatures of 80° and 90° C. for one hour. It is easily cultivated, and is believed to be taken into the body with the food, so causing the infection. Tizzoni claims that this organism is the cause of the disease, but this claim has been refuted by Wood, Raubitschek, the Illinois Pellagra Commission, and others, and therefore cannot be accepted as proven.

ALESSANDRINI'S THEORY.—From epidemiological researches mainly undertaken in Umbria, Alessandrini has come to the conclusion that there is some relationship between pellagra and drinking-water, and he has found a slender nematode worm in the drinking-water of pellagrous places. This worm, which he places in the family Filariidæ, he considers to be the cause of the disease. He also states that he has found a filarial egg in the skin of pellagrins.

According to Sambon, who has seen Alessandrini's specimens, the thick-shelled egg belongs to one of the nematode worms infecting pigs. Alessandrini's theory has not received much support up to date.

LONG'S THEORY.—This theory suggests that pellagra is merely a phase of amœbic dysentery, but the Illinois Commission, as well as the observations of Sambon and one of us, do not support this theory. Dysenteric-like ulcers can be found in the intestine, but they often do not contain amœbæ.

PERRONCITO'S THEORY.—Perroncito has found peculiar parasitic bodies in the skin of pellagrins. This is an important statement, and further investigation of these forms is awaited with interest.

BABÈS' THEORY.—Babès states that he has found bodies resembling a Chlamydozoon, in the skin.

SAMBON'S THEORY.—This theory is double-barrelled—*i.e.*, it brings forward the proposition that pellagra is a protozoan infection, and that it is spread by the agency of a biting fly.

Parasite.—His reasons for believing that it is a parasitic disease are almost entirely epidemiological. They are:—

1. *The Mononucleosis* present in the blood.

2. *The Presence of Long Intervals of Quiescence, followed by a Relapse.* Thus, a young pellagrin with marked symptoms who comes to London, and receives most excellent food, without any admixture of maize, suffers from a mild relapse every year in the month of April. In this case there can be no question of maize causing these relapses. Further, we may state that the young person appears to be in the very best of health at the time of writing (January). Similar, but not such convincing, cases have often been reported in gaols and asylums, as mentioned above.

Siler and Nichols in Peoria Asylum filled two cottages with about sixty insane persons in each. One cottage was placed on a generous maize diet and the other on a maize-free diet. At the end of twelve months the maize-eaters had four certain cases and one doubtful case of pellagra, while the maize-free group included five certain and five doubtful cases of pellagra. Probably these were merely relapses of the disease which had occurred long before, but as we have only seen a summary of the Illinois Pellagra Commission Report, we cannot give details.

A point has been made that, while patients in asylums develop acute symptoms, the attendants do not, and this is held to be an argument against the parasitic cause of the disease. But this is just where the experience of Sambon and one of us differs from those of many authorities, because we have seen the disease begin so often in early childhood. The youngest case seen was three months of age, and we have obtained excellent histories of long intervals occurring between one series of acute attacks and the next. We look upon these asylum cases as probably relapses of earlier attacks, and are therefore not surprised that attendants are not attacked, because probably the agent of the conveyance of the disease is not present in the vicinity of the asylum.

In other asylums, however, it is possible that, if suitable conditions were present, the disease might spread among the inmates and attendants.

3. *The Constant and Characteristic Topographical Distribution.*—We have already drawn attention to the topographical distribution, and to the fact that pellagra remains endemic in the same localities for very long periods, and we have also referred to the case of a young boy developing pellagra, though constantly residing in a town, after a brief visit to a pellagrous region. The case of the fishermen of Burano (*vide infra*) may also be quoted; and, finally, attention may be invited to many similar instances quoted by Sambon in his able 'Progress Report on the Investigation of Pellagra,' published in London in 1910. Associated with this, it may be mentioned that of two places almost contiguous one may be affected and the other not.

4. *Its symptoms, course, duration, morbid anatomy, as well as therapy, are similar to those found in parasitic diseases.*

5. *Spirochæte.*—Sambon found a spirochæte in the liquor from a bulla on the hand of a case of acute pellagrous dermatitis in Roumania.

These points will be dealt with under Pathology, and need not be discussed here.

Objections.—The principal objection to Sambon's theory is that up to the present no parasite has been definitely associated with the disease, but this may be at any time rectified in the near future.

The very few experiments performed on white rabbits, by injecting liquor cerebro-spinalis, blood from the erythema, or lymph from bullæ, subdermally or into the spinal canal, have produced no definite results, nor have attempts at intradermal inoculation of these animals with the same fluids been more successful. Neither have the attempts made by the Illinois Commission to transmit the disease to monkeys and guinea-pigs met with more success. Recently, however, Siler in a communication to Sambon has stated that injections of defibrinated blood taken from pellagrins have produced pellagra-like symptoms in monkeys.

In our opinion there is need for much more extended experiments, and we are supported in our belief by the finding of the Illinois Commission that '*Pellagra is a disease due to infection with some living organism.*'

Carrier.—Sambon, however, has not been content to remain with an incomplete theory, but has advanced the view that the disease is conveyed by some biting fly.

His reasons for this theory are:—

1. Pellagra is essentially a *disease of rural districts.*
2. It is in some way related to *moving water.*

3. It has a definite ***seasonal incidence***—spring and autumn—which coincides with the appearance of certain flies.

4. It largely affects ***field labourers*** and new residents in endemic areas.

5. It is ***not contagious***, and neither food nor water can account for its peculiar epidemiology.

6. In the endemic centres it ***affects all ages***, both sexes (as a rule, females are more frequently attacked than males).

7. An endemic centre is one in which it is usually easy to find ***young children*** with the symptoms of the disease.

8. In endemic centres ***whole families*** may show signs of the disease, but outside these only one or two individuals may be affected.

Researches on the Island of Burano in the Venetian Lagoon.—With regard to the theory of a biting fly, Sambon is supported by the inquiry into the pellagra of the Island of Burano made by himself, Colonel Belli, and one of us, in which it was found that the fishermen and the boys who went fishing with them, were attacked by the disease, while the men who worked in the Venice Arsenal were said by the medical authorities to be free from the disease. The women, the girls, and the young children showed no signs of pellagra, with the exception of two or three women, who gave a history of working on the mainland or on other islands adjoining. Many of these young children, girls, and even women, were alleged never to have moved from Burano, with the exception in some instances of an occasional visit to Venice. These points are contrary to the maize theory, as all the inhabitants in Burano eat maize. They are also against a hereditary transmission of the disease, for with pellagrous fathers it would be imagined that the young children should show signs of pellagra, especially as the male influence is said to be preponderant by those who believe in the heredity of pellagra. They are against sexual infection, as the women would acquire the disease; they are against infection by contact, by kissing, etc., because certain men and boys have the disease, but the women and girls are remarkably free; they are against a parasite being carried from the sick to the healthy by house parasites, such as bugs or fleas, or personal parasites, such as lice. The difference between the persons who suffered from pellagra in Burano and those who did not appeared to be the fact that the former either worked upon other islands or fished on the lagoon and up the streams leading into the lagoon. On the other islands and on ***terra-firma*** there are plenty of pellagrins, and everywhere there is a history of small black biting flies occurring on quiet days in the early morning or late evening.

Sambon considers that the peculiar feature of the erythema coming in the spring and the autumn must be a correlation with some insect, and considers that the Simuliidæ or some allied family would be the most likely to supply the requisite fly. He chose first the Simuliidæ because its larvæ lived in running water, and because it had two seasons, during which it appeared in swarms and attacked man and animals—viz., spring and autumn, and not in summer—a fact which we have been able to confirm for one of the regions which we visited.

The Illinois Commission and many others have been unable to support the relationship of pellagra to *Simulium.*

The epidemiological evidence in favour of the spread by a biting fly is, however, very strong.

Summary.—It appears to us that while at present the causation of pellagra is unknown, and while the modern tendency is to claim it as a deficiency disease, still the investigations of a possible protozoan parasite and its carrier should not be given up.

Predisposing Causes.—Sex would appear to be a predisposing cause, because the disease is often more prevalent in women than in men, and this would not appear to be so mysterious as it seems at first sight, for if there is anything in Sambon's fly theory, the women ought to be more exposed to the flies than the men, because they wash the clothes in the neighbouring streams. In one place where this incidence was most marked the men worked all day underground in mines, and the women presumably in and about the houses, which were on the banks of a fly-infested stream. Here the children also were much affected. In interesting contradistinction is the incidence in the women of Burano, who mostly work indoors and among whom pellagra was very rare; but it was common among the fishermen and boys who fish in the rivers, etc., where biting flies are common.

Age would not appear to have any marked influence, but it would seem as though the disease was very prevalent—in a mild form, at all events— in the early years of life, as the children of a pellagrous district are often early affected, and some of these attacks are by no means mild, but very severe.

With regard to social position, poverty, lack of sufficient food, and bad hygienic surroundings, it was long considered that these had a marked influence in producing the disease, but though they may help, as they would, with almost any form of disease, still, the American and our own experience show that they have no real connection with pellagra, which can equally well occur among the well-to-do, the well-fed, and those living in circumstances of good hygiene, though more commonly met with among the poor and those ill-fed and living in circumstances of bad hygiene.

There is a definite correlation between the lowering of the general resistance of the body against disease and an acute exacerbation of pellagra. Thus pregnancy, an attack of any illness, but especially enteric fever, may induce either an exacerbation or the first remembered attack of the disease.

Sunlight *per se* is not a causal factor, as far as we know, in the disease, but it is a powerful predisposing cause in helping to develop the dermatitis.

Pathology.—As the causation of pellagra is entirely unknown, the pathology must be purely speculative.

The *Zeists* see in the phenomena exhibited by the morbid anatomy and histopathology changes which appear to them allied to those found in scurvy, beri-beri, or ergotism, and believe that these changes support the maize theory.

The *Fagopyrists* see in the phenomena found in the skin lesions as well as in those of the rest of the body the signs and symptoms which can be produced in white animals fed on maize and exposed to sunlight, and believe that these changes support the photodynamic theory.

Those who support the *Parasitic Theory* quote the mononucleosis of the blood, the leptomeningitis, the perivascular infiltration, and the primary degeneration of the nerve cells, as well as the long intervals of apparent quiescence, as phenomena similar to those seen in syphilis and sleeping sickness, and therefore believe that these changes support the parasitic theory.

Sambon, however, has extended the parasitic theory by arguing that the erythemata appearing on the hands, feet, face, and neck, and more rarely on the genital organs, in the spring and autumn, are brought about by the combined action of the parasite, whatever it may be, and sunlight in correlation with the habits of some biting fly. From epidemiological studies he suggested that some member or members of the family Simuliidæ might be the insect in question. He came to this conclusion because of the known habits, life-history, etc., of the Simulidæ, which were in general agreement with the epidemiology of pellagra.

The reason why there is such a confusion of ideas with regard to the pathology is not difficult to understand, as a post-mortem made on a case of acute pellagra within an hour or so of death is of great rarity, and has often been performed under conditions of difficulty as regards cleanliness or preparation. Post-mortems on cases of recurrences or of chronic pellagra have been abundantly performed under the best auspices, but the main features of the disease are often obscured by secondary changes; while even in the acute cases the phenomena are complicated by the presence of malaria, typhoid, tuberculosis, syphilis, etc.

Notwithstanding all these objections, there is some evidence in favour of an early lesion of the central nervous system, especially the posterior portion of the spinal cord in the lower cervical and dorsal regions, as congestion and hæmorrhages have been found there, while in the more chronic condition degeneration of the cells in the posterior cornu, in Clarke's column, and in the spinal ganglia have been seen, as well as the later degeneration of some of their axones. Further, according to Brugia, acute degenerative changes can be seen in the cells of the sympathetic ganglia of the cervical and abdominal regions associated with a diffuse, round-celled infiltration of the interstitial tissue, which eventually leads to sclerosis. Degenerative changes have also been recorded in

Purkinje's cells, in the cerebellum, and in the cortical cerebral cells.

If these accounts are confirmed, they might be found to stand in relationship to the angio-neurotic process in the skin, the congestion of the alimentary canal, the vertigo, and the mental condition.

However, all these points are at present extremely obscure, and are only brought forward here because they appear to require investigation.

The lesions found in post-mortems in cases of acute pellagra, in our opinion, apparently support the theory of some protozoan parasite, as suggested above, acting upon the central nervous system and the autonomic nervous system.

Morbid Anatomy.—The principal point in studying the morbid anatomy of pellagra is to attempt to distinguish between the appearances truly produced by the disease and the signs caused by complications. As we are unacquainted with either the ætiology or the pathology of pellagra, this is most difficult, and only an attempt, which may possibly be fallacious, can be made.

The Essential Lesions.—Our experience would indicate that in *acute cases* the body need not be emaciated, and that no trace of the erythema may be visible, but that the lines of demarcation can, as a rule, be easily seen on the arms, legs, and neck, as well as the thickened or pigmented areas of the epidermis, bullæ, etc.

In these cases there may be fluid, and at times hæmorrhages under the cerebral dura mater, œdema and thickening of the pia-arachnoid, which, however, is not adherent to the cortex. The cerebro-spinal fluid is usually, but not always, increased in amount. In the cord there may be subdural hæmorrhages, sometimes extensive, especially in the region of the lower cervical and upper dorsal cords, and there may be congestion of that area of the cord; otherwise the naked-eye appearances of brain, spinal cord, and nerves, may be normal.

Sometimes the alimentary canal is almost normal, but this is rare, and usually there is more or less congestion and at times even ulceration of the mucosa of the small intestine, and the valves of Kerkring may show small hæmorrhages. The ileum may be thinned, and Peyer's patches may be diminished in number and atrophied (these lesions are, of course, found in many diseases). The large bowel may be thickened, congested, and ulcerated, but the ulcers need not contain amœbæ. Pancreas, liver, and kidneys may show signs of cirrhosis (the above intestinal lesions are often associated with polyfibrosis). The mesenteric glands may be enlarged, and congested. The spleen may or may not be slightly enlarged, and the suprarenal capsules may be larger than normal, and the cortex may be black, while the medulla is whitish in colour; but, on the other hand, the capsules may appear to be perfectly normal. In *chronic cases* the body is often emaciated and anæmic, the skin rough, hypertrophied in places and atrophied in others, the changes being marked on the face, neck, arms, hands, legs, and feet. The subcutaneous fat is diminished. The muscles, heart, liver, spleen, and kidneys, are all atrophied; the stomach is usually normal, but the intestines may be atrophied, as described above, and the rectum may be ulcerated. The nervous system shows a diffuse leptomeningitis, with marked thickening in places; the frontal convolutions may be atrophied in some cases and the motor convolutions in others. The bloodvessels may show calcareous degeneration, and there may be sclerosis of the postero-lateral and postero-median columns of the cord, and in the dorsal region there may be also lateral sclerosis. The posterior nerve roots may be implicated, and the intervertebral foramina may be narrowed by a firm cartilaginous-like deposit.

The Complicatory Lesions.—Very often in pellagra post-mortems the signs of secondary septicæmia (bacillary or streptococcal), of ankylostomiasis, of malaria, of enteric fever, of bacillary dysentery, of amœbic dysentery, and of tuberculosis, may be seen, and complicate the pathological picture. In performing post-mortems, it is necessary to attempt to unravel the true lesions from those caused by complications. The so-called characteristic intestinal lesions described above are met with in many post-mortems in which there is no sign of pellagra.

Histopathology.—With regard to the autonomic nervous system, the nerve cells of the sympathetic ganglia of the neck and abdomen are described by Brugia as becoming swollen, and showing chromatolysis, with changes in the nucleus and nucleolus in acute cases. Associated with this there is infiltration of the interstitial tissue and proliferation of the endothelial cells of the capillaries and circumscribed hæmorrhages.

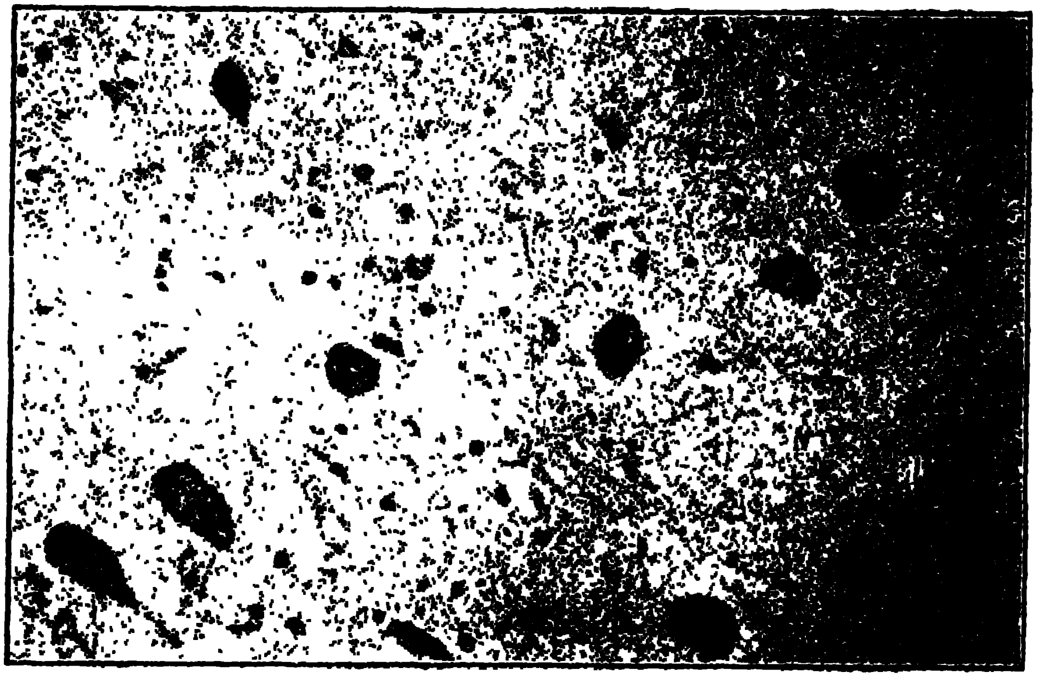

Fig. 738.—Cells of Clarke's Column in a Case of Acute Pellagra. (× 250.) (After Sambon and Chalmers.)

With regard to the chronic cases, there is atrophy and reduction in number of the nerve cells and sclerosis of the ganglion. The atrophied cells may be pigmented, but this is by no means constant.

In the spinal cord our own observations, as well as those of others, show that the posterior area is congested, and hæmorrhages are often present. Degeneration has been met with in the cells of the spinal ganglia, in those of the posterior cornu, and in those of Clarke's column. In these cells the Nissl bodies and the fibrils disappear, while the nucleus is placed excentrically, and often peripherally. Degenerated nerve fibres have been found in the posterior roots, in Lissauer's tract, in Burdach's column, and in Goll's column, and less commonly in the lateral columns. Some of the cells of the anterior cornu also degenerate. Degenerated nerve fibres may also be seen in the peripheral nerves.

In the brain the cortical cells have been found to be degenerated, swollen, and even disintegrated; while Purkinje's cells in the cerebellum are also said to degenerate. Mott has shown that while the fibrils surrounding these cells may be intact, those passing through the cells disappear. A perivascular infiltration around the vessels of the brain has been described by some authors, but was not present in our specimens nor in those described by Mott. There is also an increase in the neuroglia tissue in our specimens, but there is no cellular infiltration into grey or white matter, or any sign of acute inflammation.

The cerebro-spinal fluid is usually present in considerable quantity, and exhibits a medium amount of tension. It is alkaline, specific gravity varying from about 1004 to 1007; it generally gives reactions indicating the presence of some protein and butyric acid, and it generally reduces copper sulphate. The number of cells per cubic millimetre varies, but is about thirty-five, according to Hindman, whose differential count is: Small lymphocytes, 36·3 per cent.; polymorphonuclears, 18·6 per cent.; large mononuclears, 19·2 per cent.; plasma cells, 7 per cent.; lymphocytes, 5·1 per cent. The liquor is sterile, and injections into rabbits have been negative.

The skin has been reinvestigated by the Illinois Commission, who find that the changes can be described as due to an angio-neurotic process. There is infiltration of the true skin, and especially the pars papillaris, and œdema of the connective tissue. The rete Malpighii is infiltrated with cells, but otherwise normal. The stratum granulosum is normal, but the stratum corneum is thickened, and shows parakeratosis.

In the blood there is a reduction in the numbers of the red cells, which usually appear quite normal. There is mononucleosis, and Low has described granules in the mononuclear leucocytes, which, however, he has also found in other diseases. Fatty degeneration and cloudy swelling have been recorded in the liver, but no constant changes have so far been found in the spleen.

Symptomatology.—The incubation period of pellagra is unknown, but it cannot be of long duration, as we have known it to occur in a child three months of age, and, as we have already advanced arguments against heredity, this case is in favour of a short incubation period. We have also met with a case in which the skin symptoms are said to have appeared about two weeks after return from a visit to a pellagrous area in a person who was said to have always lived in a non-pellagrous area. We are always very sceptical of these histories, and should not have mentioned it if it had not curiously coincided with the case recorded by Sambon, where he states that a child born in an Italian gaol was nursed by its own mother in gaol until five months old, and then sent to some peasants living in a pellagrous area, when it developed pellagra in two weeks.

The description of a typical case is something of this nature:—A person, male or female, young or old, in apparently excellent health or in bad health; living or working in the sunshine of a spring day, notices that a sunburn appears on the backs of his hands, and perhaps the dorsa of his feet, if bare, and more rarely, also, on his face or neck. He thinks little of it, though the inflamed area burns, and may even blister. Perhaps he has a sore mouth, and perhaps he has a little diarrhœa or constipation. Perhaps he feels a little giddy in the morning, and perhaps he is easily tired. In a week or so the redness dies down, and the affected area is seen to be pigmented, and perhaps to have the skin thickened in places. In the course of a few days, or a week or so, these thickened areas desquamate, and the skin underneath may be found to be normal, or may be found to be slightly atrophic, and to appear whiter than the surrounding pigmented area.

The patient thinks no more of his troubles, the autumn comes, and he feels well, and during the winter there is no alteration in his good health. Perhaps the next spring may pass without a recurrence, and perhaps even several springs may elapse before the patient, who all this time may consider himself to be in excellent health, has a return of his symptoms. But though the interval may be long or short, this relapse will surely occur, and often it will be in a severer form than it was at first. It will usually recur in the spring, but it may take place in the autumn, or, much more rarely in our experience, in the summer.

This time the symptoms may be mild, as before, but, on the other hand, they may be severe: the erythema appears with severe burning sensations, and a real dermatitis, with bulla formation, may develop.

The tongue, lips, mucosa of the mouth and palate, may become inflamed, and show the presence of vesicles and ulcers. The parotid gland may enlarge (this is common in Egypt, but rare in other countries), the saliva may be so increased in amount that it pours from the mouth. There may be signs of dyspepsia, pains in the abdomen, and diarrhœa, or even dysentery may develop. The vertigo already mentioned

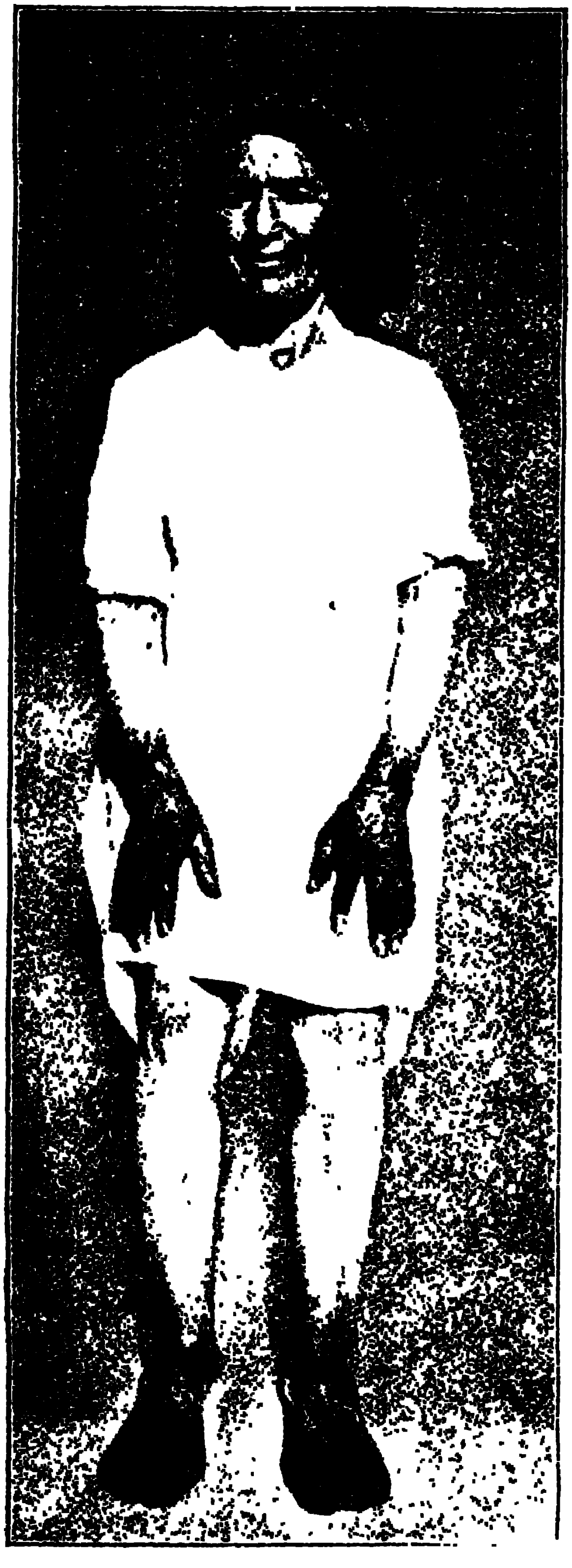

FIG. 739.—ACUTE EXACERBATION OF PELLAGRA.

Note the marked erythema on the hands and feet, and the less evident erythema on the neck and face.

(From a photograph by Terni.)

may become quite distressing to the patient, who, upon quickly rising from a sitting or a lying posture, may even fall to the ground. The muscular power may now be diminished, and the patient may no longer be able to do his work; tremblings in various parts of the body, but more especially in the head and arms, may be noticed, and the legs seem scarcely able to support the victim, who now shows decided melancholic symptoms, avoiding his fellows, becoming highly emotional, and perhaps threatening, or actually committing, suicide, often by drowning in water.

Pains are felt in various parts of the body, but especially in the head, the stomach, and the feet. A most unpleasant symptom is the burning sensation complained of by the patient after retiring to bed at night. So severe is this that patients have been known to strip off all their clothes and lie naked on their beds. By this time the unfortunate victim will have learnt by bitter experience that sunlight is deleterious to his condition, and will try to avoid it as much as possible.

Again, as winter approaches, the symptoms will diminish and die away, and the patient will feel better; but this time the skin does not recover itself, but remains thickened and pigmented in places, and thinned, whitened, and atrophic in other places.

Again, there may be only an interval till the next spring or autumn, or the succeeding spring, or there may be a longer interval, and again mild or severe symptoms may appear.

With repeated attacks the skin changes become marked, the mind becomes often permanently affected, and melancholic or maniacal symptoms are often observed.

Pain is often complained of in the back, and tenderness is found on pressure over the spinal nerves on either side of the dorsal or lumbar portions of the vertebral column. Muscular weakness is noted, especially in the legs. The knee-jerk is at first exaggerated, but later is diminished, and finally lost. Ankle clonus and wrist clonus are rare, and only occur when the knee-jerk is exaggerated, when there is tenderness on both sides of the dorsal and lumbar cord, and when abdominal and epigastric reflexes are also increased.

There is no special gait, but there is a tendency to fall backwards or forwards, and hence, though the patient walks with the legs well apart, in a very bad case he can only take a few steps without falling down. There may be tremors in the legs and tongue. The bladder and rectum are not as a rule affected until the end, but there are exceptions to this, and contraction of the limbs does not take place till bedridden; but moderate rigidity of the muscles of the arms and legs, associated with stiff and at times irregular spasmodic movements, has been recorded as occurring early in rare acute cases. A sudden rigidity of the body associated with retraction of the head has also been observed. These attacks last only a short time, but are recurrent. Trophic lesions, such as bedsores, are of rare occurrence. Hyperæsthesia may occur in different parts of the body, and pains (even of a lightning nature) may exist in the head and back, and be associated with cramps.

The facies of the pellagra patient is one of anxiety and mental worry. He cannot sleep, and there is often great mental depression and discontent; but some are excitable and irritable, while others are stupid and morose. He loses his memory, and has vague feelings of pressure, weight, or pulsation about his head. From this he proceeds to refusal of food and suicidal tendencies, with delusions of sorcery and persecution, and has a tendency to suicide by drowning. Melancholia may now become confirmed, and may eventually pass into dementia.

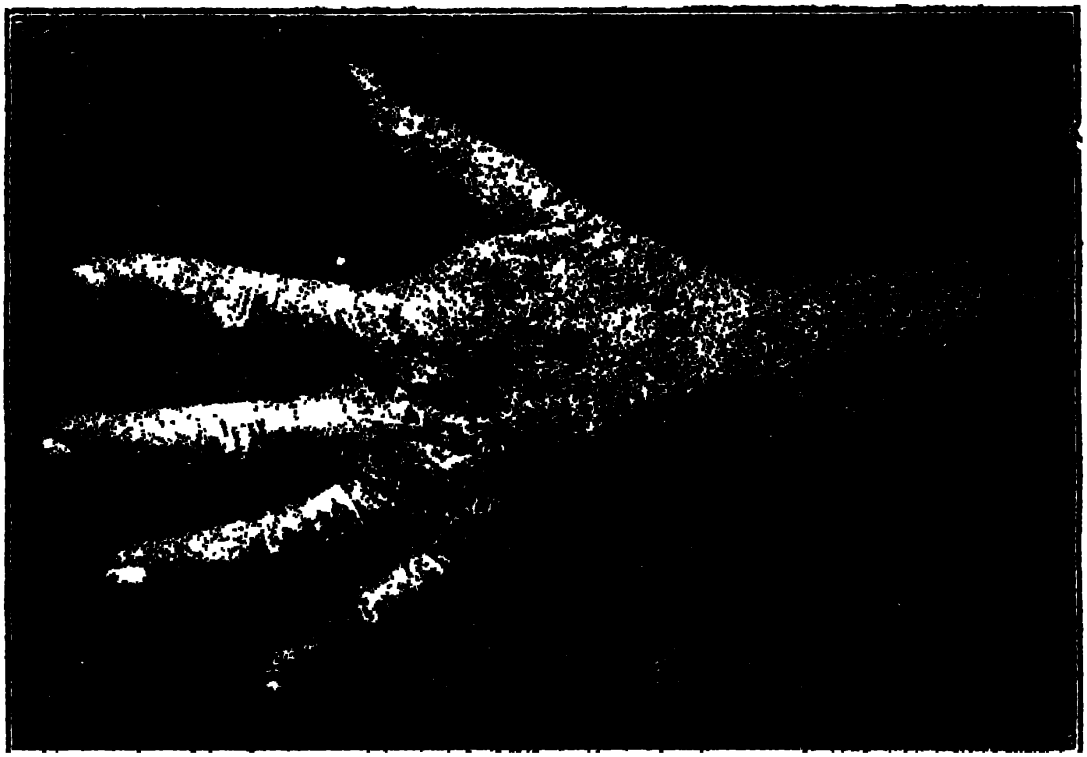

Fig. 740.—Hand in Chronic Pellagra.
(From a photograph by Sambon and Chalmers.)

Various paralyses develop, such as spastic paralysis, ptosis, hemianopsia, diplopia, amblyopia, and mydriasis. The extremities and bladder now become paralyzed, and the demented, paralyzed, rapidly emaciating patient, suffering from bad sweats, profuse diarrhœa, and sometimes dropsy, obtains a relief from his sufferings in death, the disease has usually lasted from ten to fifteen years.

Such is a general account of this rather protean disease, and we note that there is an onset in the spring, or more rarely in the autumn or summer, an intermission in the winter, and a relapse in the next or some following spring or autumn.

Very rarely a case of pellagra may be acute, lasting only a few months.

Children.—The disease is so common among young children in bad pellagrous districts, and so often can one, by careful inquiry, elicit curious facts that tend to show that pellagra, though occurring in the person in question in adult life, probably really began in infancy, that we are inclined to believe that the cases in young children are often overlooked, and we are supported in this belief by the mildness of the symptoms which we have observed in some children, which indicate merely a sunburn on the face, hands, arms, feet, legs, and perhaps the neck, associated with a little diarrhœa or constipation. The child recovers, the skin becomes normal, the attack is forgotten, and does not return until adult life, when the patient may have grown up and been living for years in a town, when a typical relapse appears—a new case (a town case it would be classified by many authors), but a careful inquiry into the history of the case may elicit the fact from intelligent people that the first attack began in childhood, when it may be explained by the friends as being in reality a sequela of Jenner's vaccination.

F 741.—HAND IN CHRONIC PELL.

Note the thickening of the epidermis and the line of demarcation. The hands in both figures had been vigorously scrubbed by the patient to try to remove the scabs.

(From a photograph by Sambon and Chalmers.)

Inquiry may often elicit the fact that when this occurred the patient, at that time a child, was living in the country, and often in close proximity to a stream—a fact which may be confirmed by a visit to the locality.

Another curious point with regard to some of these early cases is the history given by the friends of the development of some extraordinary habit of dietary, to the influence of which the disease is often assigned. These extraordinary cravings appear to us to be due to the dyspepsia (hypochlorhydria) so commonly met with in pellagrins.

We have rather insisted upon the occurrence of pellagra in young children because we are of the opinion that it is often overlooked.

Skin Eruption.—The skin eruption is usually limited to the regions exposed, being at first delineated in a most exact manner by the clothing: but in very rare cases it may be universal, and it is said sometimes to appear limited, as though by clothing, in naked gipsy children. It appears on the dorsum of the forearms, and on the hands and feet, only reaching the flexor aspect after several attacks. The most common sites are the hands and forearms, elbows, feet, legs and knees, the upper part of the chest, the shoulders, neck, and face. More rarely it appears on the genital organs and around the anus in both sexes. Sandwith points out that in Egyptian peasants the ungual phalanx of the hand is seldom affected, due to the fact that when the hoe is grasped it is protected against the sun's rays. The nails and hair are not affected, but rarely there is a dry, scaly condition of the palms of the hands.

The skin eruption may show the following conditions:— (1) Congestion: (2) inflammation: (3) thickening and pigmentation; (4) atrophic thinning.

The affected part turns a bright, dark, or livid red colour, which at first disappears on pressure, and is generally delineated by a very clearly raised limiting line. Associated with this erythema there is a burning sensation, but usually no pain. In course of time the part becomes swollen and tense, and bullæ may form. After lasting a variable period of days or weeks, the eruption gradually subsides, leaving the skin rough, pigmented, and thickened, and thus earning the names of 'pell'agra' and 'qushuf.'

This erythema disappears in the winter, but reappears the next spring with increased virulence, and in due course develops into a dermatitis, which produces an exfoliation of the epidermis in grey or brown flakes. Every attack leaves the affected area a little more pigmented, a little more thickened, and a little less elastic.

After lasting about four or five years the skin begins to atrophy, and becomes wrinkled and inelastic. This atrophy is most marked on the back, hands, and feet. Special terms have been given to the eruption when in certain areas—*e.g.*, the 'glove,' the 'boot,' Casall's 'necklace,' or 'cravat,' and the 'mask.'

Roberts has introduced the rather useful term 'dermotagra' for the dry, scaly, thickened skin seen over the olecranon process, over the knees, and more rarely on the palms of the hands. Over the elbow and knee the skin is rough, thickened, and wrinkled; on the palms of the hands it is merely rough and thickened.

Another interesting dermatological feature of pellagra is the frequency of nasal or facial seborrhœa, which is to be especially noted in the nose where the sebaceous follicles are very prominent and filled with plugs of sebaceous material.

The Mouth.—The tongue is generally coated with a whitish fur during the onset of an attack, but later it becomes abnormally clean—'*Sandwith's bald tongue*'—red, swollen, and sometimes ulcerated near the tip. It may also become fissured, but in mild cases it recovers as soon as the attack is over.

During attacks the gums may become spongy, and may bleed, and ulceration may appear, both here and on the palate, as well as on the pillars of the fauces. There may be pharyngitis, and more rarely œsophagitis.

The Blood.—The red cells are usually reduced in number, and the hæmoglobin proportionally reduced. Usually the form of the red cells is normal, but microcytes, and more rarely megalocytes, may be found. There is usually only a slight leucocytosis in uncomplicated cases, but there is in our experience generally a distinct mononucleosis. When the polymorphonuclear cells are increased, it would appear to always indicate a complication.

Circulatory Organs.—The blood-pressure is usually low, and the heart-rate may be markedly increased. Vasomotor changes can be observed in the coldness of the extremities, the bluish congestion of the feet and hands, the goose skin, and the neuroparalytic dilatation of the vessels of the face often giving rise to an appearance seen in alcoholics.

Respiratory Organs, etc.—The respiratory organs are not affected in pellagra unless there is some complication, but there may be an exudation of fluid into the pleural cavities in the late stages of the disease, as well as œdema of the bases of the lungs.

Urinary Organs.—Usually the urine is normal, or nearly so, and any great change must be considered to be a complication.

Sexual Organs.—Sexual power is usually diminished, especially in the later stages. Amenorrhœa, metrorrhagia, and inflammatory conditions of the vagina, uterus, ovaries, etc., are described, but must be considered as complications.

Special Senses.—The eyes suffer most in pellagra, but the changes—*e.g.*, weakness of vision, photophobia, etc.—are not dependent upon the disease *per se*, but upon the weakness which it produces. The patients often complain of a saltish taste in the mouth.

Fever.—As a rule the temperature is but little altered from normal in pellagra, but it may be raised at intervals as high as 101° to 102° F. (Wood) for two to three days at a time, but it may also be subnormal in other cases.

Complications.—As may be imagined, in a disease of such long duration as pellagra, the complications are numerous, and include malaria, tuberculosis, ankylostomiasis, bilharziosis, eye affections, and many skin diseases, including itch.

The most interesting complication is enteric fever, which may give rise to the form often called 'typho-pellagra,' which is apparently simply a pellagrin with an infection with one or more of the organisms causing enteric fever.

Terminal infections with various micro-organisms have been noted, and complicate the post-mortem findings. Thus, Bon records the occurrence of *Streptococcus pyogenes* in the blood as found by examination immediately after death.

Diagnosis.—Everywhere since pellagra was first recognized there has been great difficulty in its diagnosis, and it would appear necessary to consider not merely the signs exhibited by the patient, but the frame of mind in the observer in attempting to write upon this subject.

For the diagnosis of pellagra two conditions are necessary in the observer. The first is that he must suspect its presence, and be on the outlook for it in any and every country; and the second is that he must not be unduly swayed by any ætiological theory, and must be prepared to make a diagnosis of pellagra in a person of any age, any race, any social condition, living in any place, whether tropical, temperate, or frigid; resident in a town or in the country; and he must do this without consideration of the dietary or the surroundings, with perhaps the sole exception of being more intently awake to the possible occurrence of the disease in lunatic asylums.

As there are at present no microscopical, bacteriological, parasitological, hæmatological, or chemical reactions which can be said to be diagnostic of the disease, with, perhaps, the sole exception of the pellagra-like symptoms produced by one of the American Commissions, by injecting defibrinated blood into monkeys, and as these animal injections are not within the range of practical politics for purposes of diagnosis, we must trust entirely to clinical manifestations.

The cardinal signs of the disease may be summarized into—(1) *the cutaneous signs*, (2) *the gastro-intestinal signs*, and (3) *the nervous signs*.

In order to make a definite diagnosis, there must be either the presence or a definite history of the cutaneous signs of pellagra associated with symptoms belonging to one of the other groups.

1. *Cutaneous Signs.*—When a person shows more or less symmetrical erythema, dermatitis, pigmentation, or a condition more or less resembling chronic dry eczema on either the backs of the hands, the dorsa of the feet, the face, the back and sides of the neck, or the front of the chest, especially if these eruptions are limited by a more or less definite elevated margin to the areas habitually exposed to light, suspicion should at once be aroused that the disease is pellagra. If a history can be obtained that this eruption appeared for the first time in spring or autumn, and more especially if a history of recurring attacks can be obtained, the suspicion becomes almost a certainty. If to these signs there are added the fact that the skin symptoms become worse on exposure to the sun, or that there are at the same time disturbances of the

alimentary canal or of the nervous system, and especially if there is the presence or the history of *vertigo*, then the diagnosis is certain.

2. *Gastro-Intestinal Signs.*—Gastro-intestinal symptoms are usually present, but they may be extremely mild, and they may be absent. Those most commonly met with during exacerbations are—Salivation, stomatitis, dyspepsia due to hypochlorhydria, diarrhœa, dysenteric symptoms, alternating with constipation, or simply constipation appearing or recurring in the spring or autumn. A diagnosis cannot be made by these symptoms alone, which must be considered in conjunction with the cutaneous in order to arrive at a conclusion. If no cutaneous symptoms are visible, it is justifiable to place the patient in strong sunlight in order to see whether the dermatitis will appear.

3. *Nervous Symptoms.*—Of all the nervous symptoms early exhibited, the vertigo is the most common, and should be carefully inquired for, as the patient often does not associate slight morning vertigo with the disease, and will therefore omit to mention the fact.

Other important symptoms are the melancholia, the myasthenia, the tremblings, and often curious delusions, and the irritable condition of the temper, recurring in the spring or autumn; but these must be associated with evidence of skin lesions before a diagnosis can be made.

It will thus be observed that, while the diagnosis may be a matter of extreme simplicity in a typical case, it may also be one of great difficulty in atypical cases. Perhaps the greatest difficulty is met with in lunatics and young children.

1. *Lunatics.*—In these cases the patient has been admitted into the asylum suffering from one of the well-known forms of mental disease, but most probably from melancholia or dementia, more rarely from attacks of mania. It may be noted that at times he suffers from diarrhœa or dysentery, which is often assigned to what used to be called 'lunatic asylum diarrhœa' or 'dysentery.' It may also be noted that at times he spits considerably, which simply means that he has an excess of saliva; but, much more importantly, it is noticed that he suffers from *chronic eczema* on the back of his hands, from *angioneurotic œdema* so called, both of which are often common in lunatics. Such cases require careful investigation, not with a view of making a diagnosis of pellagra, but with a view of excluding, if possible, the diagnosis that the case is really pellagra.

2. *Young Children.*—In young children the disease is very apt to be overlooked, and the red eruption on the face and hands, etc., followed by pigmentation, is generally attributed to sunburn or to eczema, while the alimentary disturbance is assigned to infantile gastro-intestinal derangements, and not connected with the skin lesions. A careful inquiry will show whether these symptoms have or have not a seasonal incidence, and in any case they should arouse suspicion of pellagra, which should only be eliminated after careful inquiry.

Differential Diagnosis.—As the symptoms are divisible into three groups, so the discussion of the differential diagnosis is equally capable of arrangement under the same three headings.

SKIN DISEASES.—The skin diseases which are to be differentiated from pellagra are classifiable into those resembling the acute cutaneous symptoms and those resembling the chronic cutaneous appearances.

1. *Resembling the Acute Dermatitis.*—Under this heading comes, first of all, *erythema solare*, from which pellagra may be distinguished by the inflammation of the mouth, by the presence of the alimentary canal symptoms, and by the vertigo, as well as by the fact that the pellagrous eruption at times appears on parts not usually exposed to the sun, and by the fact that the lesions in sunburn are usually very superficial.

The same diagnostic points will help to differentiate pellagrous dermatitis from *erythema* or eczema due to winds, salt air, etc.

The erythema on the face, hands, arms, etc., in cases of *dermatitis venenata* may simulate pellagra closely. The pellagrous condition may be differentiated by the presence of gastro-intestinal nervous symptoms, by the less general extension of the eruption, by the less involvement of the eyelids, and by the more acute course.

From *acarine dermatitis* pellagra may be distinguished by the localization of the eruption, which does not appear on the trunk, by the absence of the vesiculo-papules and pustules, and by the absence of itching.

From *alcoholic erythemata* it may be recognized by the history of the attack and by the presence of the typical eruption on the hands and feet.

Some authorities have, however, described, under the term *pseudo-pellagra*, of alcoholic origin, an erythematous eruption on the hands associated with nervous symptoms which is indistinguishable from true pellagra, being, in fact, the same disease.

From *angioneurotic œdema* it may be differentiated by the absence of marked œdema and the presence of more inflammation in the skin, as well as by the more regular distribution of the eruption, and by the limiting line.

2. *Resembling the Chronic Dermatitis.*—From *chronic eczema* occurring in mentally sound persons or in lunatics pellagra is recognized by the typical distribution of the eruption, by the line of demarcation, and by the marked pigmentation, when present, and absence of pruritus. From *chronic syphilides* by the distribution of the eruption, and by the absence of any reaction to mercury. Here mention may again be made of the *dermotagra* on the palms of the hands, over the olecranon, and about the knee, in chronic cases of pellagra, which is apt to be overlooked, or to be considered as points in favour of a diagnosis of eczema rather than of pellagra.

From biotripsis (*vide* p. 2282), which it closely resembles, pellagra is differentiated by the limitation of the eruption to the areas so often mentioned above, by the presence of the line of demarcation. In biotripsis the skin is dry and wrinkled, and may be thickened in places with dark-coloured patches, alternating with shining, smooth, inelastic, atrophic areas; but this condition is by no means limited to the hands or feet, but spreads up the arms and legs, and is not visible on the face.

It is hardly possible that *Kaposi's disease* (xerodermia pigmentosa) could be mistaken for pellagra, nor is *ichthyosis* likely to be confounded with it.

The wrinkled skin of the *washerwoman's fingers* is hardly likely to be confused with the chronic thickening found in pellagra, though this disease is often found in women who wash clothes, and who explain their own dermal condition in this way.

GASTRO-INTESTINAL DISEASES.—Of all the gastro-intestinal diseases, *sprue* is the only one which in any way resembles pellagra, which can be readily distinguished therefrom by the presence of the skin eruption. It must, however, be remembered that the psilosis linguæ pigmentosæ of West Indian writers is really pellagra.

Attacks of *diarrhœa* or *dysenteric-like attacks* can only be recognized as belonging to the syndrome of pellagra if the dermal signs are present at the same time, or if they can be produced by exposure to the sun, or if there is a very definite history of their previous occurrence; unless, indeed, they are associated with marked ptyalism or bilateral swelling of the parotid glands, or some other symptom tending to indicate that pellagra was the cause. The special cases in which diarrhœa and dysentery require careful diagnosis are those in which they occur in lunatics.

TYPHO-PELLAGRA.—In this disease the dermal signs of pellagra are sufficiently evident to enable its diagnosis to be made, as a rule, without difficulty, while the diagnosis of typhoid fever can be made by the methods already described on pp. 1389-1394.

NERVOUS DISEASES.—Melancholia, dementia, mania, etc., can only be diagnosed as pellagrous when associated with its skin lesions; but here care must be taken not to mistake the dermal signs of pellagra for chronic eczema, etc.; but this point, having been already discussed above, need not again be argued.

Prognosis.—This would appear to be good in early cases in mild cases, and even in moderately severe cases, if the patient can be removed from the pellagrous area and placed in good condition of food and hygiene in a non-pellagrous area.

But predictions as to a cure must be guarded, and it must be remembered that cases have relapsed after two, five, and even fifteen, years' intervals.

In severe cases the prognosis must be guarded, and the low blood-pressure remembered, as well as the possibility of sudden death from exertion after lying down.

Cases of typho-pellagra have a high mortality, and here the prognosis is obviously bad.

Complication with ankylostomiasis, tuberculosis, etc., also render the prognosis more unfavourable, as does continued residence in a pellagrous area.

Treatment.—There can be no doubt that the essential basis of the treatment of pellagra is to remove the patient from the pellagrous area in which he has been living to a non-pellagrous area; and, secondly, to give a good and liberal diet, preferably without any admixture of maize, although Devoto has shown that good maize not merely does no harm to pellagrins, but is very suitable for some of them, as it is their usual diet. If this is done, most early cases quickly improve, and apparently are cured, but, unfortunately, this is not so, because, even if they remain under these excellent conditions, sooner or later a recrudescence occurs. These recrudescences may be mild, but at any time they may become severe, even when maize is excluded from the dietary.

Arsenic.—This being so, it is obvious that some medicinal treatment is necessary, in addition to change of locality and diet, and apparently the best remedy is arsenic in some form. Of all forms of the drug, that most commonly in use, and also much vaunted, is 'atoxyl,' which is administered by intramuscular injection of 3 grains per diem.

Other methods of giving arsenic are salvarsan, neosalvarsan, and soamin.

Other methods are the cacodylate of sodium, administered in 3-grain doses by intramuscular injection every third day until three doses have been given, and then every second day until three more doses have been administered, and then increasing to 5-grain doses every second day until the symptoms have improved.

Associated with these injections, it is as well to give liquor arsenicalis in small doses internally, and to continue this interruptedly for some three months after the symptoms have disappeared. In addition, it is as well to repeat the liquor arsenicalis some weeks before the advent of spring, and to continue it intermittently into the summer for a few years after an attack, in order to attempt to guard against the almost inevitable relapse.

Radio-Active Serum.—Nicolaidi has devised an artificial organo-mineralized radio-active serum from horse serum, together with all the organic and mineral salts of the blood, in a solution saturated with carbon dioxide gas, which was then rendered radio-active. This serum is administered by injections until twenty to twenty-five are given, when, according to the author, supported by several eminent authorities, most remarkable improvement in the cases resulted.

Symptomatic Treatment.—The patients must be protected from the sunlight by clothing, veils, hats, gloves, etc., and the dermatitis must be treated by emollient lotions, such as calamine, soothing and dark ointments, such as ichthyol in lanoline.

The indigestion should be treated by a mixture containing dilute hydrochloric acid and infusion of gentian.

The diarrhœa and dysentery should be treated as indicated on p. 1854 for bacillary, or on p. 1834 for amœbic, dysentery.

With regard to the nervous symptoms, the irritation on retiring to bed and the sleeplessness should be remembered, and combated with cool bathing, and, when necessary, by doses of bromides, which, however, are apt to increase the depression.

The vertigo should be borne in mind, and precautions taken to prevent accidents being caused by it.

The mental condition should be cheered by pleasant surroundings, and in severe cases a watch taken to prevent the suicidal tendencies taking action.

Diet.—The diet must vary with the condition of the digestion and the bowels, and during attacks of dysentery or diarrhœa that laid down on p. 1858 should be adopted.

Complications.—Search should be made for signs of ankylostomiasis, ascariasis, etc., tuberculosis, malaria, etc., and these should receive their appropriate treatment.

Typho Pellagra.—This serious complication, which is really only an attack of enteric fever in a pellagrin in whom the acute symptoms at once become aggravated, must be treated by a combination of the treatments laid down for enteric fever on p. 1309, and pellagra, as above.

Prophylaxis.—As the ætiology of pellagra is unknown, it is obvious that remarks as to prophylaxis must be more or less speculative. It does not appear to be directly contagious, and therefore isolation, quarantine, etc., appear to be useless. In accordance with certain ætiological views, it is advisable to attempt to avoid being bitten by flies in the early morning or late evening in the endemic areas by the use of protective veils, fly-brushes, etc. Protection against the sun, as described above, is also of great importance.

It is obvious that the consumption of diseased or damaged maize must be injurious, and the action taken by the Italian Government to prevent the sale of bad maize is not merely highly commendable, but must be most beneficial to the community at large.

Further, the excellent attempt to find out every pellagrin by means of local lists is good, as it enables the Government to know exactly the condition of this dreadful malady, provided the lists are carefully compiled; on the other hand, if these lists are inaccurate, they may result in much misconception of the incidence of the disease. The provision of one good meal a day to poor pellagrins during the spring and autumn is, in our opinion, highly to be praised. That these meals are good, we can certify from personal experience. We fail, however, to see the utility of the free distribution of salt, but it does no harm.

The methods adopted by the Italian and other Governments may be summarized as follows:—

1. *Laws and Regulations.*

(*a*) **Prohibiting the importation and sale of spoiled corn.**

(*b*) **Government inspection of all corn dried, stored, or consumed. This includes the erection of public storehouses.**

(*c*) **Provision of desiccating plants to dry corn.**

(*d*) Cases of pellagra to be reported, and lists to be kept and emended every year. Unfortunately, they are not always very accurate.

(*e*) Formation of *locande sanitarie*—*i.e.*, kitchens where excellent free meals are given to pellagrins, and, it is to be hoped, to other deserving poor people also.

(*f*) Free distribution of 17½ pounds of salt to every adult pellagrin and 11 pounds of salt to every child pellagrin per annum. This distribution is arranged by a ticket system.

(*g*) Establishment and upkeep of *pellagrosaria*—*i.e.*, special hospitals for the treatment of pellagrins

(*h*) Establishment of *pellagrological commissions* in every province affected with pellagra, with powers to work the laws and to investigate the disease.

(*i*) Financial supply.

2. *Formation of Rural Bakeries.*

Model central bakehouse, controlled by Government, in which the only bread allowed to be used is baked from good, wholesome wheat-flour. The best model we have seen was in the Tyrol.

3. *Improvement of Agriculture.*

(*a*) By *cattedre ambulanti*, or farmers' institutes, designed to teach *locally* modern methods of agriculture, with the result that the farmers become less poverty-stricken.

(*b*) Advising the farmers no longer to plant second crops of inferior qualities of maize, called *quarantino* (*Zea mais v. præcox*) and *cinquantino* (*Z. mais v. subpræcox*), which, being gathered in the wet month of October, were often only half-ripe, and soon decayed.

(*c*) By organizing *agricultural shows*, which include the exhibition of *maize*.

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SECTION C

SYSTEMIC DISEASES

DISEASES OF THE ALIMENTARY CANAL.
DISEASES OF THE SYSTEMS.
SKIN DISEASES.

DIVISION I.: DISEASES OF THE ALIMENTARY CANAL.

Diseases of the Mouth and Stomach.
Helminth Infections.
Sprue and the Diarrhœas.
The Choleras
The Dysenteries.
Intestinal Schistosomiasis.
Epidemic Gangrenous Rectitis.

CHAPTER LXXIV

DISEASES OF THE MOUTH, THROAT, AND STOMACH

General remarks—Oral infections—Thrush—Gingivitis—Lingual affections—Halzoun—Tonsillar affections—Gastric diseases—Earth-eating—Belyando spew—Entalação—References.

GENERAL REMARKS.

In this chapter we make some remarks concerning the diseases of the mouth and the stomach, which we will preface with a few general statements concerning the intestines, as this is the most convenient place for so doing, though we describe the more important diseases of these parts of the alimentary canal in separate chapters.

External hernia is common, but internal hernia is rare: we have only met with one example, and then of a most unusual form, the displacement being through a rupture in the transverse mesocolon, forming a hernia into the lesser sac. This hernia probably took place through the recessus intermesocolicus transversus (Bröscke). *Intussusception* and *volvulus* are known, as well as intestinal obstruction due to bands, and we have met with one unique case of fatal intestinal obstruction in a native found dead, caused by the compression of the rectum against the pelvic wall by an enormously distended bladder, which we had not thought to be possible.

Cancer of the bowels is by no means uncommon. *Tuberculosis* of the bowel is generally secondary to tuberculosis in some other regions, but we have seen primary tuberculosis. *Appendicitis* is quite common in both Europeans and natives, and is caused by bacteria acting either directly, or introduced by the action of *Trichuris* and *Ascaris*. Appendicitis of schistosomic origin has been recorded by Mursell.

In previous editions we called attention to the frequency of *intestinal sand*. The true intestinal sand of animal origin composed of dark grey or colourless gritty particles, and largely composed of lime salts, is occasionally met with, but far more common is the so-called *pseudo-intestinal sand* composed of undigested remains of vegetable food (bananas, etc.), which may become encrusted with earthy salts. Delgado Palacios has called the condition 'fæcal sarcoma.' In these cases there may be diarrhœa and colicky pains.

Uronema caudatum has been recorded by Fischer, in 1914, in the diarrhœic stool of a European in Shanghai. Two days later only cysts were present.

ORAL INFECTIONS.

The protozoal parasites reported as being found in the mouth are:—

Loeschia gingivalis Gros.
Leishmania tropica Wright, var. *americana* Laveran and Nattan-Larrier.
Spiroschaudinnia dentium Miller, and many other spirochætes.
Spiroschaudinnia buccalis Steinberg.
Treponema mucosum Noguchi.
Treponema macrodentium Noguchi.
Treponema microdentium Noguchi.

Flagellates have also been recorded.

Gongylonema pulchrum.—This filarial worm is a parasite of the pig in Europe and America, but was described, in 1916, by Ward as occurring in the lower lip of a girl, aged sixteen years, at Jefferson in Arkansas. The worm was 42·1 millimetres in length, and tapered slightly at each extremity, of which the anterior was ornamental, by a system of cuticular tubercles, while a cuticular ridge ran along the lateral line.

The most common and perhaps most serious affection is *Pyorrhœa alveolaris*, in which condition pus wells up from alongside the roots of the teeth, while the gums become swollen, reddish, and inflamed, the teeth loose, and general septic absorption or infection may result.

The organisms associated with this lesion are innumerable—amœbæ, spirochætes, bacteria, etc.—and, therefore, the causal germ is unknown, but the treatment is quite clear—viz., to remove all teeth which are too far decayed to allow any hope of improvement, or which are viewed as dangerous from a general health point of view. Having done this, the next and most important point is *ionization* with zinc sulphate.

Apart from this, all bridges, crowns, and fillings have to be viewed with suspicion in the tropics, and vague septic conditions, diarrhœal or even dysenteric-like symptoms, and more especially inflammatory changes about the jaw, should lead to careful examination of teeth treated in this manner.

It will be remembered that streptococci are apt to enter the system alongside the teeth and via the tonsils, and, therefore, the streptococcal infection should be thoroughly and carefully treated.

The *inflammations of the tonsils*, diphtheritic, pseudodiphtheritic, and streptococcal, are common in the tropics, though diphtheria is somewhat rarer than in temperate climates, and require careful treatment with local antiseptics and either serums or vaccines.

Salivary calculi have been reported by Christopherson, and are certainly not uncommon in Europeans and natives, and are apt to recur after removal. A favourite seat appears to be the sublingual duct, where the calculus is apt, on superficial examination, to be mistaken for an enlarged lymph gland.

Espundia or oro-nasal leishmaniasis is fairly frequently met with, and is described on p. 2175; while *gangosa* or its syphilitic counterpart is frequently seen, and is described on pp. 1876-1879.

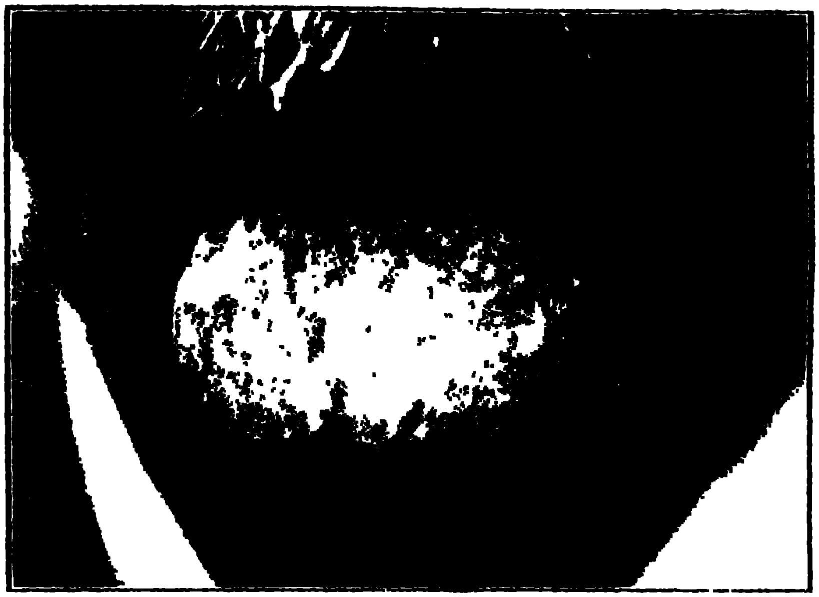

FIG. 742. LEUCOPLAKIA.

Leucoplakia and *cancers* of the lips, cheeks, and tongue are frequently met with in the tropics, and appear in a curious way to be related to mycetoma, via the condition called *paramycetoma* (*vide* Chapter XCIII., p. 2145).

THRUSH.

Synonyms.—Saccharomycetic stomatitis, Oral oidiomycosis. *French*, Muguet, Millet blanchet; *Italian*, Mughetto; *German*, Schwämchen.

Definition.—A stomatitis, or, more correctly, a group of stomatites, characterized by the presence of creamy white patches, believed in the past to be produced by *Oidium albicans* Robin, while at the present time it is recognized that they may be produced by a multiplicity of fungi.

Historical.—The affection was clinically known to Hippocrates, forming part of the στόματα ἀφθώδεα described by him. It was also certainly known to Galen under the term of *aphthæ albæ infantum*.

Sauvage called the affection *aphthæ lactamen*, and Bateman *aphthæ lactantium*.

In 1839 Langenbeck first discovered that the condition was due to a fungus. It is interesting to note that the thrush case, microscopically investigated by Langenbeck, was a patient suffering from typhoid, and that Langenbeck suggested that the fungus might be the cause of this malady.

Berg in Stockholm, in 1842, studied the condition very carefully and gave some details on the morphology of the fungus, while Vo demonstrated the contagiousness of the malady. Gruby, in 18. considered the fungus to belong to the genus Sporotrichum, an called the affection aphthaphyte.

Robin gave a full description of the fungus in 1847, and considered it to be closely related to *Oidium tuckeri*, which attacks the leaves of vine-trees, and to *Oidium lactis*. In 1853 he called it *Oidium albicans*.

In 1866 Hallier considered the fungus to be a Stemphylium, and called it *Stemphylium polymorphum*. In 1868 Quinquaud created a new genus, *Syringospora*, and named the fungus *Syringospora robini*. In 1877 Grawitz considered the organism to be identical with *Mycoderma vini*.

In 1878 Rees placed the fungus in the genus *Saccharomyces* (*S. albicans*). In 1885 Plaut grew it in pure culture and considered it to be identical with *Monilia candida* Bonorden, which is often found in cow-dung.

In more recent times the condition has been studied by Klemperer, Roux, Linossier, Vuillemin, and others, while Castellani has shown that the affection may be caused by a multiplicity of fungi. Pijper has recently described a case of thrush in South Africa due to *Hemispora rugosa* Castellani.

Climatology.—Thrush is very common throughout the tropics, but it is found also very frequently in temperate and cold climates.

Etiology.—It is generally stated that thrush is due to *Oidium albicans* Robin (synonyms: *Monilia*, *Saccharomyces*, *Parasaccharomyces*, *Endomyces*, *Syringospora albicans*, *Syringospora robini*, *Stemphylium polymorphum*), but the researches of Castellani carried out both in the tropics and in temperate zones have shown that the term *Oidium albicans* has been used to cover a multiplicity of fungi, and that the affection may be caused by hyphomycetes belonging to different species, genera, and families. The fungi capable of producing thrush may be classified as follows:—

Fungi Imperfecti :—
  Genus *Monilia* Persoon.
  Genus *Oidium* Link.
  Genus *Hemispora* Vuillemin.
Ascomycetaceæ :—
  Genus *Endomyces* Link.

Fungi of Genus Monilia Persoon.—Fungi of the genus *Monilia* Persoon are by far the most frequently met with, and there is little doubt that the fungus described by Robin under the name *Oidium albicans* belongs to this genus. For details on fungi of this genus the reader is referred to Chapter XXXIX., p. 1079. The species most commonly found in the tropics are of the types *Monilia tropicalis* Castellani, *Monilia pinoyi* Castellani, *Monilia parapinoyi* Castellani, less frequently of the *Monilia bronchialis* Castellani type and other types, while *Monilia albicans* Robin *sensû stricto* is seldom found.

In cases of thrush in London Castellani isolated in 1913 fungi of the types *Monilia pinoyi* Castellani, *M. parapinoyi* Castellani, *M. londinensis* Castellani, *M. metalondinensis* Castellani, *M. bronchialis* Castellani, occasionally *M. tropicalis* Castellani, and rarely other types.

Fungi of Genus Oidium Link.—The following fungi of the genus Odium have been found in a few cases of thrush:—*Oidium matalense* Castellani, *Oidium rotundatum* Castellani, *Oidium asteroides* Castellani. The same species have been found in the expectoration of certain cases of bronchitis, and *Oidium rotundatum* and *Oidium asteroides* also in the fæces of certain cases of enteritis.

Fungi of the Genus Hemispora Vuillemin.—The fungus *Hemispora rugosa* Castellani, found by Castellani in certain cases of subacute tonsillitis and cases of bronchomycosis, has been recently observed by Pijper in a peculiar case of thrush in South Africa.

Fungi of Genus Endomyces Link.—Vuillemin in old cultures of so-called *Oidium albicans* Robin found asci, and, therefore, considered the thrush fungus to be an endomyces. Vuillemin's findings were not confirmed, and Landrieux created a new species for the fungus in which Vuillemin found asci: *Endomyces vuillemini* Landrieux.

Predisposing Causes.—General weakness, marasma, and the late stages of tuberculosis and diabetes, favour the development of thrush, though at times perfectly sound individuals may suffer from it.

Symptomatology.—On the mucous membrane of the cheeks, soft palate, and tongue, white small spots appear, which gradually spread. There is often a certain degree of inflammation, and the oral mucosa may be red and swollen and the saliva very acid. Nursing and chewing are painful, and infants and children with thrush have often diarrhœa. Certain authors, however, maintain that the severe signs of stomatitis are not due to the thrush fungi; bacteria and other organisms would be the real cause of the oral inflammation, which would prepare the ground for the fungus to thrive, and by abundantly growing produce the white patches. Thrush not rarely spreads to the pharynx and the upper portion of the œsophagus. It is interesting to note that the fungus grows from the surface downward fairly deep into the mucous membrane. It was believed at one time that thrush never affected cylindrical epithelium. Thrush runs a variable course, and in many cases shows little tendency to spontaneous cure.

Clinical Varieties.—In cases of thrush due to *Oidium rotundatum*, *Oidium asteroides*, and *Monilia zeylanica*, the colour of the patches may be yellowish instead of creamy white. The same appearance has been recently noted by Pijper in an interesting case of thrush he has carefully described in South Africa, due to *Hemispora rugosa* Castellani.

Diagnosis.—The diagnosis can often be made clinically, the creamy white patches being characteristic, but it should always be confirmed by the microscopical examination, which will reveal a large amount of mycelial threads and conidial forms. If it is desired to know the ætiological variety of thrush the patient is suffering from, cultural methods are necessary. These are described in the chapter on Bronchomycosis (see p. 1888).

Prognosis.—Thrush *per se* is not a serious affection, but its occurrence in cachectic patients is a bad omen.

Treatment.—Glycerine of borax applied to the patches several times a day is efficacious in many cases, or an aqueous solution of borax (1 in 30) may be used. The addition of honey to the latter is to be deprecated. In resistant cases the addition of carbolic acid to the glycerine of borax, 10 minims to the ounce, will be found useful. In marasmic children or adults suffering from some incurable disease any treatment may fail to bring about a complete disappearance of the thrush.

Prophylaxis.—In the case of infants there is no doubt that in many cases the infection is carried by contaminated nursing bottles and their rubber nipples. These should, therefore, be kept scrupulously clean. As regards children, and more especially adults, quite a number of them, although in apparent perfect health, harbour thrush fungi in the mouth, and are, therefore, carriers. In them the use of alkaline tooth-pastes and mouth-washes is to be recommended.

GINGIVITIS.

During the last few years much attention has been paid to gingivitis, or inflammation of the gums, which may be divided into simple gingivitis, pyorrhœa alveolaris, and ulcerative gingivitis. They are all of tropical importance.

Simple Gingivitis.

In this disease the gums are bright red in colour, especially near the margin, becoming normal when traced towards the buccal mucosa. The interdental papillæ are swollen, but are neither painful nor ulcerated. There is no odour, no pain at night, and no enlargement of lymph glands, but the teeth may be covered with tartar and show food débris. A carbolic rose-water mouth-wash (½ per cent.) will be found useful.

Pyorrhœa Alveolaris.

This is a chronic condition, in which there is little sign of inflammation of the gums, but in which pus can by pressure be made to exude from the peridental pockets. If it is allowed to proceed unchecked it will produce ulceration of the bottom of the peridental sulcus and destruction of the periodontal membrane, and will set up a rarefying osteitis, which will injure the bony socket and loosen the teeth.

Ulcerative Gingivitis.

Synonym.—Mal de Bocha.

This was studied by Miller, an American dental surgeon, in 1882, who first saw the spirochætes and the fusiform organisms which were subsequently described by Vincent, in 1898, as the causal agent of a membrano-ulcerative pharyngitis and tonsillitis, a membrano-ulcerative stomatitis, and a membrano-ulcerative gingivitis, two of which are commonly present when a case comes to be noted, although the gingivitis is nearly always the primal disease.

All forms are common in the tropics, and their relative frequency has been investigated in Palestine by Schimeoni-Meckler, in 1917, who found that 78 cases of mouth disease could be resolved into 28 cases of ulcerative gingivitis, 17 of ulcerative stomatitis, 6 of Vincent's angina, and 27 of mixed types. The whole subject has been ably studied by Barlow in 1914, Bowman in 1916, by Taylor and McKinsty in 1917, and by Colyer, in 1918. There are three varieties of the complaint—viz., the acute, the subacute, and the chronic.

Acute Variety.—This is an acute inflammation of the margins of the gums, of gradual onset, but which spreads rapidly and causes ulceration of the interdental papillæ and sloughing of the gums around the necks of the teeth, and in severe cases ulceration of the oral mucosa, associated with malaise, fever, and enlargement of the lymph glands, hæmorrhage from the gums, and pain therein, especially at night, bad taste in the mouth, offensive breath, difficult and painful mastication, and loose and tender teeth. There is œdema of the interdental papillæ, which are bluish-red in colour or covered with a brownish friable slough. It usually attacks the gums around the upper incisor teeth, but may begin anywhere where food tends to accumulate. It spreads from person to person, but is commonly met with in persons living under bad conditions.

Subacute Variety.—The gums are spongy and tender, and a whitish pellicle often forms which on superficial examination may give the appearance of a purulent exudate. The condition often spreads to the cheeks and lips, and may involve the soft and hard palate and even the tonsils. The pellicle after a time separates, leaving an eroded surface which gradually deepens.

Chronic Variety.—If untreated the acute and subacute varieties pass into the chronic, and lead in a year or so to destruction of the bony sockets.

Treatment.—The best treatment for these infections is to remove the tartar, disinfect the mouth with a spray of peroxide of hydrogen or of glycothymoline, and then to treat by ionization with zinc sulphate, and afterwards to use antiseptic washes of sanitas or similar preparations. Roberts recommends the local application of the following: Hydrogen peroxide ʒv., vinum ipecac. ʒiii., glycerin ʒv., aq. ad ℥viii.

LINGUAL AFFECTIONS.

Patches of **Leucoplakia** of the tongue are common in natives, and may be of various origin—syphilitic, frambœtic, or due to irritation caused by smoking or chewing various substances. Case of the so-called **Circinate pityriasis linguæ** or **Annulus migrans** are not rare. **Lingua nigra** is occasionally seen. We have already called attention to the *dark patches* found on the tongue in natives, and which by some writers have been described as a sign of ankylostomiasis. These pigmented patches are roundish or oval, and may be found also on the gums, the mucosa of the lips, on the soft and hard palate, and are apparently congenital. A condition which might be called **Red or Purple tongue,** and which often puzzles the newly arrived medical man, who does not know its origin, is extremely common in Ceylon among the coolies and lower-class natives, and is simply due to chewing betel. The pigmentation slowly disappears on the native discontinuing the use of betel. Cases of **Furrowed tongue** (scrotal tongue) are not rare. We have seen a case of **Fordyce's disease** (pseudo-colloid of the lips) in a half caste. A case of **Chelitis exfoliativa** in a European lady and cases of **Perlèche** have been observed by us among European children. Under the term *seasonal recurrent ulceration of the lips*, Gros has described a very superficial ulceration on the lower lips in Algerian natives which is very common in the hot season, and is due, according to him, to a diplobacillus.

Pityriasis Linguæ Spirochætica.—This condition has been described by Castellani. There is as a rule no sign of acute inflammation and no ulcers, but the dorsum of the tongue is covered by a thick, persistent, whitish-yellowish or greyish-brownish fur, which on microscopical examination seems to consist solely of innumerable spirochaetes, with some epithelial cells. Of course, a few spirochætes are always found in scrapings from the tongue, but never in such enormous amounts.

HALZOUN.

Definition. Halzoun is the invasion of the pharynx by the adults of *Fasciola hepatica* (Linnæus, 1758), which cause dyspnœa, dysphagia, and sometimes more severe symptoms, and even death.

Historical. In 1904 Khouri described this disease as occurring in Northern Lebanon.

Ætiology.—The disease is caused by eating raw livers, especially raw goat (*Capra hircus* Linnæus) livers, which are infected with *Fasciola hepatica* (Linnæus, 1758), when the worm (p. 565) fastens itself on to the mucosa of the pharynx and sucks blood.

Symptomatology.—The patients suffer from dyspnœa, dysphagia, dysphonia, and congestion of the head, and occasionally die, but more usually, after lasting from a few hours to a few days, the victim vomits and the parasites are expelled, and recovery results.

Treatment.—An emetic will cause the parasites to come away.

TONSILLAR AFFECTIONS.

Every type of tonsillitis met with in temperate climates is observed also in the tropics, although there is no doubt that tonsillar and throat affections are less frequent in warm climates than in cold. Diphtheria is on the whole less frequent than in temperate zones, but a fairly large number of cases occur in every tropical country. We have seen a number of cases of **follicular tonsillitis** and other streptococcal affections; **quinsy** or tonsillar abscess is not rare, and cases of **Vincent's angina** occur, due to Vincent's *Bacillus fusiformis* in association very often with spirochætes. We do not propose giving a description of Vincent's angina, which may be found in any text-book on general medicine, but we would call attention to the possibility of mistaking it for a syphilitic condition. Certain authorities state that Wassermann reaction is positive in Vincent's angina, but in our experience this is not so, and we can confirm the researches of Taylor and others, according to which Wassermann reaction is negative in Vincent's angina, except, of course, when it develops in a syphilitic person. Cases of tonsillitis possibly due to amœbæ and flagellates have also been recorded. We propose saying a few words on certain affections of the tonsils to which little attention has so far been paid—viz., mycotic infections.

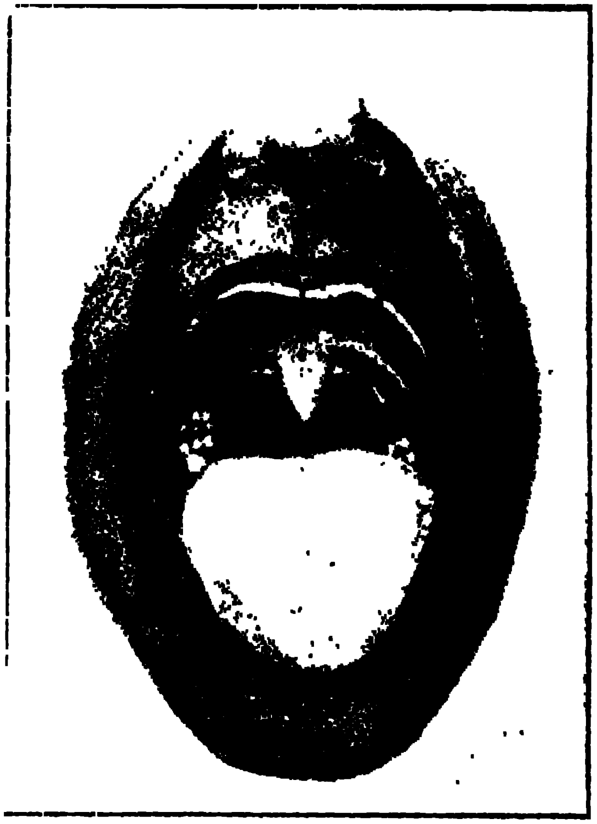

FIG. 743.—TONSILLAR AFFECTION CAUSED BY *Hemispora rugosa* CASTELLANI.

Tonsillar nocardiomycosis and lesions of the tonsils due to *Nocardia bovis* and other species of the genus Nocardia and Cohnistreptothrix have been placed on record, but we desire to call attention to the comparative frequency of a granular Nocardiasis of the crypts which may lead to the formation of tonsillar calculi. The affection, which is not new, but is little known, runs a chronic course and is not painful. The patient often does not come to consult the doctor because of sore throat, but because of the unpleasant odour of the breath. On examination the teeth and gums may be quite healthy, but on examining the throat small whitish-yellowish spots will be seen on the tonsils; these spots are in reality the surface portion of granules contained in the crypts, and may be extracted with more or less ease. These bodies when squashed have a very offensive odour; under the microscope they consist of masses of Nocardia-like organisms at times, at other times masses of leptothrix; in certain cases both Nocardial fungi and Leptothrix are seen and various bacteria, and even protozoa such as amœbæ and flagellates The nocardia fungi are very difficult to grow. After several years the masses in the crypts may become calcified, and real calculi may be formed, which at times are the starting-point of some very severe inflammation.

Varieties of Tonsillonocardiasis.— Clinically the usual form is the yellow or whitish type. A case observed by one of us was characterized, however, by the presence of black granules, from which a nocardia similar or identical to *Nocardia nigra* Castellani, 1912, was grown.

Tonsillar moniliomycosis.- Moniliasis of the tonsils has been described by Castellani. Three types may be distinguished: the acute, the subacute, the chronic. The *acute type* is important, as such cases have often been taken for diphtheria. The tonsils are covered by creamy white patches, which at times extend to the soft palate, the pharynx, and larynx. There is difficulty in swallowing, and the patient may have some fever. Diphtheria is often suspected, but the microscopical and cultural examination clears the diagnosis at once. The fungus most commonly found in Ceylon is *Monilia tropicalis* Castellani. Cases of mixed infections of diphtheria and moniliasis have occasionally been seen by us.

In the *subacute* and *chronic* types of moniliasis the subjective symptoms are often nil. The diagnosis is based on the microscopical examination. The treatment consists in applications of glycerine of borax and of carbolic acid.

Tonsillar Oidiomycosis.- The condition is due to fungi of the genus *Oidium* Link. Clinically the affection is very similar to moniliasis, but in the case in which *Oidium rotundatum* Castellani was found the patches were yellowish and not white.

Tonsillar Hemisporomycosis.- In certain cases of tonsillitis in Ceylon Castellani found a fungus which he had previously observed in cases of bronchomycosis. He was doubtful about the classification of the fungus, and at first placed it temporarily in the genus Monilia, naming it *Monilia rugosa* Castellani, 1909. Recently Pinoy has placed it in the genus Hemispora, the name of the fungus becoming *Hemispora rugosa*.

The case in which the fungus was first observed had been suspected by the house physician to be a case of diphtheria, as the patient complained of great pain in swallowing. There was fever, the submaxillary lymphatic glands were enlarged, and on examination of the throat several greyish patches were seen on the left tonsil and on the soft palate. At times, however, the patches are yellowish. Under appropriate treatment they become smaller and smaller, but one or two small spots remain often for weeks and even months. As regards treatment, painting with a 5 or 10 per cent. solution of carbolic acid is found useful.

GASTRIC DISEASES.

All forms of **Dyspepsia** are common, but hyperchlorhydria and fermentation are especially common in our experience.

Ulcers and **Cancers** of the stomach are met with at times, as well as dilatation of the veins at the lower end of the œsophagus, leading to severe hæmatemesis. In children **Pyloric stenosis** has been seen several times by us. We have met with one case of diffuse inflammation which resembled 'phlegmon of the stomach' in its gastric symptoms, but which was associated with other signs pointing to a more general poisoning of the system.

EARTH-EATING.

Synonyms.—Geophagy. *French:* Mal d'estomac.

Remarks.—Earth-eating is common in many parts of the tropics, especially in certain parts of Africa (*e g.*, the Sudan and Southern Tunisia) and Asia (Malasia, Java, Borneo), but is observed also in Temperate Zones, in Europe, Northern China, and Japan. It is common in children and pregnant women. It is believed to be acquired by the children being left to crawl about and eat anything which comes to hand. It is also acquired by being taken as a remedy for syphilis and other diseases.

Christopherson says that it is common in the Sudan, where two forms of earth are eaten: (1) Karkooti (Nile mud), (2) taffel (some form of calcium carbonate). In Giava the earth eaten consists of bituminous clay, called 'ampor,' which is taken especially by pregnant women, who believe it will benefit their unborn babies. In Guatemala and other Central American countries natives occasionally eat a yellowish earth containing sulphur as a prophylactic against disease. In Japan it is said that the Ainus used to eat a paste made of starch and of diatomaceous earths in famine years.

Symptomatology.—The symptoms are usually emaciation and anæmia, with pain in the epigastrium and a sensation of hunger, while constipation is common. Earth-eaters frequently suffer from ankylostomiasis, and often have a yellowish muddy or earthy colour.

BELYANDO SPEW.

Synonyms.—Grass sickness (Western Australia). Gastric spirochætosis (Ernest Black).

Definition.—A gastric disturbance characterized by vomiting; occurring suddenly after meals, and unaccompanied by nausea in certain tropical regions without any immediate cause.

History.—Under the above terminology Dr. Ernest Black has described to us a disease which he has met with in Western Australia.

Geographical Distribution.—It has long been known as a distinct disease in Queensland under the name derived from the Belyando district, 250 miles inland, and in Western Australia in certain tropical districts, chiefly coastal, where it is called 'grass sickness.' It also exists in some tropical districts in Brazil.

Ætiology.—The cause of the disease is unknown. Black has found a spirochæte in the mucous membrane of the stomach. This spirochæte is of variable size, small and slender.

Black thinks that, like other members of that class, it generates no free toxins, but its pathological effect is produced, on its death and disintegration, by the liberation and absorption of toxins.

The mode of conveyance is not conclusively determined, but it seems to be by means of contaminated food or water. In one district in Western Australia all the evidence pointed to milk as the medium. In Queensland, on the other hand, many years ago there was no fresh milk used in a district where the disease was common.

Climatology and Incidence. In Queensland it persisted in the past in an endemic area in spite of a drought lasting several years. In Western Australia the outbreaks are strictly limited to the wet season, and start with the rapid growth of grass after the first rains. Hence its local name in that district.

Persons of both sexes, any age, and all races may be affected, those in robust health equally with those in ill health.

Symptomatology. The solitary symptom is vomiting, which occurs only after taking food. This may be within a few minutes, or may be delayed for some time after a meal. The character of the vomiting is quite distinctive, and reminds one of the action of apomorphia. It is very sudden, and rarely preceded, accompanied, or followed by any nausea, straining, or pain. There is seldom any premonitory sensation, consequently it is so sudden as often to be extremely embarrassing. It may occur after every meal or only after one or two meals in a day. It may be every day, or there may be intervals of one or several days between the attacks, which also vary in their duration. From the results of experiments, Black has come to the conclusion that the attacks are concurrent with and due to the death of some of the organisms, and that the intermissions are periods during which none or too few die. In the intermittent form there is little if any interference with the general health, but in the more or less continuous cases there is sometimes considerable loss of weight, the malnutrition then resulting in ill health. There is no loss of appetite, but rather the reverse. If the attacks are short and the intermissions long, patients, especially children, sometimes increase in weight.

Treatment. According to Black, the aim of the treatment is to destroy the causal organism in the mucous membrane of the stomach. Cyllin in palatinoids of 3 minims each with a wineglassful of water three times a day is generally effectual and convenient. Thymol may be given in 1 grain doses three times a day, the patient being warned not to take any alcohol or oil. Chlorine solution, freshly prepared, has been strongly recommended. Other drugs suggested are carbolic acid, creosote, and β-naphthol. Whatever drug is used, it should be given at least half an hour before meals.

Prophylaxis. Nothing is known about this.

ENTALAÇÀO.

Synonyms. – Mal d'engasgo, Dysphagie Tropicale, Tropical Cardiospasm.

Remarks. This disease has been known for a long time in certain parts of Brazil, having been described by Botelo, Langard, and by Paranhos. Bouchard has noticed a somewhat similar disease in pheasants which is due to a worm.

Climatology. –It appears to be localized to some districts in the interior of Brazil.

Ætiology. – The causation is unknown, but it has been suggested that it is a parasitic disease, that it is a neurosis, or that it is connected with eating diseased manioc. The last theory has been brought forward by Paranhos.

Morbid Anatomy. –No macroscopical lesions have so far been discovered.

Symptomatology. –The patient complains of severe difficulty in swallowing even liquids, and feels as though the food had stopped in the œsophagus and had not reached the stomach; hence the name 'd'engasgo,' meaning choked. During the attack the patient becomes anxious-looking, throws the arms about, and becomes dyspnœic. The face is congested and the eyes protrude. The swallowed food is brought up by a process of regurgitation rather than of true vomiting. The attacks are recurrent, with intervals of freedom. After a time the patient may become cachectic from lack of nutrition, and die.

Treatment.—This is very unsatisfactory, and merely symptomatic. Bromides and chloral have been given, but a change of climate is essential.

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CHAPTER LXXV

HELMINTH INFECTIONS

General remarks—The intestinal trematodiases—The intestinal cestodiases—The intestinal nematodiases—Trichuriasis—Ankylostomiasis—Ascariasis—Oxyuriasis—Intestinal polyparasitism—Rare infections—References.

General Remarks.

In the present chapter we propose to consider the helminth infections of the intestines and in so doing exclude those found in the liver or the bloodvessels of the intestines, though it is true that the eggs in both cases may be found in the fæces.

The Intestinal Trematodiases.

Definition.—An intestinal trematodiasis is an infection of the alimentary canal with adult trematode worms.

Remarks.—The intestinal trematode worms of man are:—

1. *Watsonius watsoni* (Conyngham, 1904).
2. *Gastrodiscus hominis* (Lewis and McConnell, 1876).
3. *Fasciolopsis fülleborni* Rodenwalt, 1909.
4. { *Fasciolopsis rathouisi* Poirier, 1887.
   { *Fasciolopsis buski* Lankester, 1857.
5. *Heterophyes heterophyes* (von Siebold, 1852).
6. *Metagonimus yokogawai* (Katsurada, 1913).
7. *Echinostoma ilocanum* Garrison, 1908.
8. (?) { *Echinostoma* (*Euparyphium*) *malayanum* Leiper, 1911.
   { *Artyfechinostomum sufrartyfex* Clayton Lane, 1915.

Eurytrema pancreaticum (Janson), fully described by Loos (*Annals of Trop. Medicine*, 1907, vol. i., p. 128), has occasionally been found in man in China.

In addition to adult worms, the ova of the Schistosomidæ (Chapters XXIV., LXIV., LXXVII., and LXXXIII.) and those of the liver flukes (Chapter LXXXI.) pass down the alimentary canal and escape in the fæces.

Fasciola hepatica is the cause of halzoun, described in Chapter LXXIV., p. 1746.

Symptomatology.—Diarrhœa has been described as being caused by ***Watsonius watsoni*** (p. 562), while ***Fasciolopsis buski*** (p. 568) causes dysenteric diarrhœa, ***F. rathouisi*** (p. 568) colic, ***F. fülleborni*** (p. 569) fever, and ***Kwan's fluke*** (p. 569) gastric disturbance, but the recorded cases are few, the method of infection is unknown, and the symptomatology has still to be carefully studied.

Diagnosis.—The presence of trematode worms can only be diagnosed by the discovery of the eggs or the adult in the fæces.

Treatment.—The treatment must be on the same lines as that described for ankylostomiasis.

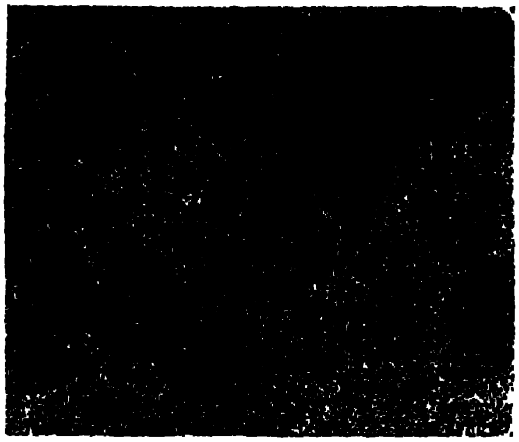

FIG. 744.—EGGS OF *Eurytrema pancreaticum* IN THE FÆCES OF A CHINESE COOLIE. (× 250.) (From a photograph by J. J. Bell.)

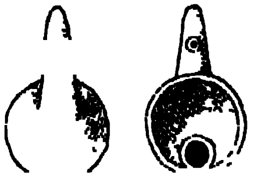

FIG. 745.—*Gastrodiscus hominis*. (After Leuckart.)

Intestinal Tæniiases.

Definition.—An intestinal tæniiasis is an infection of the alimentary canal by adult cestode worms.

Symptomatology.—*Cestode parasites* cause gastric and reflex symptoms, mostly of a vague nature. The former comprise salivation, diarrhœa, or constipation, with colicky pains, nausea, vomiting, or dyspepsia, while the latter include faintness, unequal pupils, disorders of vision and hearing, headache, itching of the nose or anus, vertigo, epilepsy, etc. Anæmia and skin eruptions have also been recorded. Christopherson and Izzedin have recorded a case of acute intestinal obstruction due to *Tænia saginata*.

Treatment.—The treatment is the usual anthelmintic remedy of *Filix mas*, in capsules (six 10-minim capsules) or emulsion—such as olei filicis ʒi. to ʒi.ss., gummæ acaciæ q.s., syrupi zingiberis ʒi., aquæ ad ℥ii. Fiat haust. To a child six to eight years of age olei filicis ʒss. may be administered, followed by a saline purgative six hours later. Filmaron, which contains the active principle of filix, may be given in capsules (two or three). Turpentine may be given in doses of 20 minims three times a day, or kousso 2 drachms, or kamala 1 drachm. Thymol has also been recommended. Naphthalene in 2-grain doses has been used in children.

Tæniasis is extremely common in certain parts of the tropics—as, for instance, Abyssinia—where some natives take every two months kousso flowers (*Brayera anthelmintica* Kunth). Several other native drugs have been used, among which, according to Annaratone, the following are the principal ones: Bulbs of *cossala* (Mollugoliro), *habbeciacco* (seeds of *Oxalis anthelmintica*), the bark of

OVA OF INTESTINAL WORMS AS SEEN IN THE FÆCES.

TREMATODA

F, Schistosoma japonicum (after Leiper).
P, Schistosoma mansoni (after Holcomb).
G, Fasciolopsis buski (after Looss).
H, Heterophyes heterophyes (after Looss).
Q, Dicrocœlium lanceatum (after Looss).

CESTODA

J, Dibothriocephalus cordatus. (Outline only to show relative size. Figure K is placed inside it in order to economize space.)
L, Tænia solium (after Leuckart).
M, Tænia confusa (modified after Guyer).
N, Dibothriocephalus latus (modified after Schauinsland).
O, Tænia saginata (after Leuckart).
R, Hymenolepis nana (after Stiles).
T, Hymenolepis lanceolata (after Railliet).
W, Hymenolepis diminuta (after Blanchard).
S, Dipylidium caninum (after Diamare).
V, Diplogonoporus grandis (after Brumpt).

NEMATODA

A, Ancylostoma duodenale.
B, Strongyloides stercoralis (after Thayer).
C, Oxyuris vermicularis (after Leuckart).
D, Necator americanus.
E, Trichostrongylus instabilis (after Ward).
I, Gigantorhynchus gigas (after Ward).
K, Trichuris trichiura. (Placed inside the outline of Dibothriocephalus cordatus for the sake of economy in space.)
U, Ascaris lumbricoides.
X, Ascaris, sp.? (We have seen large eggs of this nature in Ceylon.)

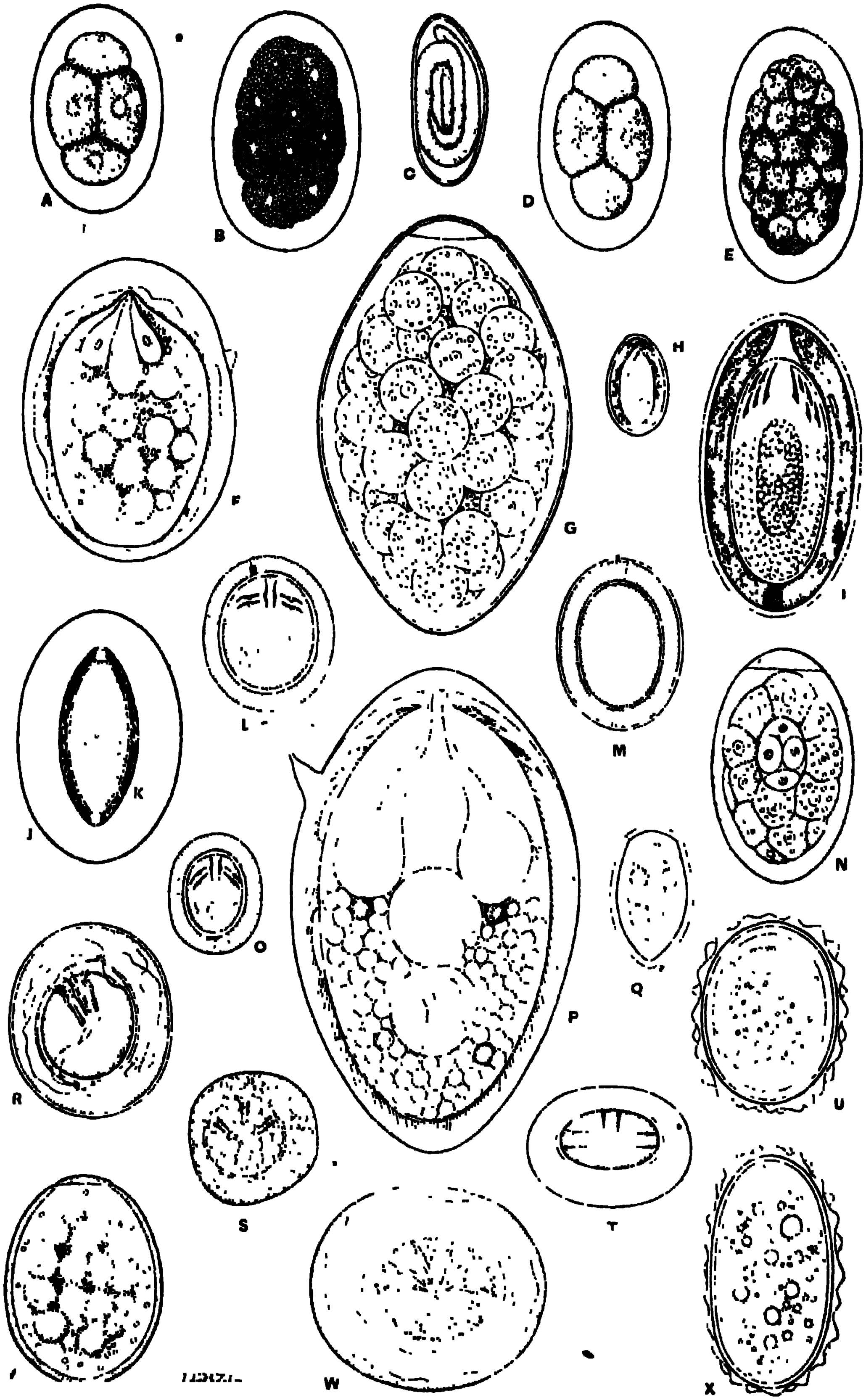

FIG. 746.—OVA OF INTESTINAL WORMS AS SEEN IN THE FÆCES.

Albizzia anthelmintica (Bessina), flowers and leaves of buddleia, polistachya (*mattari*), the bacchæ of *Mœsa lanceolata* (Saoria), and of *Nijrsine africana* (*ssa'hlso*), leaves, flowers, and fruits of *Celosia ervgina* (*bellilda*), efficacious also for ascarides. Large doses of melon seeds are also used.

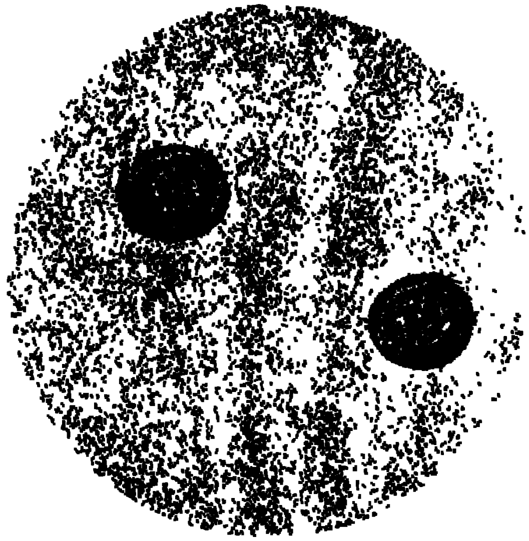

FIG. 747.—FÆCAL EGGS OF *Tænia solium*.
(From a microphotograph by J. J. Bell.)

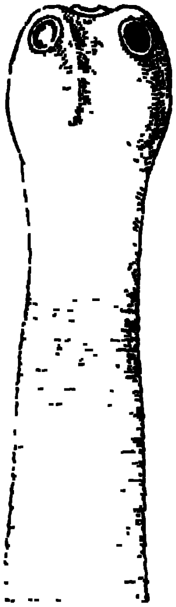

FIG. 748.—*Tænia saginata*.
(After Braun.)

Rare Tæniiases.

Some of the Tæniiases—*e.g.*, those due to *Tænia philippina*, *T. confusa*, *T. bremneri*, *T. hominis*, and *T. africana*—are so rare that no further mention is necessary beyond the descriptions which have been given in Chapter XXV., p. 614.

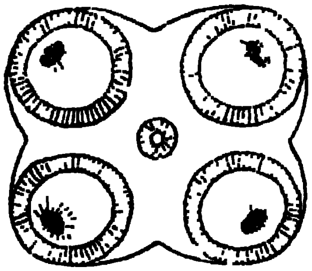

FIG. 749.—*Tænia africana*.
(After von Linstow.)

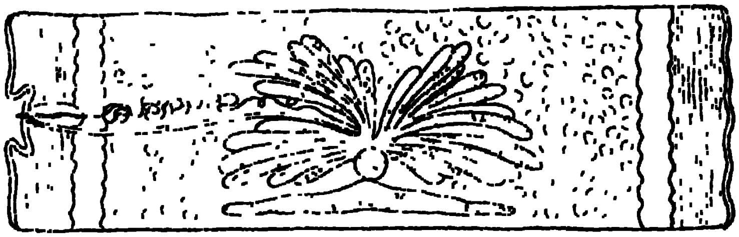

FIG. 750.—*Tænia africana*.
(After von Linstow.)

The Dibothriocephaliases.

The Dibothriocephaliases are produced by *Dibothriocephalus latus*, *D. cordatus*, and *D. parvus*. *D. latus* (p. 604) causes severe anæmia, and at times fever associated with serious symptoms, but this infection is not common in the tropics. The treatment is the same as for Tæniiasis.

The Diplogonoporoses.

Diplogonoporosis is found in Japan, where it is due to *Diplogonoporus grandis* (p. 605), and in Roumania, where it is caused by *D. brauni* (p. 605). The recorded symptoms somewhat resemble those produced by *Dibothriocephalus latus*.

Hymenolepsiasis.

Hymenolepsis nana (p. 610) may give rise to severe reflex nervous symptoms, but only when present in considerable numbers. It has been found in Egypt, Siam, Japan, North and South America, and Europe, and is by no means a rare parasite in man. *H. diminuta* (p. 609) is a common parasite in rats, but does not occur so frequently in man, though a number of cases have been recorded in America and Europe. It does not cause any appreciable symptoms.

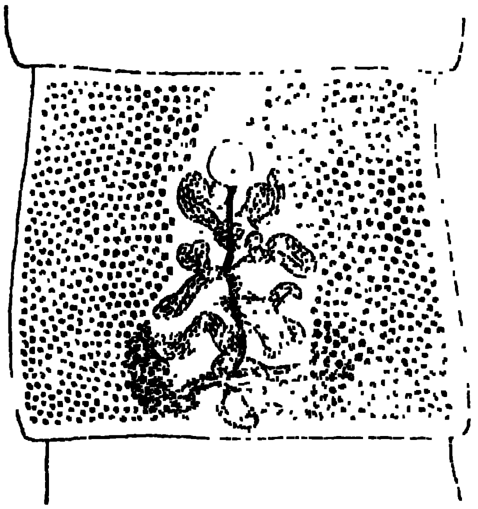

FIG. 751.—*Dibothriocephalus latus* (PROGLOTTIS).
(After Braun)

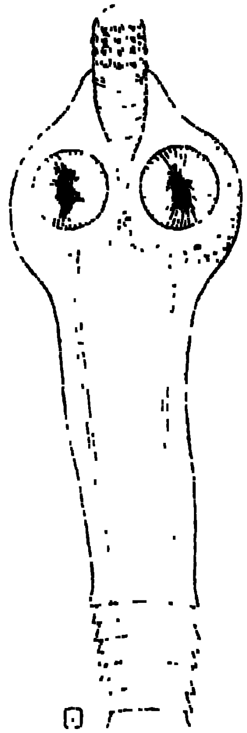

FIG. 752. *Dipylidium caninum.*
(After Diamare)

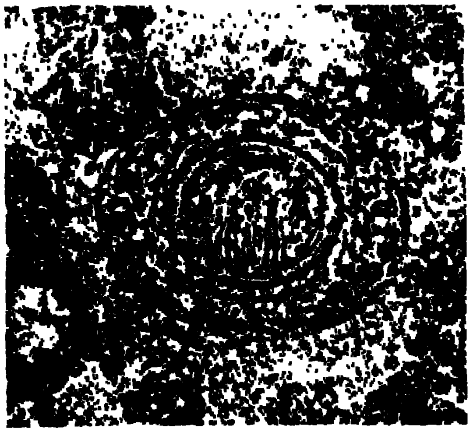

FIG. 752A.—EGG OF *Hymenolepsis nana* IN HUMAN FÆCES. (× 300)

Dipylidiasis.

Dipylidium caninum (p. 608) has often been found in man, but is harmless.

Davaineiasis.

Davainea madagascariensis (p. 611) is normally found in birds, but about nine cases have been recorded in children in Madagascar, Mauritius, Siam, and New Guinea.

Intestinal Nematodiases.

Definition.—Intestinal nematodiasis is the invasion of the alimentary canal by adult nematode worms.

Strongyloidosis.

Synonym. Intestinal anguillulosis.

Strongyloidosis, usually called intestinal anguillulosis, is the infection of man with *Strongyloides stercoralis* Bavay, 1876 (*vide* p. 628), which produces no symptoms if present in small numbers, but induces an intestinal catarrh leading to anaemia and an intermittent diarrhœa when in large numbers. The disease is met with all over the tropical world, and even in the temperate zone. Diagnosis can only be effected by finding the rhabditic embryo (the so-called *Anguillula stercoralis*) or the eggs in the fæces, in which the latter will only be found when violent diarrhœa is present. The treatment is the same as for ankylostomiasis.

Trichuriasis.

Synonyms. Whip-worm infection, Trichocephaliasis.

Nomenclature.—Büttner in 1761 first named the worm *Trichuris*, or thread-tail, for he mistook the posterior end for the anterior. Linnaeus in 1771 called the worm *Ascaris trichiura*, but Goeze in 1782 changed the name to *Trichocephalus trichiura*, because he recognized the error made by Büttner. The term *Trichuris trichiura* Linnaeus must, however, stand, and the term for any disease associated with this worm must be ‘trichuriasis’

Definition. Trichuriasis is an infection of the large intestine appendix, or ileum by *Trichuris trichiura* Linnaeus, 1771 (*vide* p. 677), which produces no symptoms unless it is present in large numbers, when anæmia, nervous and gastro-intestinal symptoms may appear.

History.—From the time of Barth, who, in 1845, was the first to ascribe a pathogenic rôle to the worm, there have been a large number of observers who have considered it to be the cause of gastro-intestinal and nervous symptoms, while Metchnikoff and Guiart in 1901 considered it to be a cause of appendicitis. In the same year Girard drew attention to the possible transmission of pathogenic bacteria into the tissues via the wounds produced by the worm. In 1902 Schiller ascribed a case of high fever to the action of a heavy infection with the parasite. In 1908 Musgrave, Clegg, and Polk contributed an excellent monograph on the whole subject of trichuriasis, together with full accounts of four cases. Our own experience is in favour of the worm being occasionally directly the cause of appendicitis, for several times we have found it in the inflamed appendix removed by operation.

Geographical Distribution.—*Trichuris trichiura* is cosmopolitan in its distribution.

Ætiology.—Trichuriasis is caused by *Trichuris trichiura* Linnæus, 1771, which, as far as is known, is really a parasite of man and monkeys, while allied forms exist in other animals. The eggs escape with the fæces, and require three to six months for the development of the embryo, which can then remain alive for years inside the shell if kept on moist earth. Usually the eggs gain access to man by means of contaminated food, especially uncooked vegetables, and to a less extent fruits This is especially likely to occur in the tropics, where human fæcal matter is often allowed to be deposited in vegetable gardens. Musgrave, Clegg, and Polk report finding the ova in washings from fresh vegetables. Domestic animals, insects, flies, dust, etc., are also considered to be possible means of infection. When taken into the alimentary canal, it hatches and reaches sexual maturity in sixteen days.

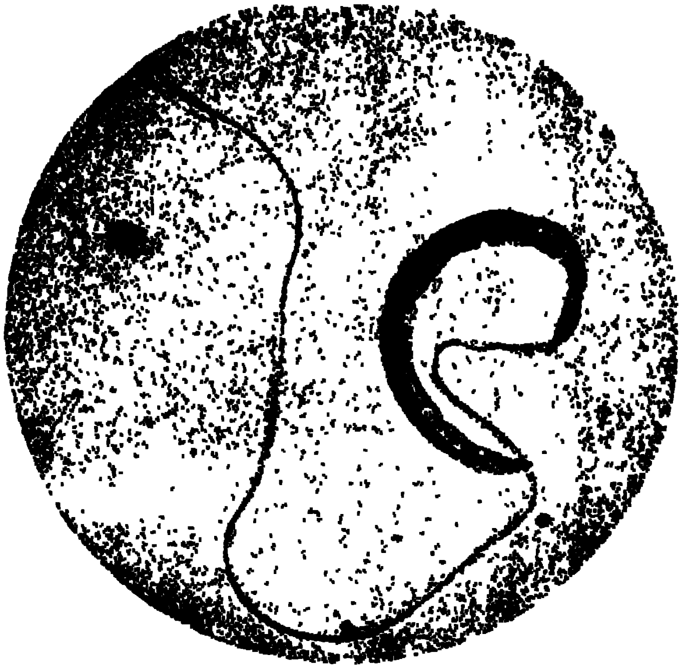

FIG. 753 *Trichuris trichiura.*
(Microphotograph by J. J Bell)

It occurs more commonly among children than adults, women than men, and native races than European. But all these factors appear simply to depend upon good or bad sanitation, for the latter is the principal factor in producing infection.

Pathology. It is believed that the worms attached themselves to the mucosa of the bowel by the head penetrating deeply into its tissue either via a gland or directly. In this position the worm is firmly fixed, and is more or less protected against the action of anthelmintics. They do not appear to be blood-suckers, nor is there any evidence that they produce toxins—at all events, in sufficient quantity to affect man. On the other hand, it is believed that micro-organisms can gain entrance to the blood through the wounds produced by the head, and this secondary infection may be the cause of the appendicitis and other pathological phenomena.

Morbid Anatomy.—A post-mortem simply reveals anæmia and dropsy, with at times appendicitis. The most marked feature is the presence of large numbers of *Trichuris trichiura*.

Symptomatology.—The symptomatology may be subdivided into the intestinal and appendicular varieties.

Intestinal Variety. The illness begins with dizziness, tinnitus aurium, and a sensation of weakness, which may be followed by slight daily fever and later by œdema of the face and extremities, while anæmia appears and gradually progresses. Seen at this stage of the illness, the mucosa of the lips and tongue appear pale, the appetite is poor, and dyspepsia, followed later by nausea and vomiting, with or without slight diarrhœa, occurs.

The liver and spleen are normal, but a hæmic murmur may be heard at the apex of the heart, while the blood examination reveals a great decrease in the number of red cells and the presence of poikilocytes, but as a rule no nucleated elements. The hæmoglobin is also reduced, while the leucocytes are increased, and also in most cases there is an absence of an eosinophilia. The urine is normal. There is mental depression, restlessness, headache, and at times insomnia. As the disease progresses the anæmia becomes more and more marked, and death may eventually ensue.

Appendicular Variety. The symptoms of this variety are the same as those for appendicitis arising from other causes. Operative treatment reveals the nature of the malady. The symptoms are the same as those for appendicitis due to other causes—viz., severe pain in the region of the appendix, tenderness on pressure, with often vomiting and fever.

Diagnosis.—The disease closely resembles ankylostomiasis, from which it may be differentiated by finding trichuris ova and no ancylostome ova in the fæces, and also by the absence of marked eosinophilia.

Prognosis.—The ordinary slight infection which is frequently met with may be considered to be harmless, but the prognosis is grave in those rare cases of very heavy infection presenting the symptoms described above.

Treatment.—The treatment at present advised is the administration of thymol by the mouth in the manner presently to be described for ankylostomiasis, and enemata of solutions of benzine.

Prophylaxis.—Good sanitation and proper disposal of sewage, associated with cleanliness in the preparation of food, as well as with personal cleanliness, constitute important prophylactic measures. Uncooked vegetables and skins of fruits should not be eaten.

Ankylostomiasis.

Synonyms.—Ancylostomiasis (this is the latinized Agchylostomiasis, and is a term much recommended by many authorities), Agchylostomiasis, Anchylostomiasis, Uncinariasis, Dochmiosis, Dochmiasis. *Latin*: Anemia intertropicalis, Hypoæmia intertropicalis, Geophagia (*pro parte*). *English*: Ceylon anæmia, Negro consumption, Tropical chlorosis, Egyptian chlorosis, Miners' anæmia, The Great-lazies (Florida), Tunnel-workers' anæmia, Hook-worm disease, Porto Rican anæmia. *French*: Anémie des Pays Chauds, Cachexie Africaine, Mal de Cœur, Mal d'estomac, Ankylostomasie. *Italian*: Anchilostomanemia, Anchylostomiasi. *German*: Ankylostomen-Krankheit, Tunnelkrankheit, Wurmkrankheit. *Spanish*: Aquilostomiasis. *Portuguese*: Oppilação, Amerellao, Cançação. *Arabic*: Ribâgan, Sulura, Tun-tun.

Definition.—Ankylostomiasis is a toxæmia resulting in a progressive anæmia, caused by *Ancylostoma duodenale* Dubini, 1843, and *Necator americanus* Stiles, 1902.

History.—The history of the discovery, together with the structure, life-history, and geographical distribution of the two parasites, has been described on pp. 666-673, and it now remains to give an account of the history of the disease produced by them in man.

If the references contained in the Ebers papyrus, as well as those in the 'Harita Samhita,' really refer to ankylostomiasis, they would make the history of the knowledge of the disease very ancient. It was, however, early recognized that there was a fatal disease of unknown causation in the New World. Thus in 1648 Piso, in his work 'Historia Medica Brasiliae,' gives an account of a fatal disease, Oppilatio (or Oppilação), present in Brazil, by which he probably meant ankylostomiasis. After him it was described by Père Labat in Guadeloupe in 1742, by Chevalier in St. Dominique in 1752, by Desportes in the same place in 1770, by Bayon in Cayenne in 1780, by Hunter in Jamaica and Rodschield in British Guiana in 1796, by Bryon Edwards in Jamaica in 1799, by Pitt in 1808 in the United States, and by Moreau de Jonnès in 1816 in Guadeloupe, while Chabert's celebrated account appeared in 1821. In Peru Castelnau found it in 1820, Jobim in Brazil in 1835, and Clarke in West Africa in 1860. In the meanwhile a peculiar anæmia had been found among miners, first of all in Hungary in 1786, and later in France, Belgium, Germany, and Cornwall, which for a long time was misunderstood, until Dubini's worms were found in the victims. In fact, nothing certain could be said about this peculiar form of 'tropical anæmia' or 'miners' anæmia' until Dubini found *Ancylostoma duodenale* as the cause of the disease, thus definitely separating ankylostomiasis from 'malarial cachexia,' and also clearing the diagnosis of miners' anæmia and tunnel disease. He proposed the name *Agchylostoma* for his new worm, deriving it from ἀγκύλος, meaning 'bent,' and στόμα, meaning 'mouth,' which he latinized into *Agchylostoma*, which therefore ought to have remained as the name of the worm, though *Ancylostoma* is doubtless a better rendering. Still, whether he misspelt the word or not, his name, according to the old rules of nomenclature, ought to have stood, but the Zoological Committee decided otherwise, and we have no choice in the matter, and simply carry out the rules for the time being in force. After his discovery the recognition of the disease spread, at first slowly, but later rapidly. Thus Bilharz in 1853 and Griesinger in 1854 recognized it in Egypt, and Wucherer in 1872 in Brazil, while Grassi and Parona, in 1877, drew attention to the importance of finding the ova in the fæces as a method of diagnosis, and in 1899 Ashford drew attention to the importance of the high eosinophilia. In 1898 Looss traced the method of infection by the skin, the lungs, trachea, etc., while more recently Sambon, Fülleborn, and v. Schilling-Torgau have traced a subsidiary route from the lungs via the blood-stream to the alimentary canal. In 1902 Stiles described *Necator americanus*, and in the same year Boycott and Haldane found the disease in the mines of Cornwall.

Climatology.—The disease will be found wherever there is a suitable temperature and moisture for the development of the parasites. It is therefore spread throughout the tropics of America, Africa, and Asia, and is also found in Queensland, New Guinea, and Fiji, and also in mines or tunnels in Europe, where the conditions of temperature and moisture resemble the tropics.

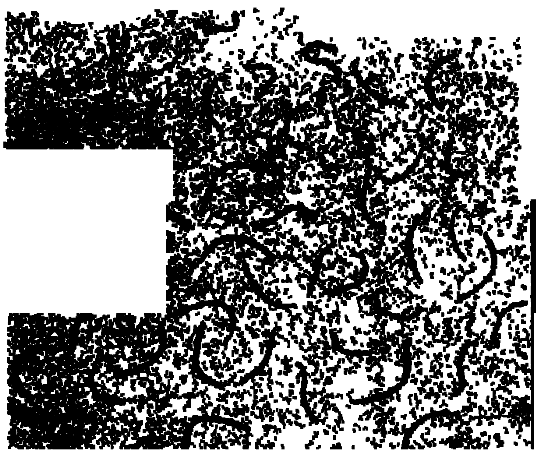

FIG 754.—*Necator americanus.* (Natural size.)

Ætiology.—The disease is due to the presence of *Ancylostoma duodenale* and *Necator americanus* in the body. These parasites, as far as is known, live entirely in human beings, and are therefore kept alive by '*patients*' suffering from the disease and by '*carriers*' or persons infected with so few worms that little or no symptoms are produced. As already noted, the larvæ live in earth, and infection takes place by two routes either through the skin or by the mouth. In the latter instance, it is generally acquired by eating contaminated vegetables, or through the habit of geophagy met with in some natives. It is probable, in our opinion, that the pathological phenomena may, partly or principally, be due to toxins, either set free by the embryo in its travels from the skin to the alimentary canal, or inoculated into the blood-stream from the cephalic glands of the adult worm as it grips the villi of the intestine. But absolute proof is still required of the presence of these toxins, notwithstanding the work of De Giovanni, Loeb, Gabbi, Noc, Alessandrini, and many others. Weinberg's researches on various helmintotoxins must be specially mentioned. The Porto Rico

Commission confirms the suspicion which had long existed as to a relative racial immunity, finding 71 per cent. of the cases in Europeans, 54 per cent. of the cases in mulattoes, and 41 per cent. of the cases in negroes, to vary from medium to very severe, though the degree of infection of the three races was in the proportions of 78 per cent., 72 per cent., and 76 per cent.

With regard to the two worms it is useful to note that *Ancylostoma duodenale* is larger and coarser looking, with thicker and coarser head, armed with four hooks on the buccal rim, and with the dorsal conical tooth not markedly projecting into the mouth. Female with sexual opening in the posterior third. Male with larger caudal bursa, with dorsal lobe. Ova slightly smaller. *Necator americanus* is smaller, with small and finely tapering head, simple chitinous lips on the buccal rim, dorsal conical tooth projecting well into the mouth. Female with sexual opening in the anterior half of the body. Male with smaller bursa and subdivided dorsal lobe. Ova slightly larger.

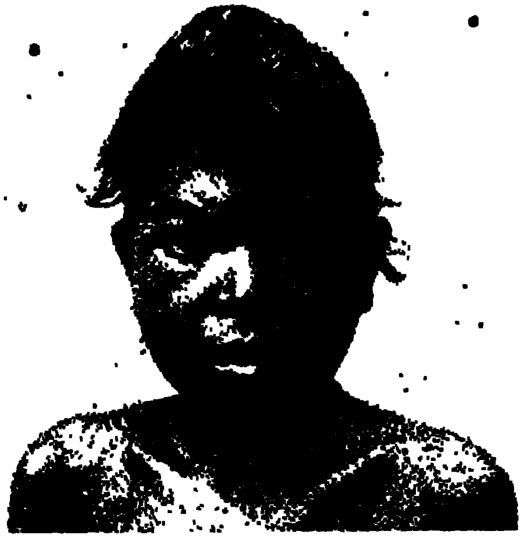

FIG. 755.—CASE OF ANKYLOSTOMIASIS.
(Note the swollen face.)

Pathology.—When the embryos enter the skin in sufficient numbers they cause an eruption of papules or vesicles, but some of these are more probably due to the pyococci and bacteria introduced along with the larvæ, which are the true cause of the dermatitis, as alcoholic extracts of the larvæ are said to produce similar lesions. These skin lesions are called 'bunches' in Cornwall, 'mazamorra' in Porto Rico, and 'ground-itch' in Assam. Smith has shown that experimental dermal infection with *N. americanus* causes local itching and a macular eruption, followed next day by a vesicular rash and swelling of the part, and on the fifth day marked swelling and enlargement of the lymph glands. This dermatitis disappears by the twelfth day. There may be sore throat and uneasy sensations in the stomach for a few weeks, and the ova appear in the fæces about the middle of the seventh week.

It is not known what effect the journey from the skin to the alimentary canal has upon the host, but it is certain that in course of time a marked effect upon the blood and the organs of the body is produced, which often appears out of proportion to the number of worms which can be found in the intestine. Loeb and Smith find that the worm produces a substance which hinders the coagulation of the blood. Some observers—*e.g.*, Gabbi—have found that the blood of ancylostome patients is more toxic than the blood of healthy people, and contains more hæmolytic substances, but this has been denied by Marini. Padoa and others have observed that the processes of intestinal putrefaction are very marked in ankylostomiasis. In our opinion the anæmia is due to a complex of causes—viz., the hæmolytic toxins secreted by the worm, actual loss of blood from the bites of the worms, and microbic secondary infections.

Morbid Anatomy.—An eruption about the feet, œdema about the ankles, with a peculiar dead-white appearance of the conjunctiva, are often seen on the post-mortem table. On opening the abdomen, it will be noted that the tissues are damp, the peritoneum sodden, the intestines very pale, and some straw-coloured fluid will generally be seen in the peritoneal cavity. All the organs appear damp and pale. The lungs are œdematous, the heart pale and fatty, with sometimes hypertrophy of the left ventricle The liver is fatty; the spleen presents various appearances, but generally is shrunken; the pancreas is normal, as are the suprarenals; the stomach shows chronic gastritis; the jejunum and ileum are usually contracted; and the mucosa is often dark red in colour, and marked by small hæmorrhagic points, which indicate the position of the bites. The ancylostomes may be found in large numbers, or may require considerable looking for. Sometimes they are firmly attached to the mucosæ. The kidneys are usually enlarged, pale, and fatty.

Symptomatology. The first stage or invasion of the body by the embryos may be marked by dermatitis of various types, papulo-vesicular or pustulo-ulcerative. The dermatitis is generally situated on the soles of the feet, and called by the natives of the West Indies 'mazamorra' (ground-itch), and is also known as 'pani-ghao' and the sore feet of coolies. It is probable, as remarked by Balfour, that the symptoms of the initial dermatitis, urticarial wheals, redness, and itching, are due directly to the larvæ, while the pustular stage is caused by secondary pyogenic infection. The second stage is the development of a leucocytosis and an eosinophilia before the definite disease begins. The third stage is when the anæmia begins to be appreciable.

The patient becomes pale, weak, and dropsical, the pallor being most marked in the conjunctiva of the lower eyelid, which becomes of a peculiar dead-white appearance. The emaciation may be marked, but, on the other hand, it may be concealed by the dropsy. In many cases there is œdema round the ankles, and in others there may be general œdema, with often ascites, œdema of the legs, scrotum, or face. When the ascites is marked, the patient has a protuberant abdomen, and looks at first sight not unlike a person suffering from malarial cachexia or kala-azar. The tongue is said by some observers to have two purplish smears, one on each side of the median line, and to be pigmented, but this in our experience can be seen in normal natives. The appetite may be perverted and geophagy result, and in addition there are signs of dyspepsia due to the chronic gastritis, and there may be nausea, vomiting, heartburn, and pain over the pit of the stomach. The bowels may be constipated, or there may be diarrhœa. Ova of *Ascaris* and *Trichuris*, together with those of *Ancylostoma*, are often seen in the fæces. Occasionally a little blood and mucus are present, and Charcot-Leyden crystals may also occur.

Blood.—There is marked anæmia, which has been shown by Boycott and Haldane, by using Haldane and Lorrain-Smith's method of estimating the total volume of the blood, to be due to a hydræmia; that is to say, the total volume of the blood is increased without a corresponding increase in the cellular elements and hæmoglobin. This is analogous to the blood condition found in chlorosis, and is the reverse of that found in pernicious anæmia, the features of which are very rarely met with in ankylostomiasis.

The counts given by different observers vary. Thus, Ashford gives as the average of nineteen cases the following figures: Erythrocytes, 1,776,000, hæmoglobin, 21 per cent.; colour-index, 0·6; leucocytes, 7,000; eosinophiles, 10·3 per cent. Boycott and Haldane in seventeen cases found erythrocytes from 4,072,000 to 1,533,000; hæmoglobin from 58 to 17 per cent.; colour-index from 0·71 to 0·56, leucocytes from 44,800 to 3,800; polymorphonuclears, 48·7 per cent.; lymphocytes, 14·4 per cent., mononuclears, 5·9 per cent.; transitionals, 7·4 per cent.; eosinophiles, 23 per cent.; mast cells, 0·6 per cent. Ashford, King, and Gutierrez found erythrocytes from normal to 754,000; hæmoglobin from 8 to 101 per cent., leucocytes from 5,000 to 10,000; polymorphonuclears, 54·5 per cent.; lymphocytes, 16·3 per cent.; mononuclears, 8·6 per cent.; eosinophiles, 17·1 per cent.; other forms, 3·5 per cent.

The red cells may show pathological changes and poikilocytes; megalocytes and polychromasia may be seen, as well as normoblasts and megaloblasts. The diminution of the colour-index is said to be the first pathological sign in the blood. In some very rare cases a condition of hyperglobulia has been observed instead of the usual oligocythæmia.

Boycott has shown that the principal leucocytic changes are to be seen in the blood before a condition of marked anæmia has set in, when it is found that there may be high leucocytosis—20,600 to 56,000—with a very high eosinophile figure of 56·2 to 66·2 per cent., while the hæmoglobin was from 98 to 80 per cent. When anæmia sets in, a leucocytosis is much less frequent, being met with in cases in which anæmia develops quickly. On the other hand, a leucopenia may be seen if the case is very anæmic. The reason for this alteration from a high state of leucocytosis without anæmia to that of leucopenia with severe anæmia might at first sight be thought to be explicable by the hydræmia producing the anæmia. Boycott, however, considers that this is not so, for he points out that leucocytosis can occur with marked anæmia, and that there is always a tendency on the part of the blood to restore its average volume and composition when altered from the normal, and comparing the normal leucocytic count of the hydræmia of chlorosis, says that, if there was no other factor, the leucocytic count of ankylostomiasis would not be affected by the hydræmia.

He thinks that the true explanation is probably exhaustion of the bone-marrow produced by the anæmia, and that it is partially due to a failure on the part of the individual to react to the stimulus to produce the eosinophile leucocytes. In any case, the leucocytic reaction does not bear any relationship to the anæmia. According to Boycott and Haldane, if the eosinophiles are deducted from the total number of the leucocytes, and the percentage of the remainder then calculated, it will be found to be nearly normal. The eosinophilia has been found to remain after the ova have quite disappeared from the fæces. Any inflammatory complication which leads to a polymorphonuclear increase may hide the true eosinophilia. The leucocytes are normal in structure, a few neutrophile, but no eosinophile myelocytes are to be seen. Wemberg and Mello have shown that the injection into guinea-pigs of extracts of various worms induces a certain degree of eosinophilia.

Reviewing this description of the blood, we would point out that it looks as though toxins were stimulating the production of the eosinophiles, and at the same time preventing a proper formation of hæmoglobin, and finally producing the hydræmia. We must state, however, that occasionally we have come across severe cases showing no eosinophilia. Low has demonstrated that eosinophilia is generally well marked in children, while it may be absent in adults, and suggests that the eosinophiles, which are tissue cells at first, come into the blood in response to some stimulus set up by the infection, but gradually disappear as this stimulus weakens with the prolongation of the infection. As a result of the diminution of the production of hæmoglobin, the iron in the liver is diminished.

Patients often complain of palpitation or difficulty in breathing. The lungs will be found normal, but the heart may be displaced downwards and to the left, and be feeble, with a hæmic bruit at the base. The vessels of the neck may be seen to pulsate markedly. The pulse is quick, and may be weak, thready, dicrotic, and intermittent. The liver is very often enlarged, especially in children.

Fever.—Fever in ankylostomiasis was described years ago by Manson, Fernando, and others, and more recently attention has been called to it by Gabbi and one of us. In some cases there is no fever, while in others this feature is present. In our experience three types of ankylostomiasis fever may be met with:—

1. The low intermittent type, which is the commonest, and in which the temperature seldom rises above 100° F.

2. An irregular type, at times intermittent, and at times subcontinuous.

3. An undulating type. This is very rarely observed.

Great care should be taken in making the diagnosis of ankylostomiasis fever to exclude other conditions—*e.g.*, malaria, Malta fever, kala-azar, trypanosomiasis, etc. There is much diversity of opinion on the origin of this fever. In our experience the fever is not due to the worm itself. It is of bacterial origin, being probably due to infections by intestinal bacteria entering the general circulation through the small wounds produced in the intestinal mucosa by the worm. The term 'ancylostoma fever' is, therefore, not quite appropriate. In several cases the fever continues long after the patient has got rid of the ancylostomes by adequate treatment.

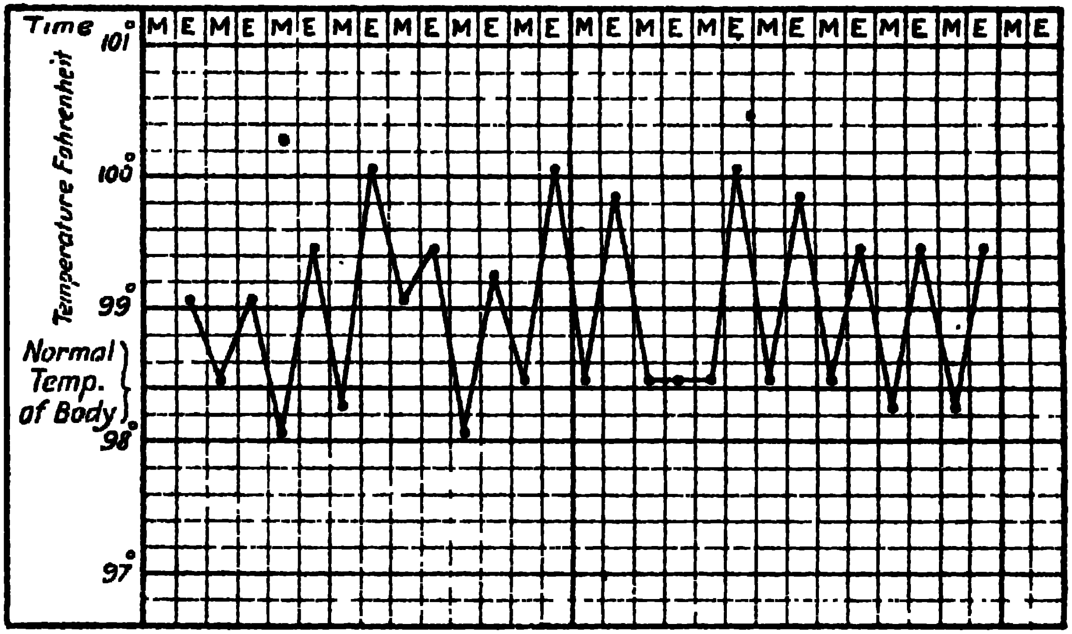

Fig. 756.—Temperature Chart of a Case of Ankylostomiasis Fever.
(From a case in the Clinic for Tropical Diseases, Colombo.)

Urine.—The urine is copious, pale, and often alkaline, with a specific gravity varying from 1010 to 1015. Albumen is rarely seen, but there is an increase of indigo-blue and urobilin, and there is albumosuria at times. The excretion of nitrogen is said to be much increased. Lussana believes that there are toxins in the urine which can be separated by the following method: The urine is condensed in a water-bath at 60° to 70° C. to a syrup, and then extracted with absolute alcohol, which is driven off, and the residue dissolved in sterilized water, and injected subcutaneously into rabbits. This is believed to produce diminution of the red corpuscles, loss of hæmoglobin, and poikilocytosis, which speedily disappear on stopping the injections. These findings of Lussana have been confirmed by some and refuted by other observers.

Mental and physical hebetude are marked, and other nervous symptoms may be observed. Children do not develop properly, and sterility, with delayed menstruation, has been noted.

When the anæmia becomes profound death may ensue from cardiac failure, but any intercurrent affection hastens the end in a case of ankylostomiasis.

Complications.—Any intercurrent disease is a serious complication, as also is pregnancy.

Diagnosis.—The definite diagnosis depends upon finding the ova in the fæces.

Anæmia in tropical countries, especially if associated with dropsy, should at once lead the practitioner to suspect ankylostomiasis. It must be remembered, however, that it is by no means easy to find the ova in the fæces at the first examination, and that sometimes, even in the worst cases, they require to be looked for on several days. Occasionally it is useful to give an aperient to make the eggs appear in the stools.

To facilitate the search for the eggs in the stools several methods have been elaborated by Fulleborn, Pepper, and others. *Pepper's method* is based on the stickiness of the ova; a portion of the sedimented fæces is placed on a slide for a few minutes, and then gently immersed in water; after this, although all other materials are washed away, the ova still adhere to the slide. If this process is repeated several times, numerous eggs may accumulate on the slide. It is to be noted that eggs of *Ascaris*, *Trichuris*, etc., do not possess this physical property, and therefore do not remain on the slide.

Telemann's method is to shake up a small portion of fæces with equal parts of ether and hydrochloric acid, filter, centrifuge, and examine the bottom deposit.

Bass's method is to dilute the fæces with ten or more times their bulk of water, strain through two or three layers of gauze in a funnel, centrifuge, pour off fluid, fill up with diluted fæces, shake, centrifuge, repeat a third time, then examine deposit removed by a clear pipette.

It must be admitted, as noted by Miss Porter and other observers, that concentration methods for the detection of ova are of relatively little use, as in practice they take too long.

Prognosis.—There is no doubt that ankylostomiasis is one of the great factors in producing the death-rate of a tropical native community, very often because it is not diagnosed. Ashford, King, and Gutierrez placed the deaths of Porto Rico caused by ankylostomiasis at 30 per cent. of the total death-rate, and we are not at all surprised at this, for our experience indicates that the disease is frequently entered in death certificates as anæmia, general dropsy, and malarial cachexia.

Treatment.—The aim of the treatment is to kill and remove the parasites, and this can be effected by thymol, eucalyptus oil, eucalyptol, beta-naphthol, or male-fern. A case must not be considered cured until the fæces show no ova on repeated examination after two or three weeks.

In all cases the patient should be carefully examined as to the condition of all his organs before treatment is begun, and should be placed on low or liquid diet for a day or so, and while being treated should be kept in bed, and care taken that the bowels have been well opened.

Thymol, introduced by Bozzolo, should be given in cachets, or as an emulsion. Generally 15 to 30 grains are given, and two hours later another 15 to 30 grains, followed in some cases by a third dose of 15 to 30 grains after another two hours. If the bowels do not act within four hours of the last dose, a saline aperient should be given. The treatment may be repeated on the following day. Another method is to give 10 grains in cachets at night until the desired result is attained. Yet another method, recommended by the International Health Board, is to mix it with an equal quantity of bicarbonate of soda, as this addition is believed to aid the cure and prevent unpleasant symptoms.

Thymol is a very poisonous drug in large doses, causing first irritation of the cerebral centres, with excitement and vertigo, while a dark colour may appear in the urine, or, according to Blum, may be produced by the addition of hydrochloric acid to the urine. According to the same authority, this colour exists in the form of a chromogen in the urine, the chemical nature of which is threefold: thymolsulphuric acid, thymolhydrochinon sulphuric acid, and thymolglycuric acid. In larger doses the nerve centres are paralyzed, the blood-pressure falls, and the patient dies of collapse.

Thymol, however, is very insoluble in water—only 1 in 1,500 of cold water—but it is easily soluble in alcohol, ether, chloroform, glycerine, and turpentine; hence no alcoholic stimulant whatever must be given to a patient who is to take or has taken thymol, and not merely must care be taken not to order stimulants, but the nurses must be warned of the danger of giving them. Thymol is also soluble in oil. Hence no purgative of castor oil should be ordered after its administration. Thymol certainly should never be given if there is marked visceral disease, nor do we think that it should be given in very profound anaemia—*i.e.*, when the number of red cells is below 1,500,000 per cubic millimetre. It is, however, very satisfactory in its lethal action on the worms, but the treatment must be repeated in many cases in a week, and again repeated if ova are seen in the fæces. Sandwith recommends a hypodermic injection of strychnine before thymol is administered.

Eucalyptus Oil and Chloroform.—A much less dangerous treatment is by oil of eucalyptus and chloroform, which may be preceded by a saline purgative given a few hours earlier.

The usual formula is:—

Olei eucalypti	♏xxx.
Chloroformis	♏xlv.
Olei ricini	ʒx.

One half to be given first thing in the morning, and the other half in half an hour. The chloroform is probably the active principle of this mixture. It does not work as satisfactorily as thymol, but it is safer, and can be used several days in succession. We use it often in children and debilitated adults. We have not seen the alarming symptoms described by some authorities as occurring in children and debilitated subjects. Some physicians prefer eucalyptol instead of the oil of eucalyptus. The difference is that eucalyptol is that portion which passes over between 347° to 351° F. when the oil is being distilled from the leaves.

Chenopodium Oil.—The International Health Board of the Rockfeller Foundation in 1917 stated that this oil was the most effective remedy for the treatment of *ascaris, oxyuris*, and *trichiuris*, but that its utility for the treatment of ankylostomiasis was conflicting, and, further, that it produced at times alarming symptoms and even death.

It is either used alone or with oil of eucalyptus in the proportion of three parts of chenopodium to one part of eucalyptus. The method of administration is to forbid all solid food after midday, to give a purge of Epsom salts at 4 p.m., and then at 6 p.m. the first dose of sugar containing chenopodium; this is continued at hourly or two-hourly intervals until the full dose has been taken, and finally, two hours after the last dose, more than 1 ounce of Epsom salts is taken by an adult and repeated if necessary in another two hours.

The dosage of oil of chenopodium is as follows:

1-2 years of age		..	..	..	2 minims for three doses.		
3-5	,, ,,	..	..	..	3-5	,, ,,	,,
6-10	,, ,,	..	..	.	6-9	,, ,,	,,
11-16	,, ,,	..	..	..	10-13	,, ,,	,,
17-50	,, ,,	..	..	..	14-16	,, ,,	,,
Over 50	,, ,,	..	..	..	12-14	,, ,,	,,

It can be given on sugar or in gelatine capsules. The Epsom salts administered are in a solution of 5 pounds in 5 gallons of water, 4 drachms being given to a child one to five years of age, 8 drachms to one of six to ten years, 12 drachms to one of eleven to fifteen years, 16 drachms to one of sixteen to twenty years, and 24 drachms above that age. Castor oil may be given instead of salts, 2 drachms for a child of one to three years, 3-5 drachms for a child of four to eight years, 6-10 drachms for nine to sixteen years, and above sixteen years 8-16 drachms, while 1½ ounces is considered to be the maximum for a female.

No alcohol or acids are to be ingested for a period of twelve hours antecedent to and after the treatment. Pregnant women should not be treated in this way.

Treatment should be repeated after ten days, and one week after the second course the fæces should be examined microscopically to see whether further medication is necessary, and if so it should be repeated at ten days' intervals according to the microscopical findings.

Beta-naphthol, finely powdered, can be given in cachets in 15 to 20 grain doses, administered in the same manner as thymol—viz., one cachet every two hours for two or three times, with the same precautions as with thymol. The patients often complain of severe burning of the stomach after taking them. The drug should *never* be given to individuals suffering from diseases of the kidneys, as it may cause fatal hæmorrhagic nephritis.

In debilitated patients beta-naphthol may be given in 5-grain pills made up with pulvis tragacanthæ composita and syrup. One to three pills, according to age, should be administered early in the morning on six successive days. No preliminary preparation is necessary. The results, however, as regards the destruction of the parasites, are not brilliant.

Nicol recommends:—

Beta-naphthol (finely powdered)	ʒiv.
Mucilaginis tragacanthæ	℥i.
Aquæ menthæ piperitæ	ad ℥vi.

of which 6 drachms (gr. xxx. of beta-naphthol) is given to an adult male, 5 drachms to an adult female, and 1 to 2 drachms to children, for a dose. Three doses are given at intervals of two hours. Two hours after the last dose a saline aperient is given. Beta-naphthol does not keep well, and should be stored in ½-pound bottles, and kept in a cool place.

Male fern, followed by castor oil, or calomel, or infusion of senna, has also been strongly recommended, and was generally used before Bozzolo introduced thymol in 1880. The Porto Rico Commission found it useless even in doses which produced toxic symptoms.

Nattan-Larrier recommends the following method of administering *Filix mas*:—

First day: Milk diet and saline purge. Second day: Milk diet; a capsule containing 0·30 centigramme of oil of *Filix mas* every ten minutes until twenty have been taken, followed in one-quarter of an hour by a capsule of ether every three minutes until eight have been taken. After the last capsule, 15 grams of castor oil are administered, and, after half an hour, 25 grammes of castor oil. Third day: A saline purge. Fourth day: Examination of the fæces and repetition of the treatment. Brimont recommends the essence of *Melaleuca viridiflora*.

Worms in the Fæces.—Whatever treatment be adopted its effect must be judged by the worms found on examining all the fæces passed during the first twelve to twenty-four hours after dosage. These fæces are stirred up with water, allowed to settle, and the water decanted, and this process repeated several times, after which the deposit is placed on a flat dish with a black background, and the whitish or greyish little worms looked for.

Treatment of the Skin Eruption.—The area showing the eruption should be painted with a solution of salicylic acid in collodion (1 in 6) in the early stages, or later it should be soaked in a weak solution of carbolic lotion (1 in 100), and the vesicles, pustules, etc., should be opened and cleaned with 1 in 40 carbolic lotion, and the whole area dressed with a carbolic lotion or carbolic ointment dressing. The itching may be relieved by an ointment of salicylic acid gr. v. in ʒii. of zinc oxide ointment and vaseline. The dressing should be performed twice daily, and the internal treatment, as described above, begun at once, and repeated every week for some time.

Treatment of the Mouth.—For about two weeks after infection the patient should use a mild antiseptic gargle several times a day, and should be instructed to spit out his saliva, sputum, etc., and not to swallow it. The gargling should be performed before drinking or eating anything. The sputum should be collected and examined for larvæ.

Prophylaxis.—Prophylaxis must be based upon an attempt to kill the parasites in the human being, and to prevent the infection of the human being by the parasite, but in order to be successful in these methods it is absolutely necessary to educate both the rich and the poor of a district in the essentials of the disease. This must be done by illustrated lectures and pamphlets in the vernacular. An appeal must also be made to the people to come at once for treatment when suffering from skin eruptions or anæmia.

The first method is the most feasible, and has been tried on a large scale at Porto Rico, and on many estates and in mines. The quickest way is to examine the people for anæmia, and treat the anæmics with thymol, the eucalyptus-oil mixture, or β-naphthol, after the examination of the fæces. On estates the method of examining the blood of non-anæmic persons for an eosinophilia might be adopted, as the worms may be present before the anæmia shows itself. The fæces of persons showing eosinophilia should then be examined for ova, and treatment instituted on the findings. Of course a certain degree of eosinophilia is also present in cases of ascariasis and other kinds of helminthiasis.

With regard to the second method, the formation and use of proper latrines may do much. With regard to estates, tea-bushes, etc., should not be allowed to grow right up to the coolies' lines, but a clear area should be left, and this should be treated from time to time with quicklime. Further, every alternate row of bushes might be left out in the half-acre adjoining the lines, and in the vacant spaces latrine-holes lined with lime might be dug. The use of bucket-latrines and the destruction of the fæces in a small crude incinerator would be better, and could be easily managed on estates. The best cheap latrine is 'Bailey's patent,' manufactured by the Empire Engineering Company of Cawnpore, at a cost of 118 rupees for a two-seat, and 300 rupees for an eight-seat latrine.

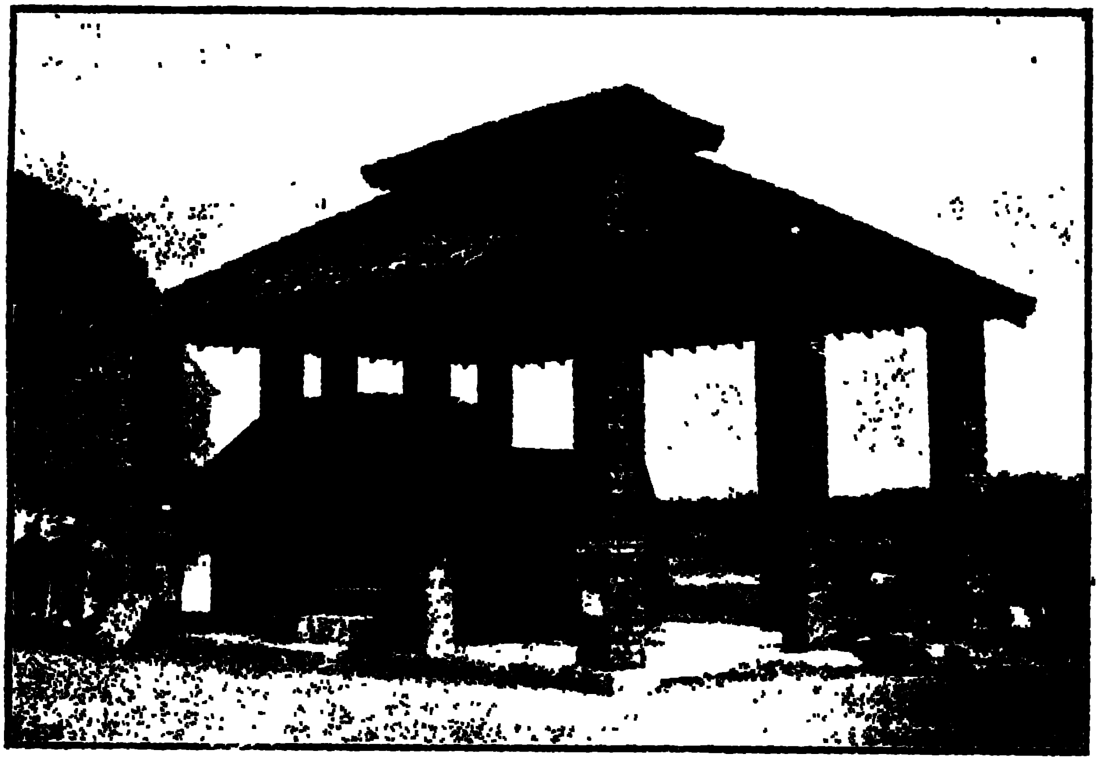

FIG. 757.—A CHEAP AND EASILY CONSTRUCTED INCINERATOR.

Leiper has suggested that fruitful results would be obtained from a more detailed study of the larvicidal effects of chemical manures such as 'nitroline,' etc. According to certain experiments made by this author, it would seem that after treatment with such chemicals human ordure could perhaps be used on the land with safety.

The figures show small incinerators in use in a mill and in a gaol in Colombo, but it must be remembered that fæces require a considerable amount of fuel and a considerable draught before they are properly burnt. There is, however, no need to go to great expense, and a simply constructed incinerator will often work well, if a little smell is not objected to. In order to calculate the size of latrine required, it must be remembered that an Indian community is estimated to pass 8 ounces of fæcal matter per diem in a mixed population of races, sexes, and ages, and 40 ounces of urine. The usual size of a galvanized iron latrine-bucket is 14 inches high by 12 inches broad at the mouth and 9 inches at the base, and it has a cubic capacity of 0·9 cubic foot, and is said to weigh 10 pounds when full. Coir fibre is often mixed with the fæcal matter in the proportion of 2½ pounds of coir to 1 pound of fæcal matter or 1 gallon of urine.

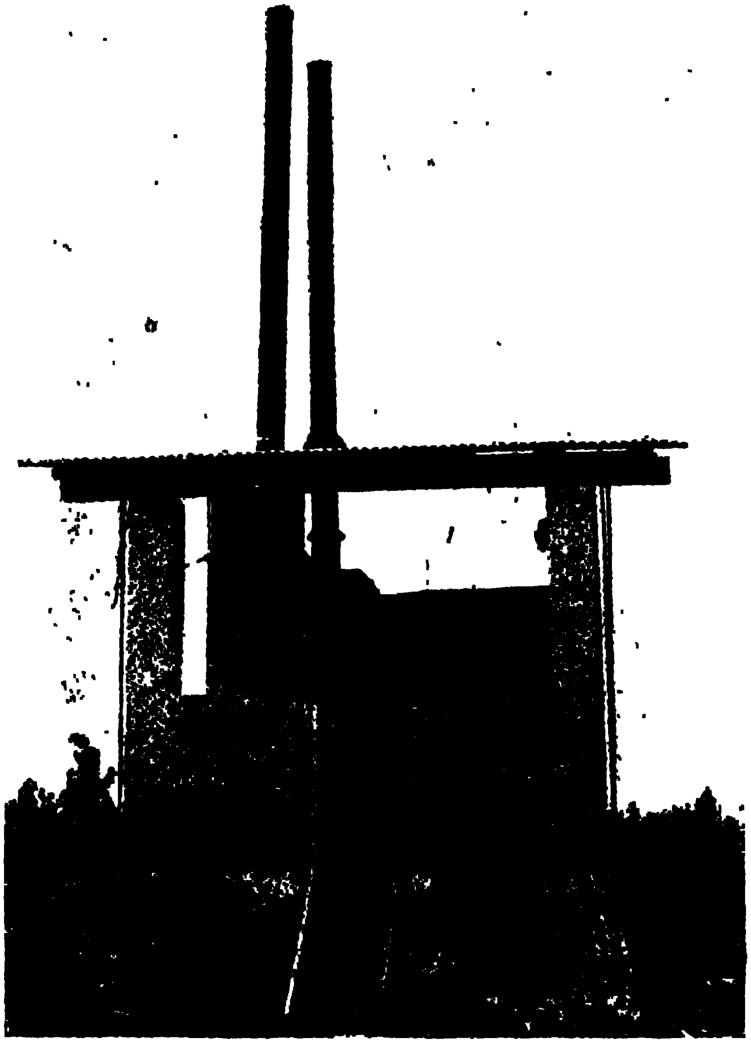

FIG. 758.—ANOTHER CHEAP AND EASILY CONSTRUCTED INCINERATOR.

Messrs. Freudenberg and Company, of Colombo, use a simple incinerator, and they have kindly supplied us with the following details of their process, which is carried out at night:—

Average number of buckets of fæcal matter burnt per night, 20.
Average weight contents of a bucket, 26 pounds.
Average quantity of ash left after burning the above, 5 buckets.
Average amount of coir dust used per bucket, 2 pounds.
Average amount of firewood used per burning, 2 hundredweight.
Average amount of rubbish burnt at the same time, together with a few old gunny bags, 1½ hundredweight.
Average number of coolies whose fæcal matter is dealt with, 400.
Latrine coolies at 62½ cents per diem to do the work, 2.
Firing starts at 7 p.m., and is finished by 8 a.m.; the highest temperature recorded was 1,050° C.

The urine can, of course, be separated from the fæces by using a Donaldson's separator latrine. The urine can then be disposed of by burial, and the fæces burnt.

There is no doubt that some such method would have excellent results in dealing with the problem in small communities and estates if carried out properly.

Badly infected lands might be treated with lime. It has been recommended that coolies should protect their feet by first dipping them in a bucket of tar, and then in one with sand.

The method of dealing with a large community is best exemplified by quoting the excellent work of the two Porto Rico Commissions, temporary and permanent, the former consisting of Ashford, King, and Igaravdez, and the latter of Igaravdez, Martinez, and Sein y Sein.

Patients attend at a central, or one of the outlying depots or dispensaries, where their stools are examined, and they are given medicines, and a card with the following instructions

1. Take one of the two purgatives given to you to-night (sodium sulphate).
2. Take at 6 a.m to-morrow half the capsules [all the capsules equal 45 to 60 grains (3 to 4 grammes) of thymol, or 23 to 45 grains (1·5 to 3 grammes) of β-naphthol].
3. Take the other half at 8 a.m the same morning.
4. Take the other purgative at 10 a.m.
5. You should neither drink wine nor any alcoholic liquor during the time you are taking these medicines.
6. Come for more medicines until the physician says you are cured.
7. Have a privy in your house. Do not defæcate on the surface of the ground, but in the privy.
8. Do not walk barefooted, so that you may avoid catching mazamorra in your feet. Wear shoes, and you will never suffer from anæmia.

In addition, farmers were requested to stop the pollution of the ground, and to introduce the use of shoes

The result was that 11 per cent of the population were treated in the year 1906-07 (89,233), and of these, 25·7 per cent. were cured, 17·4 per cent. practically cured, 40·5 per cent. were under treatment, 16·2 per cent. ceased to return, and 0·2 per cent. died, at a total cost of £9,600, of which £7,200 went in salaries and £1,100 in drugs.

Again, the highest credit must be given to the Americans for the fearless way in which they spend money on the prevention of disease and the free hand which they give to the sanatarian in the tropics.

In mines Oliver recommends that a solution of iron sulphate be used as a wash for the floors.

Salt has also been recommended by Perroncito, and later by other observers, but as a solution of at least 2 per cent. is necessary to kill the larvæ, this method is too expensive.

SUMMARY OF PREVENTIVE MEASURES.

Educational :—

Instruction of rich and poor with regard to the methods of infection, symptoms, treatment, and prophylaxis.

Personal Prophylaxis :—

1. Protection of the feet.
2. Protection of the hands.
3. Immediate treatment of the eruption on feet or hands.
4. Necessity of early treatment.

Public Prophylaxis :—

1. Search for and treatment of carriers.
2. Search for cases of the skin eruption and treatment of the same.
3. Search for cases of anæmia and treatment of same.
4. Provision of sanitary conveniences kept in good condition, and associated with a good system of conservancy.

Ascariasis.

Definition.—Ascariasis is infection with *Ascaris lumbricoides* Linnæus, 1758; *Toxascaris canis* Werner, 1782: or *Belascaris mystax* Zeder, 1800, the first named being much the most common.

Symptomatology.—The symptoms may be nil, or may resemble those of cestode infections, being partly gastro intestinal, partly reflex, while skin irritation and eruptions may also be present. If, however, the number of parasites be very considerable, signs of toxic poisoning, or even of intestinal obstruction from interlacing of the worms, may develop, but the great danger is from the wandering of the parasites. If they wander up the bile-duct and into the liver, they may cause abscesses in the liver. We have found as many as eleven worms in the bile-duct, with a large number in the liver, three of which lay in abscess cavities. They may also enter the duct of Wirsung, and cause slight inflammation of the pancreas, or go into the appendix, and cause appendicitis. Further, they may pierce the bowel in cases of ulcerative conditions of the bowels, and enter the peritoneum or the bladder, or enter the lung, the nose, or the ear by the Eustachian tube—in fact, they may wander all over the body. The observer must, however, be careful to distinguish between the post-mortem and ante-mortem wanderings of these worms: in the former case the worms are generally found alive. The most important reflex symptoms are the convulsions so commonly met with in children, and attacks of so-called 'wormy' cough are not rare. We have seen cases of fever resembling typhoid (typho-lumbricosis) which on post-mortem examination have shown no lesions of typhoid, but enormous numbers of ascaris.

Diagnosis.—The diagnosis will depend upon the discovery of the eggs in the fæces.

Treatment.—The best treatment is santonin, with some form of purgative. Usually santonin is mixed with an equal quantity of calomel, and given in doses of 1 to 3 grains for an adult, and $\frac{1}{6}$ grain for every year of life for a child. The dose is given every morning for two or three days, and repeated again in a week if eggs still appear in the fæces. It is as well to remember that santonin may cause blue or yellow vision.

Oil of chenopodium may be given in gelatine capsules or in castor oil. (For dosage see p. 1770.) In China *Quisqualis indica* is at times used: 2 drachms of the powder.

Oxyuriasis.

Definition.—Oxyuriasis is infection with *Oxyuris vermicularis* Linnæus, 1767 (see p. 857), and is common all over the world.

Symptomatology.– The symptoms are irritation in the region of the anus, with sometimes a distinct entero-colitis, and sometimes slight fever. It is usually stated that there is a sense of irritation in the nose. The diagnosis is to be made by finding the worms in the motions after a purgative. In girls the worms may enter the vagina and cause vaginitis.

Treatment.– The gravid females can be killed by rectal injections of quassia, alum (ʒi. to a pint), salt (ʒii. to a pint), but the young forms require internal treatment with santonin and calomel, as described under Ascariasis. Flynn recommends sulphur (gr. iii.) three times a day in adults, and gr. i.ss. in children, given as a cachet or lozenge. A 10 to 20 per cent. calomel ointment, diluted unguentum hydrargyri (1 in 4), may be applied to the anus, or iodoform and naphthalin suppositories may be used.

Intestinal Polyparasitism.

Definition.—Intestinal polyparasitism is the invasion of the alimentary canal by more than one species of parasite.

Remarks.– We have, since 1903, investigated the question as to which parasites are commonly present in natives of tropical Africa and Ceylon, and find that it is the rule rather than the exception for their intestines to harbour more than one species of parasite.

Statistical information with regard to the prevalence of the various forms in different tropical regions is still wanting, but some valuable observations have been made, especially in the Philippine Islands by Garrison, and in South Africa by Miss Porter. The relative prevalence of the various intestinal parasites in the Philippines has been carefully studied by Garrison, who finds that 84 per cent. of the investigated persons were infected with fifteen genera and about twenty species, multiple infections being the rule, the average number of infections being 2·25 per head.

The prevalence of the various parasites were as follows:—

	Per Cent.
Trichuris	59·0
Ancylostoma and Necator	52·0
Ascaris	26·0
Amœbæ	23·0
Flagellates and Ciliates	21·0
Strongyloides	3·0
Oxyuris	0·8
Tænia	0·7
Schistosoma japonicum	0·6
Paragonimus	0·4
Opisthorchis	0·2
Hymenolepsis	0·1

Besides these, however, there were a number of undetermined forms. The infection with *Trichuris* is variously given in different countries—*e.g.*, Porto Rico (Commission), 7·27 per cent.; India (Fearnside), 6·95 per cent.; India (Dobson), 4·4 per cent.; Central Africa (Daniels), 2·79 per cent. The infection with *Ancylostoma* and *Necator* is given in India (Calvert), 83 per cent.; (Dobson), 57·58 per cent.; (Fearnside), 65·83 per cent. *Ascaris* infection in West Africa (Wellman) is 50·97 per cent. Garrison considers his figure of 26 per cent., which is based upon adults only, as much too low. *Strongyloides* is placed in Central Africa at (Daniels) 1·5 per cent.; West Africa (Wellman), 0·65 per cent.; Porto Rico (Commission), 0·8 per cent. *Oxyuris* is given in India (Dobson) at 15·37 per cent.

Ætiology.—*Ascaris lumbricoides* is, in our experience, by far the most common parasite, and it is often associated with either *Trichuris trichiura* or *Necator americanus* (or *Ancylostoma duodenale*) in double infections, but triple infections with these three parasites are not uncommon, and quadruple infections of the three associated with *Strongyloides intestinalis* are also common.

Associated with one or more of these worms it is by no means unusual to find *Loeschiæ* and flagellates, especially *Trichomonas hominis*, and more rarely ciliates—*e.g.*, *Balantidium coli*. *Oxyuris vermicularis* is fairly common in children, but tapeworms are not so frequently met with in Ceylon, India, and Equatorial Africa, while they are extremely common in Abyssinia.

In China and other countries *Trematode* infections must also be considered, and in the West Indies and Africa infection with *Schistosoma mansoni*.

Symptomatology.—The symptoms presented by the patients may be nil if the parasites are few in number, and will in any case depend mostly upon the action of that species which is known to be the more pathogenic or which is most abundant, but it may be very difficult or impossible to separate the symptoms caused by one parasite from those due to another. Cases may show signs of fever, anaemia, diarrhœa, and even dysenteric symptoms may appear if the infection is heavy.

Treatment.—The treatment must commence with that laid down for the parasite which is the more important from a pathogenic point of view—*e.g.*, in the case of a double infection with *Ancylostoma* and *Ascaris*, the ankylostomiasis must be treated first and then the ascariasis.

Rare Infections.

Gordiaceiasis and Acanthocephaliasis (see pp. 678 and [illegible]).

Infections with species of the Gordiacea and Acanthocephala are rare. Treatment would be on the same lines as for ascariasis.

Intestinal Diplopodiasis and Chilopodiasis (see pp. 689 and 739).

Diplopodiasis and chilopodiasis are rare and unimportant, giving rise to intestinal pains and diarrhœa. The diagnosis is only possible on discovery of the parasites in the fæces. The treatment is the chloroform mixture, as for ankylostomiasis.

These infestations are placed here only for convenience.

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CHAPTER LXXVI

SPRUE AND OTHER DIARRHŒAS

Sprue—Pseudo-Sprue—Hill diarrhœa—Low-country morning diarrhœa—Flagellate diarrhœa—Famine diarrhœa—Cœliac disease—References.

SPRUE.

Synonyms.—Ceylon sore mouth, Aphthoides Chronica, Tropical aphthæ, Impetigo Primarum Viarum, Diarrhœa Alba, Psilosis Linguæ et Mucosæ Intestini, Phthisis Abdominalis, Blastomycosis Intestinalis, Endemic diarrhœa, Cochin China diarrhœa.

The term 'sprue' (sprew, sprau, sprulf, spru, spre, spree, spro) is a phrase used in Holland and Scotland for aphthous stomatitis in children, Aphthæ tropicalis der deutschen, and was applied to this disease by Manson and Van der Burg, the latter calling the disease in Batavia 'Indische spruw.'

Definition.—Sprue is a chronic catarrhal inflammation of the alimentary canal, of unknown cause, characterized by a peculiar ulcerative condition of the tongue and mouth, and by the passage of large, pale, frothy motions, the symptoms waxing and waning periodically.

History.—According to Hiatt, sprue was first mentioned in the writings of John Bicknell, in America, in 1737. Hillary, of Barbados, in 1766, in a most remarkably able manner, describes the disease for the first time under the name 'aphthoides chronica.' His account is well worth reading, and there can be no possible doubt that his description refers to the disease we now call sprue. The Indian physicians Twining (1835), Grant (1854), Cunningham (1877), mention symptoms indicating that they were acquainted with a disease of this nature, while Elliott of Ceylon gave a very good account of the malady, which he called 'phthisis abdominalis.'

At the same time—*i.e.*, 1864 to 1883—French physicians noted a peculiar form of diarrhœa, commonly met with in Cochin China, which perplexed them considerably, a large number believing that it was dysenteric in nature, while others considered that it was probably a new disease.

In 1880 Manson was the first after Hillary to clearly define the disease, which he called 'sprue'; and in the same year, and independently, Van der Burg described it under the term 'Indische spruw' in Batavia. In the next year (1881) Sir Joseph Fayrer delivered the Lettsomian Lectures on chronic white tropical diarrhœa. These three authors permanently established the disease as a clinical entity. Since then many important papers and articles have appeared, notably Roux's 'Traité' in 1888, Thin's 'Psilosis' in 1897, and Cantlie's papers, and the publications by Brown, Begg, Castellani, Low, Bahr, Ashford, Rogers, Nicholls and many others.

Climatology.—The endemic home of sprue appears to be Asia; especially Malaya, Sumatra, Java, Siam, and Annam; but it also extends into Burma, India and Ceylon, China, Australia (East and South), New Caledonia, the Fiji Islands, and Japan. Possibly it exists in the West Indies, where Hillary originally described it, and it may occur all through the tropics; but if so, it must be rare in certain regions—as, for example, West Africa. Rare cases of sprue occur in Europe.

Ætiology.—The etiology of sprue has not yet been elucidated, but of the many etiological theories brought forward, the one which at the present time receives more acceptance is the monilia or oidium theory, also known as *Kohlbrugge's theory*. Kohlbrugge, in 1901, found in cases of sprue in Java a fungus which he identified with *Monilia albicans* Robin, at that time better known under the name of *Oidium albicans*. He made a very complete histological study of one of his cases which ended fatally, and emphasized the fact that the fungus in sections of the tongue, etc., had invaded the deep strata of the mucosa, the glands, and portions of the submucosa. He concluded that the fungus was the cause of the disease. Kohlbrugge's findings were speedily confirmed by many observers, especially French and Dutch, and Le Dantec gave to the malady the name of *blastomycosis intestinalis*.

In 1905 and 1912 cases of sprue with presence of monilia fungi were placed on record by Castellani, who, in 1912, described several species, *Monilia intestinalis*, *M. enterica*, etc. This author's opinion was that such fungi were the cause of some of the symptoms of sprue, as, for instance, the frothy appearance of the stools, but doubted their being the primary cause of the malady. He believed them to be the cause of the frothy diarrhœa, because he had noted that this symptom generally improved after large doses of bicarbonate of soda. He thought that sodium bicarbonate given in large doses might decrease the acidity of the intestinal contents, and in this way check the growth of fungi, which, as is well known, grow better on acid than on alkaline media. In 1913 Castellani and Low described a new monilia found in a case of sprue, *M. decolorans* Castellani and Low, 1913. They came to the conclusion that this and other monilias (*M. intestinalis*, etc.) were the cause of certain important symptoms of the disease such as frothiness of the stools, etc., but they were not inclined to consider them to be the primary cause of the malady: they quoted in analogy the example of scabies, in which the main part of the symptoms is due to the secondary invasion by staphylococci, and not to the primary cause, the acarus.

In 1914, Bahr, in a series of interesting publications, supported Kohlbrugge's theory, believing that the cause of the malady was probably *Monilia albicans* Robin.

From 1915, Ashford, in several able papers, has supported the same theory, though he does not consider that *M. albicans* is the cause of the malady. He calls the monilia observed in his cases *M. psilosis*, but, according to the laws of nomenclature, the correct term would seem to be *Monilia enterica*.

Monilias found in Sprue.- The principal species of monilia so far found in sprue are the following.

1. *Monilia albicans* Robin.
2. *Monilia decolorans* Castellani and Low.
3. *Monilia intestinalis* Castellani.
4. *Monilia fæcalis* Castellani.
5. *Monilia insolita* Castellani
6. *Monilia tropicalis* Castellani.
7. *Monilia enterica* Castellani (probable synonyms: *Monilia psilosis* Ashford, *Parasaccharomyces ashfordi* Anderson).

For description of these fungi see p. 1079.

Species of the Genus Oidium found in Sprue. - The principal species of the genus *Oidium sensu stricto* so far found in sprue are:—

Oidium rotundatum Castellani.
Oidium asteroides Castellani.

For description of these fungi see p. 1093.

Remarks.—Kohlbrugge's theory is the one finding most support at the present time, and, according to various authors, agglutination and complement fixation tests are supporting it, and certain observers have claimed to have succeeded in reproducing the malady in the lower animals by injection of intestinal monilias. We believe that if the malady is eventually demonstrated to be a moniliasis, then a group of monilias, and not one only, will be found to be capable of producing the affection: this in analogy to what one sees in bacillary dysentery, and in affections due to the higher fungi, such as ringworm

It must be noted that fungi, especially in tropical countries, may be found also in stools of normal individuals and persons suffering with affections which are not connected with sprue. Such fungi mostly belong to the genera Monilia, Saccharomyces, Cryptococcus, Willia, Mycoderma, Oidium.

The Helminthic Theory. Some authorities consider *Strongyloides stercoralis* to be the cause of the disease, but in our experience the worm has nothing to do with the malady, being found in all sorts of pathological conditions.

The Bacterial Theory.- Numerous different cocci, bacilli, etc., have been described as the causative agents of sprue, but so far none has been demonstrated to be the primary cause of the malady. Rogers and Nicholls have suggested that the disease may be a *streptococcal infection*, both authors having obtained good results by using streptococcal vaccines. The streptococci found by Nicholls were of the viridans type, as found also in normal mouths. Complement fixation tests carried out by Nicholls would seem to support the streptococcal theory. Nicholls believes the etiology to be in reality twofold, there being an infection factor and a dietary factor.

Attention must be called to certain cases of pseudo-sprue, described by one of us, and due to a bacillus of the Flexner group. These cases are not true sprue, as they get well either spontaneously without leaving the tropics or by a course of vaccine treatment prepared with the Flexner-like bacilli isolated from the stools.

The Protozoan Theory. Various protozoan organisms have been found in cases of sprue, amoebae, spirochaetes, flagellates, etc., but none have been demonstrated to be the cause of the malady.

The Climatic Theory. This does not need to be discussed, though a hot damp climate is an important predisposing cause.

The Food Theory.—This also does not need to be discussed, though spicy foods and alcohol may be predisposing causes, and dietary errors, as emphasized by Nicholls, may lower the resistance of the alimentary mucosa to germ infection.

The Deficiency Theory.—This theory has been ably brought forward by Cantlie, who noticed in certain cases signs of scurvy.

Syndrome Theory. Finally, the theory must be mentioned according to which sprue is not a separate disease, but is a syndrome met with in various pathological conditions, such as chronic dysentery and pernicious anaemia. This theory is not supported by any medical man of long tropical experience. The disease presents typical symptoms and a typical course, but, as in dysentery, so in sprue, it is in our opinion probable that the clinical term covers several closely allied conditions, e.g., it is possible that there may be a sprue of hyphomycetic origin, a sprue of bacterial origin, and a sprue of protozoan origin.

Pathology.—With an unknown causation, it is not easy to write an account of the pathology. It would appear as though the primary lesions are beneath the epithelium in both the tongue and the intestine, and cause the superficial desquamation and catarrh. In the intestine the disease begins with submucous congestion, after which follows thrombosis of the vessels, and exudation of haemoglobin, and a round-celled infiltration. The mucosa suffers because its blood supply is damaged, and therefore necrosis takes place, the glands and villi being affected. The oesophagus and stomach also suffer. The liver is at first enlarged and congested, but later becomes atrophied and small. The fact that the tongue, oesophagus, stomach, and intestines are affected would indicate that something deleterious is being carried by the blood stream to these organs, rather than that something is acting from the surface. The irritation of the liver may be due to the same cause.

When once the mucosae are damaged, the chemical processes of digestion and the absorption of their products must be interfered with; while at the same time the absorption of poisons from the alimentary canal must be easier. Indeed, there is evidence of this in the increase of indigo blue in the urine, which is at times marked.

These two conditions would lead to an atrophy of the liver, which organ is one of the great safeguards against a toxæmia of intestinal origin. When the liver is sufficiently damaged, a toxæmia is possible, and occurs; hence, possibly, the advantage of the treatment by liver-soup or other preparations of liver.

The damaged condition of the mucosa of the mouth and tongue makes mastication difficult. The denuded condition of the œsophagus causes the burning pain during swallowing; the condition of gastric and intestinal mucosæ causes the dyspepsia and diarrhœa of the disease. The diarrhœa is characterized by pale, frothy motions, the explanation of which is as follows:—

On opening the bowels post mortem, the observer is struck by the fact that, though there may be plenty of bile in the duodenum and in the higher portions of the bowel, this gradually disappears until, in the lower parts of the small intestine, the contents appear white. In normal fæces bilirubin should be changed into stercobilin (hydrobilirubin), which is urobilin, and is identical with that found in the urine. The white appearance of the intestinal contents is probably partly due to certain bacteria, especially *B. albofaciens*.

Vaughan Harley has shown that in the upper third of the small intestine the normal fæces are of a yellowish colour, due to bilirubin. In the middle third they are of a whitish or greyish colour, probably owing to the bile-pigments being converted into chromogens, which become green in the lower third. After passing the ileo-cæcal valve, the bile-pigments are converted into urobilin by the action of putrefactive bacteria, but a considerable quantity of this is in the form of a chromogen. If the pancreatic juice is absent a colourless form of urobilin is found, called leuco-urobilin; the blood pictures in the last stage closely resemble that of pernicious anæmia. A very common feature is the presence of true chromatin granules in certain red cells.

Histopathology.—The histopathology of the disease requires much further study. The principal histopathological feature of the malady is a severe process of desquamation of the mucosæ of the digestive tract, together with atrophic changes of the mucosæ, glands, pancreas, and liver. One of us, in association with E. H. Ross, Low, and Cropper, has studied certain histological features of the epithelial cells of the tongue and the condition of the blood.

Changes in the Epithelial Cells of the Tongue.—These cells present often a fatty degeneration, but an interesting feature is the great increase in the presence of certain inclusions, which, as demonstrated by one of us, may be found also in various kinds of stomatitis, including the usual tobacco variety, and even in normal people. These peculiar inclusions are of two types.

Type I.—This is by far the commoner. The cell presents a various number—one to twelve or fifteen—of roundish or oval formations of variable size, 2 or 8 μ in diameter, which in preparations coloured by Leishman's stain take up a reddish or purplish colour. They are apparently structureless, but they may present one or two small vacuoles. These inclusions stain beautifully by using H. C. Ross's jelly method, but even with this method do not show any structure. They are not fat drops, as they colour deeply with Leishman's stain instead of becoming dissolved in the alcohol. They do not appear to be of nuclear substance, as the masses are structureless. They do not seem to be parasitic, as they are structureless and homogeneous. The severer the inflammation of the tongue, whatever the cause, the more numerous are these bodies. The greatest probability is that they are merely masses of keratohyalin.

Type II.—Occasionally instead of structureless homogeneous masses, granular agglomerations somewhat resembling chlamydozoa are seen. Whether these are a stage of the former inclusions is not known, but they appear to be merely cell degenerations.

Changes in the Cells of the Blood.—These have already been mentioned under the heading Pathology.

Morbid Anatomy.—The body is emaciated, and the skin often hangs loosely, and there may be œdema about the ankles. The tongue shows small areas of infiltration into the connective tissue, vesicles, and small ulcers. The filiform papillæ atrophy, and the fungiform papillæ become swollen and prominent. The pillars of the fauces and the tonsils may show subepithelial inflammation, and even suppuration and ulceration. The œsophagus is inflamed, and its mucosa is attenuated in places. The mucosa of the stomach may be pale and atrophied, or rough and cirrhotic. The mucosa of the small intestine may be slightly eroded, or may be so destroyed that the whole bowel is diaphanous with vascular arborizations; or there may be effusion into the solitary and agminated glands. The contents are bile-stained in the upper parts, and whitish lower down. The large bowel may be ulcerated. The liver is atrophied, but otherwise normal. The pancreas may be normal, inflamed, or cirrhotic. The peritoneum may be thickened and chronically inflamed, and in some cases show adhesions. The other organs are normal as a rule, but sometimes they are atrophied.

Symptomatology.—The incubation period of sprue is quite unknown, and the onset is insidious, without marked symptoms, which are usually merely failing strength and an undefined sense of illness. The disease may begin with diarrhœa and intestinal symptoms, or with mouth symptoms only.

Usually it begins with slight attacks of sore mouth, indigestion, and morning diarrhœa, often of a bilious nature; but as none of these are severe, and all are evanescent, the patient thinks little or nothing about them, and does not consult a medical man until the disease is well established. Three symptoms now worry the patient—viz., sore mouth, indigestion, and morning diarrhœa.

On examining the mouth, the dorsum of the tongue will be seen to have a whitish fur, through which the swollen fungiform papillæ are projecting. The sides and tip of the tongue are red and inflamed, with often small vesicles, small ulcers, and bare patches, which are very tender. Similar patches may be noted under the tongue near the frenum, on the inside of the cheeks, on the palate, and on the pillars of the fauces. A little ulcer, called Crombie's molar ulcer, may be seen near the two last upper or lower molar teeth. So tender is the mouth at times that deglutition, mastication, warm or spiced foods, acid or alcoholic liquors, cause much pain. In addition, mucus may be noticed clinging to the pillars of the fauces and to the back of the pharynx. This mucus is a source of great distress to the patient, as it accumulates in considerable quantities especially if some warm fluid has been taken, and the effort to get rid of it makes him almost sick. On swallowing food, a burning pain is felt along the course of the œsophagus and over the sternum, as though there was something raw inside (as, indeed, there is). The voice is said by Thin to be altered at times, but we have not specially noted this.

The neck, thorax, and arms may show signs of emaciation. The abdomen is swollen, sometimes markedly so, especially in the epigastric region, and the wall is soft and relaxed. The patient complains of dyspeptic symptoms, viz., a sensation of discomfort and distension after meals, with acid eructations and sometimes vomiting. Early in the morning he feels symptoms of intestinal discomfort, and passes a few copious, greyish, offensive, frothy motions, and no more for the rest of the day. After these motions he may feel much better, and have a good appetite.

Examination of the fæces shows mucus, epithelial débris, and many bacteria, and often yeast-like fungi, and in some cases eggs of various worms may be present. The quantity of fæces passed varies with each motion, but is in excess of the normal, this being due to solids rather than liquids. The excretion of nitrogen and fat is increased. Fat constitutes over 20 per cent., often 40 to 50 per cent. of the stools, while in normal individuals on a mixed diet it averages 6 to 8 per cent. Some observers believe that this is not due to the fat-splitting enzymes non-acting, but to the absorptive power of the upper parts of the intestine being interfered with.

The analysis of gastric contents may show a decrease in hydrochloric acid and pepsin. The pancreatic juice may show absence of diastase, trypsin, and lipase.

The most complete analysis of urine and fæces has been carried out by V. Harley and Goodbody. The patient, weighing 30·87 kilogrammes, was on a milk diet, containing 12·00 grammes of nitrogen, 70·44 grammes of fat, 82·32 grammes of carbohydrates, and 1,900 c.c. of fluid. The urine passed measured 1,050 c.c., specific gravity 1012, urea 10·8 grammes, uric acid, 0·8 gramme; ammonia, 0·44 gramme, phosphates, 1·27 grammes, chlorides, 3·89 grammes. Total sulphates, 1·47 grammes, of which 1·35 grammes were alkaline and 0·12 aromatic. The average daily quantity of the motions was 255 grammes, of which 70·40 were water, 1·47 nitrogen, 35·92 fat. The nitrogen given in the food was 12·00 grammes, and that in the fæces 1·47 grammes; therefore 88·80 per cent. had been absorbed. The fat in the food was 70·44 grammes, and that in the fæces 35·92 grammes; therefore 53·01 per cent. had been absorbed.

The colour of the fæces was greyish-green to greyish-white, but gave a distinct urobilin reaction, due to the leuco-urobilin. Schmidt's test for urobilin is performed by adding a concentrated solution of perchloride of mercury to the fæces, when a bright red colour is developed if urobilin is present. If there is much urobilin, the colour appears within five minutes; if little, in five to fifteen minutes; if very little, in half an hour. The colour deepens for twenty-four hours. More analyses on the above lines are required. Halberkann in a case he studied found a large amount of *indican* in the urine and a reducing Fehling substance, which was not glucose, undetermined. In the stools he found presence of urobilinogen, and they contained a large amount of fat.

The *blood* coagulates slowly, and there is always some reduction of the red cells, which may fall as low as 3,000,000 to 1,000,000 per cubic millimetre. The colour-index is low, and the structure of the cells is normal. The white cells are also reduced to about 6,000 to 2,800 per cubic millimetre. The ratio of white to red is about 1 to 400 in bad cases. A differential count shows an increase in the mononuclears and eosinophiles.

The *urine* requires more investigation, but as far as evidence goes at present it is not abnormal, showing only an increase in indigo blue and urobilin, and at times Cammidge's reaction for pancreatitis.

Schmitter has often noted loss of sexual power.

The buccal, intestinal, and other symptoms may markedly improve, even without treatment, but only to get worse again; and this is repeated time after time.

In due course the patient becomes very emaciated, weak physically, and depressed and irritable mentally. The skin becomes harsh; the mucosæ anæmic, the tongue becomes smooth, glazed, reddish-yellow, and small, and is often furrowed by cracks, indigestion is marked; and the diarrhœa is worse. The patient continues to lose weight, and emaciates rapidly, the skin hanging in loose folds, the abdomen blown out with gas, the liver small and atrophied, the ankles œdematous, while the pulse becomes slow and feeble.

After this has gone on for a long time, the emaciated, worn-out, irritable person dies of an acute attack of diarrhœa or cardiac failure. Sprue is essentially a chronic disease, with remissions, intermissions, and recurrences, but, unless taken seriously in hand, goes steadily from bad to worse.

Some writers distinguish three stages—a first stage, with oral and dyspeptic symptoms; a second stage, with marked intestinal symptoms; and a third stage, with toxæmia, emaciation, and anæmia; while cases are sometimes seen which are atypical—that is to say, where there are the mouth symptoms without the intestinal symptoms, and *vice versa*.

Complications. The complications met with in the course of the disease are:—Acute diarrhœa; dysenteric diarrhœa; hæmorrhage; meteorism; pancreatitis; myalgia; insomnia; helminthiasis, especially ankylostomiasis; impacted fæces; chronic appendicitis; jaundice; diabetes; and pernicious anæmia.

Diagnosis.—The diagnosis of the disease is to be based upon the irregular chronic diarrhœa occurring especially in the morning, and associated with flatulent dyspepsia, causing distension of the abdomen, and the passage of fermenting, abundant, clay-coloured motions. With these symptoms there will be progressive emaciation and anæmia, and when to these the characteristic mouth-lesions occurring in a person living in the tropics are added, it is indeed difficult to imagine any disease with which it could be confounded. Van der Scheer considers that the discovery of fat in the motions is a diagnostic sign before the disease begins; but this condition may also be found in pancreatitis. Low says that the so-called psilosis pigmentosa of Barbados is pellagra. The diseases from which sprue should be distinguished are stomatitis, hill diarrhœa, chronic dysentery, and chronic pancreatitis.

Stomatitis.—All forms of stomatitis are very common in the tropics, and may be accompanied by intestinal symptoms such as diarrhœa. The stools, however, do not show the peculiar characteristics of sprue—viz., the white colour, the frothy appearance, and the copious amount passed in the twenty-four hours.

Thrush.—This is easily diagnosed by examination of the white patches, in which fungi of the genus *Monilia* will be found. It is, however, to be noted that in long-standing cases of sprue, as in all chronic complaints, thrush may develop.

Hill Diarrhœa.—The patient generally gives a history of residence at a high elevation, and the diarrhœa is as a rule present only in the morning, while mouth symptoms are absent. We have, however, seen several patients in whom sprue has developed after repeated attacks of what to all appearance was simply hill diarrhœa.

Chronic Dysentery.—In chronic dysentery there is an absence of the mouth symptoms, while the motions are not whitish in colour, and may contain blood and mucus during the exacerbations. The diarrhœa of dysentery is generally accompanied by griping, while that of sprue is not. In chronic dysentery pain is often felt on pressure over the sigmoid and descending colons. In some cases microscopical and bacteriological examination of the stools for entamœbæ and the Shiga-Kruse bacillus may be necessary to clear the diagnosis.

Though personally we consider sprue and chronic dysentery to be different diseases, still we have seen several cases of sprue developing in old-standing cases of chronic dysentery.

Chronic Pancreatitis.—Absence of the mouth symptoms of sprue and presence of tenderness in the region of the epigastrium and the passage of large quantities of fat in the motions, together with Cammidge's crystals in the urine, will enable the diagnosis of chronic pancreatitis to be made.

Prognosis.—The prognosis in any case of sprue is serious, because, unless the patient will honestly co-operate with the doctor, he will go from bad to worse. We are of the opinion that, no matter how mild the case may be, the patient should be warned of the danger.

If treatment is properly carried out, the prognosis improves considerably, but even then relapses are apt to occur.

Treatment.—The treatment is symptomatic.

An attempt must be made to soothe the alimentary canal, and to give it as little work to do as possible, so that it may repair itself. This line of treatment will necessitate rest in bed and a careful diet, after the bowels have been swept as clear as possible of decomposing material.

While this is proceeding, care must be taken to avoid chills, as they aggravate the disease. Lastly, an attempt should be made to treat those symptoms which worry and annoy the patient.

The treatment, therefore, may be classified into:—

1. The co-operation of the patient.
2. Rest in bed.
3. Suitable clothing.
4. Removal of fermenting bowel contents.
5. Diet.
6. Medical treatment.
7. Change of climate.

1. THE CO-OPERATION OF THE PATIENT.—The nature of the complaint and the dangers which the patient runs must be carefully explained to him, and the line of treatment sketched out. Further, he must be told that its success or failure largely lies in his own hands. If he has not the strength of will to persevere, even when at first success seems far from certain, he might as well not begin.

If he agrees to co-operate, then he must be carefully weighed, and a chart kept of his weights.

2. REST IN BED.—The second point is that the patient must remain in bed for a little time, and use the bed-pan and the urine-bottle, in order to give the bowels as much rest as possible, and warm water must be used in sponging.

3. SUITABLE CLOTHING.—The underclothes and pyjamas should be of wool or flannel, in order to avoid chills.

4. REMOVAL OF FERMENTING BOWEL CONTENTS.—The treatment should begin with a dose of castor oil, to remove the fermenting contents of the bowel.

5. DIET.—The various diets advised may be arranged as follows:—

(*a*) The milk diet.
(*b*) The milk and fruit diet.
(*c*) The fruit diet.
(*d*) The meat diet.
(*e*) The meat and milk diet.

(*a*) *Milk Diet.*—The real basis of the treatment of sprue at present is the milk diet.

In the tropics, this milk should be obtained from a cow kept for the purpose or from some really reliable dairy, as the danger of contamination is great. Even when the cow belongs to the patient, great care has to be taken that the milk is not adulterated by the household servants. We can never forget that once the milk of a peculiarly careful household, collected, apparently, under strict precautions, was found on analysis to be grossly adulterated.

The lesson we have drawn from the above is to get a sample analyzed from time to time. This analysis costs but little, and the possibility of its being carried out at any time puts a certain amount of restraint upon would-be adulterators.

There is a considerable difference between the average composition of the milk supplied by *Bos taurus*, the straight-backed cow, and *B. indicus*, the hump-backed cow, which, in general terms, may be summarized by saying that the milk of the latter is much richer than that of the former. We have investigated this point, and are of the opinion that if 3 per cent. of fat is considered to be an average for *B. taurus*, then 5 per cent. should be reckoned for *B. indicus*.

In placing a patient upon a milk diet, the composition of the milk should be carefully considered, especially as regards the fat, for, as Harley and Goodbody have shown, no less than 47 per cent. of the milk-fat is passed out in the fæces.

Milk with high percentages of fat should, therefore, be diluted with whey, when the amount of nitrogen will be kept up, while the percentage of fat is diminished. Whey is easily made in the tropics by means of the juice of limes.

Preferably the milk should not be boiled or sterilized, but boiling, apparently, does not interfere with its beneficial properties, and, therefore, if desired or thought necessary—*i.e.*, owing to the risk of typhoid—there is no harm in so doing. In cold weather it should be warmed before being taken. It can be aerated in a seltzogene if desired, and can be mixed with Vichy water. Finally, it must be remembered that milk is not a perfect food for an adult, however suitable it may be for a child.

It is as well to begin with a small quantity, and gradually to increase the amount. Every medical man sooner or later adopts his own method of carrying this out, and we will, therefore, only give general directions. If the case is very severe, with vomiting and much diarrhœa, it is as well to begin with whey only, which the patient should sip slowly, and practically *ad libitum*—*i.e.*, about 7 to 8 pints per diem. As soon as the urgent symptoms are relieved, milk must be added to the diet, as whey alone is starvation.

If the case is of moderate severity, milk can be begun at once, 3 pints per diem being given in the more severe, and 4 pints in the less severe cases—*i.e.*, 60 to 80 ounces—which should be divided into not less than ten meals at regular intervals during the day. The milk must be slowly sipped or taken through a glass tube, which, of course, should be carefully boiled after each meal. On no account must the patient be allowed to drink the milk in gulps. It is, perhaps, as well to define a limit of time—say about twenty minutes—as the minimum time for a meal.

If the symptoms improve, it is necessary to increase the milk gradually every few days until 6 to 7 pints—*i.e.*, 120 to 140 ounces—are given: but in doing this, it is better to increase the number of meals rather than the quantity at a given meal. Twelve meals in the twenty-four hours are not difficult to arrange.

If the symptoms do not improve, the milk must be reduced gradually, or whey must be tried; but as soon as the urgent symptoms of diarrhœa and vomiting abate, the milk must be gradually increased, and, indeed, the starvation must not be long continued in any case. Starvation diets are dangerous in severe cases, when the patients are emaciated and weak; and hence, while they are being employed, great care is required in nursing.

If the milk is succeeding, the diarrhœa ceases, the mouth troubles diminish, and the patient feels better. The fæces will at first be pale and grey, but, as improvement continues, stercobilin will appear, as evinced by the brown colour. This change in the colour of the fæces is a most important sign.

But even if milk is agreeing with the patient, there will be much trouble, as there is often strong objection to milk only. Another difficulty is constipation, and this must be relieved by enemata. Sometimes the milk does not agree, causing vomiting and pain. Usually this can be relieved by alkalinizing the milk with bicarbonate, 1 grain to the ounce, or the citrate of soda, 2 grains to the ounce of milk (convenient tabloids of this salt are prepared by Burroughs Wellcome and Co.), or by adding Apollinaris or Ems water in the proportion of equal parts, or lime-water, 1 to 6 of milk. As soon as a definite improvement appears, and the weight begins to increase, the patient should be allowed to sit up, but great care must be taken to avoid chills. Milk diet should be persisted in for a month or six weeks, but may be modified by the addition of fruit —*e.g.*, strawberries, bananas, or apples—as will be described later.

Then eggs may be beaten up in the milk: chicken-broth can be tried: then Benger's food, or some other simple food—Allen and Hanbury's, Mellin's, Albany food, Carnrick's soluble food, Sanatogen, or Plasmon. Then fish, chicken, or sweetbreads, with a biscuit, and, later, potatoes; and finally, the patient is put on to a diet of eggs, toast, dilute China tea, soups, white meats, custard-puddings, milk. But he must avoid dark meats, most vegetables, spiced foods, iced drinks, and all indigestible substances. Alcoholic drinks in every form are bad, both during the illness and afterwards. Nor is smoking to be encouraged: we, personally, are much against it.

But, unfortunately, a case of sprue is not so easy to treat as indicated above, for, while the food is being gradually and carefully increased, relapses are not infrequent, and a return to milk may be necessitated. The patient gets weary, and at times exceedingly angry about this dieting, and, indeed, is apt surreptitiously to kick over the traces, with disastrous results. The prohibition of alcohol also leads to trouble, but our experience about this is quite clear: if alcohol is taken, the progress of the patient is seriously hindered.

Before leaving the milk diet, two points ought to be mentioned, concerning one of which we have had considerable experience; concerning the other, none at all. First of all, there can be no reasonable doubt as to the advantages of liver soup—*i.e.*, soup prepared from calves' or sheep's livers—in the milder cases of sprue, or in the return to ordinary food of a severe case. The liver treatment is really an old native remedy in Ceylon. We do not profess to advance views as to its action, but in a certain class of cases it is of benefit. Secondly, gall-pills or inspissated bile, as suggested by C. J. Martin, and pancreatic preparations have been advocated by some: but of these we have no experience.

(*b*) *Milk and Fruit Diet.*—A milk and fruit diet has been found to be even better than a pure milk diet in many cases. The milk is administered as already described, but, in addition, fruit is given. Strawberries are most highly recommended, beginning with ¾ pound and gradually increasing to 2½ pounds per diem. They should be crushed, and eaten with sugar and cream. In lieu of strawberries, bananas (not plantains, though people often call bananas plantains, the difference being that a banana shows three cells on transverse section and a plantain five), pears, grapes, in the same weight as the strawberries or apples, from ½ pound to 1½ pounds per diem. If these cannot be obtained, the juice of oranges, papaya (1½ pounds per diem), avocado pears, mangosteens, and sapodilla, may be used.

Fresh Bael fruit is excellent, but must be carefully prepared. It may be boiled in water and then cut open and shredded by means of a fork into warm milk, in which it is pounded with castor-sugar, and finally strained through a fine strainer to remove all débris. This should be used three times a day. Preserved fruit is said to be useful, if fresh fruit cannot be obtained. Acid fruits, such as pineapples and sour-sops, should be avoided, and, personally, we do not advise the use of mangoes.

(*c*) *Fruit Diet.*—This was first advocated by Van der Burg, and usually consists of grapes and pears; but it appears as though almost any fruit which is not acid might be used.

(*d*) *Meat Diet.*—If the milk or fruit diets fail, it is advisable to try a meat diet, or this may be made the basis of treatment from the beginning. Cantlie is the great supporter of this dietary.

If the patient is very ill, it may be necessary to begin with raw-meat juice prepared by pounding sufficient good raw flesh in a mortar, so that, with the addition of 2 ounces of water and 20 minims of dilute hydrochloric acid, 6 ounces of meat-juice is obtained on straining. The quantity of meat required to obtain these 6 ounces will sometimes be quite considerable, and, as it varies in different regions, must be obtained by preliminary experiment. A little salt should be added to this juice, and 1 teaspoonful should be given every quarter of an hour in very bad cases, and rapidly increased in amount if successful.

As soon as the very serious symptoms subside, the meat diet should be started. Brown gives the following directions for preparing a meat diet: Take 2 pounds of good raw meat, free from fibrous matter, fat, and gristle, and 2 ounces of fresh suet, and mince and pound them up thoroughly. Sprinkle the pounded mass with a little salt, and divide into six portions. One portion, cooked in a small, well-buttered saucepan until the red colour has just disappeared, is given six times a day, as convenient. This portion, when cooked, is estimated as weighing 4 ounces. In addition, ½ pint of plain warm water, rice or toast water, is sipped half an hour before a meat meal, and a little tea, with lemon-juice instead of milk, taken twice daily. It may, perhaps, be as well to remind the reader that rice-water is an infusion of roasted rice.

In about a week this meat diet should be changed to a modified meat diet, which is first produced by the addition of fruit, followed in a little time by chicken, then and gradually by eggs, biscuits, and fish, until the dietary already mentioned under Milk is reached.

With a modified meat diet some people combine curdled milk. This is based upon Metchnikoff's researches, which showed that if the *Bacillus acidi lactici* is taken with milk, it generates large quantities of lactic acid in the intestines, particularly in the large bowel, and that this acid interferes with intestinal toxins. Various preparations of the germ have been placed on the market, including 'Sauerin' made by Messrs. Allen and Hanbury, and said to be a pure culture of the germ. Brown gives the following directions for its use: 2 pints of milk are heated to 100° F., to kill off any bacteria which might happen to be present, and then are allowed to cool in a jug which has been boiled. When 100° F. is reached, 6 tablets of Sauerin are added, and 2 tablespoonfuls of sugar, when the milk is curdled in about three hours. This curdled milk is taken four times a day, between the meals of a modified meat diet, and is said to be efficacious.

It may be mentioned that curdled buffalo-milk is commonly used by the natives of Ceylon as a part of their food, and curdled milk is also used in India, and, indeed, in many other places by natives

Under the heading of Meat Diets must be placed Cantlie's treatment, which consists of putting the patient to bed, applying a hot wet pack from the nipples to the groin for two hours, morning and evening, and giving three meals of 5 ounces of meat per diem, and, in addition, either beef tea, beef-jelly, calves'-foot jelly, or a plain jelly every two hours. Castor oil is administered in 1½-drachm doses every morning for the first three days, and santonin in 3-grain doses morning and evening for three days. Strawberries, to the quantity of 3 to 4 pounds per diem, are also allowed between meals. When the stools become solid, and show brown colouring matter, a poached egg and pounded chicken are added, and, later, minced chicken, and, still later, the undercut of meat, with stewed celery, seakale, vegetable marrow, pulled bread, and thin slices of bread, baked in an oven for twenty minutes.

(*c*) *Meat and Milk Diet* Cantlie now advocates that when a patient is on a meat diet, this should be stopped every third or fourth day for twenty-four hours, and that milk only be given during this period.

6. MEDICAL TREATMENT. It may be said at once that astringents as a rule are dangerous, and that antiseptics are not useful.

Santonin, which must be yellow, has been strongly recommended by Begg, who gives 5 grains night and morning in salad oil, but we have seen no benefit by this treatment. Mixtures containing bicarbonate of soda are often useful.

People complain that yellow santonin cannot be obtained, but it can be easily prepared from white santonin by exposure to the sun for a few days. The crystals are turned from time to time until yellow throughout, as demonstrated by crushing. The chromosantonin of Monte-Martini is not santonin, which, according to Lestini, is changed into formic acid and photosantonin acid and a red resinous substance Peter Sys's remedy, which is much used in China, is simply powdered cuttle-fish bone.

Cantlie has had good results by the administration of 20 grains of ipecacuanha daily for two or three days in advanced cases, and emetin has been administered by several authors. Schmidt has used oxygen introduced *per rectum*, ½ to 1 litre weekly.

Castellani has obtained in some cases a remarkable improvement by giving massive doses of bicarbonate of soda.

The mouth may be treated with any appropriate mouth-wash—*e.g.*, glyco-thymoline, glycerine and borax, diluted liquor aluminis, etc. The teeth require attention, and, if there is any pyorrhœa, this should at once be treated by syringing or spraying between the teeth with peroxide of hydrogen solution. Pain may be relieved by painting the raw surfaces with 1 to 5 per cent. solution of cocaine, novocain, alypin, or stovain. The pain along the œsophagus requires morphia. Janowski recommends 5 to 10 drops of a solution of 1 in 1,000 adrenalin, which, he says, gives prompt and permanent relief for œsophagitis. The muscular pains may be relieved by massage, or by pilocarpine nitrate, given in $\frac{1}{10}$ to $\frac{1}{8}$ grain doses three times a day. Intestinal pain may be relieved by hot packs, as recommended by Cantlie. Acute diarrhœa must be checked by a dose of liquor opii sedativus or lead and opium pills. Dysenteric symptoms must be treated as described under Dysentery.

7. CHANGE OF CLIMATE.—It is obvious that, if possible, the patient should be transferred from the tropics to the temperate zone, but only if he is strong enough to travel. There is no advantage in putting him on board a ship in such a condition that he will probably die when changing from the warm to cooler weather. Personally, we are not in favour of a patient being sent from the low country to the hills. If he is able to travel, let him go to the temperate zone.

VACCINE TREATMENT. —Vaccines have been prepared with various bacteria from the mouth, and Rogers and Nicholls report very encouraging results by the use of streptococcal vaccines prepared with streptococci isolated from the mouth lesions. Monilia vaccines have been used by Ashford, Michel, Taylor, and others, who claim satisfactory results.

Prophylaxis.—Nothing of any practical value can be said under this heading.

PSEUDO-SPRUE.

One of us has called attention to some cases presenting clinical symptoms closely allied to sprue and due to bacilli of the Flexner group. Such cases have no dysenteric symptoms, but present the white frothy motions, the sore tongue, and the anæmia as found in typical sprue, but in contrast to this disease they may recover without any change from the tropics, and a vaccine treatment is very useful.

Motility.	*Litmus Milk.*	*Lactose.*	*Saccharose.*	*Dulcite.*	*Mannite.*	*Glucose.*	*Maltose.*	*Dextrin.*	*Raffinose.*	*Arabinose.*	*Adonite.*	*Inulin.*	*Sorbite.*	*Galactose.*	*Lævulose.*
o	A	o	o	o	A	A	A	A	A	A	o	o	o	A	A

Si	*Amygdalin.*	*Isodulcite.*	*Erythrite.*	*Glycerine.*	*Indol.*	*Voges-Prosk.*	*Redn. Nitrates.*	*Neutral Red.*	*Gram.*	*Gelatine.*	*Serum.*	*Broth.*	*Pept. Water.*
	o	A	o	As*	+s	o	o	o	o	o	o	G.T.	G.T

Abbreviations.—A, acid; G.T., general turbidity; s, slight; o, negative result—viz., neither acid nor gas in sugar media, non-motile, non-liquefaction of gelatine or serum, as the case may be.

*** Certain strains are distinctly acid on ninth day.**

The Flexner-like bacillus found in these cases is identical with the typical Flexner, but for the fact that litmus milk was rendered permanently acid instead of the medium becoming first acid and then alkaline. Minor differences with regard to some sugar broths may occasionally also be noted.

HILL DIARRHŒA.

Definition.—Hill diarrhœa is a gastro-intestinal catarrh of unknown cause, occurring mostly at high altitudes in tropical regions, and characterized by the passage of several liquid, frothy, light-coloured motions in the early morning.

History.—Hill diarrhœa was first described by Grant in 1854, in the same paper as that in which he dealt with sprue and dysentery, and later as a disease quite distinct from sprue by Crombie in 1892. The latter writer held that it was liable to occur at an elevation of 6,000 or more feet in India, Europe, and elsewhere. In India he believed the monsoon to be a potent factor, associated, probably, with a diminished barometric pressure. We have seen cases in Ceylon occurring at a much less elevation—for example, at about 3,000 to 4,000 feet.

More recently Duncan has put forward the view that mica in the water is the causative agent. This mica is found in the laterite—*i.e.*, weathered gneiss—which is a common geological formation in the tropics. Singer considers that he has met this disease in four out of six Europeans on an expedition to Abyssinia, when they reached a height of about 5,000 feet.

Ætiology.—The causation of the disease is quite unknown. The theories are:—Diminished atmospheric pressure, the irritation of mica, fæcal contamination of the water, and exposure to cold.

Pathology.—Very little can be said under this heading, except to invite attention to what has already been written under the heading of Sprue with regard to the formation of leuco-urobilin, and to point out that it is obviously to the formation of this body, and not to anything wrong with the liver, that the colour of the motion is due. The morbid anatomy would appear to be totally different from that of sprue, and to be a congestion of the mucosæ of the stomach and bowels, with a proliferation of the mucosal lymph and fibrous tissue in chronic cases. On the surface of the mucous membrane of the small and large bowels there is a thick layer of mucus, but no ulceration.

Symptomatology.—The disease generally begins soon after the patient has arrived in the hills from the plains.

The onset is sudden, beginning with abdominal pain in the early hours of the morning, with the passage of large, frothy, greyish or whitish motions, which produce a sense of relief. The patient goes about his work, but in the early hours of the next morning the symptoms are repeated, and he will complain that his stomach feels blown out, and that he can hear gurgles, and this goes on morning after morning.

If now the patient leaves the hills and comes down to the plains to consult a doctor, he is astonished to find that he is quite well. and perhaps goes back to the hills without having obtained the medical advice which he desired. A relapse takes place, for which he does not as a rule seek advice, as he considers it a trivial complaint, until later he begins to feel dyspeptic, disinclined for his food or work, and now he will seek treatment, notwithstanding the fact that he feels better on returning to the plains. The disease may become chronic, and rarely may lead to a fatal result.

Sequela.—It is said that neglected hill diarrhœa may develop into sprue.

Diagnosis.—The history of the case and the absence of mouth symptoms are sufficient to enable the diagnosis as a rule to be made from sprue.

Prognosis.—The prognosis is good, as recovery is generally quick under suitable treatment, but in certain cases it is found necessary to abandon residence at high elevations.

Treatment.—The treatment is simple and effective. It consists in rest in bed, warm clothing, and ½ to 1 drachm of liquor hydrargyri perchloridi, given fifteen minutes before each meal, and 12 to 15 grains of pepsin, ingluvin, or lactopeptin two hours after the meal. The diet is to be milk, which may be diluted as advised in the treatment of sprue.

Prophylaxis.—Persons liable to the disease should avoid the hills, especially in the monsoon season, and if compelled to go to high altitudes should do so by easy stages.

LOW-COUNTRY MORNING DIARRHŒA.

This affection, described by Castellani, is common in Ceylon, and somewhat resembles hill diarrhœa, but is found in the plains.

Symptomatology.—The patient wakes up about 3 to 4 a.m. with an urgent call to evacuate the bowels, but there is no abdominal pain or straining. After an interval of one to two hours the bowels are again evacuated, and perhaps again two or three more times in the course of the morning. The motions are liquid, generally yellowish or brownish, and do not contain blood or mucus. The condition lasts as a rule for months, but usually ceases on a change of climate.

Treatment.—A dose of tannalbin (gr. xv.-xxx.) or bismuth subnitrate (gr. xv.-xxx.) may be given at bedtime as a palliative.

FLAGELLATE DIARRHŒA.

Definition.—Flagellate diarrhœa is an acute or chronic diarrhœa due to infections of the intestine with *Oicomonas hominis* (Davaine, 1854), *Chilomastix mesnili* (Wenyon, 1910), *Giardia intestinalis* (Lambl, 1859), and *Enteromonas hominis* da Fonseca, 1915, and other flagellates.

History.—From the days of Davaine, observers have from time to time drawn attention to cases of diarrhœa or enteritis thought to be caused by these parasites—*e.g.*, Roos, Epstein, Castellani, Nattan-Larrier, Brumpt, da Fonseca, Chalmers and Pekkola, Escomel, Paranhos, etc.

On the other hand, of late years a number of observers—*e.g.*, Wenyon and O'Connor—do not believe in the pathogenic action of these germs. It is quite true that flagellates may be aerial contaminations of fæces, and that others may perhaps be non-pathogenic. Still, in our opinion, when these parasites are very numerous there can be no doubt that they can and do cause irritation of the bowel and diarrhœa. It is equally true that they can live in considerable numbers in man's intestine without causing diarrhœa, but such a person, in our belief, is a carrier.

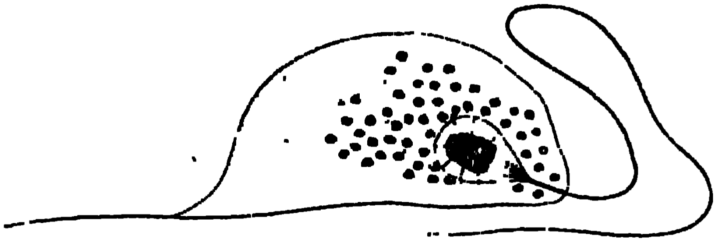

FIG. 759.—*Cercomonas longicauda* DAVAINE.

(After Wenyon and O'Connor, from the publications of the Wellcome Bureau of Scientific Research.)

Climatology.—The flagellates and their associated diarrhœas are to be found in temperate and tropical climes. They are common in Ceylon, the Anglo-Egyptian Sudan, the Balkans, and Brazil, but have been reported from many parts of Africa, Asia, and America.

Ætiology.—It is difficult to prove that the flagellate is the cause of the diarrhœa, but if one of these organisms is present in very large numbers in a case, if bacteriological research fails to demonstrate any pathogenic bacteria, and no other cause can be found, it may be provisionally admitted that they are causal. If the causal organism is killed off and the diarrhœa ceases *pari passu* with this process, and does not return, and the flagellate is either absent or only present in small numbers, the first assumption receives support, but beyond this we cannot at present go.

The difficulty is that the numbers of the parasites wax and wane in the carrier without producing symptoms, but when present in large numbers they are generally associated with diarrhœa. Infection may be by the cysts passing into the alimentary canal of flies, and so to human food, but perhaps it may take place more directly at times. We have never seen them cause true dysenteric symptoms.

From certain experiments carried out by Miss Porter, it would seem that cockroaches may play a rôle as transmitters of flagellate diarrhœas of man. This observer succeeded in transmitting Giardia, Trichomonas and Chilomastix of human origin to clean white rats by allowing their food to be contaminated with the excrement of cockroaches (*Periplaneta americana* and *P. orientalis*) which had fed on infected stools.

FIG. 759A.—CYST OF *Giardia intestinalis* IN FRESH CONDITION IN HUMAN FÆCES.

(Photomicrograph, × 70 diameters.)

Symptomatology.—When in small numbers there may be no symptoms, or the only symptoms are those of diarrhœa, with liquid brown motions, containing yellow flakes, which are composed of epithelial cells and leucocytes, around which the parasites are formed in large numbers.

Treatment.—This is not very satisfactory. It is easy in most cases to stop the diarrhœa by giving a small dose of castor oil followed after some hours by the administration of astringents such as tannalbin and salol in large doses, but it is most difficult to obtain a complete disappearance of the parasites. Methylene blue acts fairly well on flagellates of the genera Cercomonas, Oicomonas, Trichomonas and Chilomastix, but has practically no action on Giardia (Lamblia). It is given in 1 or 2 grain doses twice daily in cachets or gelatine capsules, and in addition enemata of 3 pints of 1 in 3,000 solution of methylene blue may be given twice daily. The patient should be told that the urine will become blue, otherwise he will be much alarmed.

Another method of treatment is to administer calomel at night, a saline purgative in the morning, and during the day powders or cachets of salol combined with bicarbonate of soda. This is done for several days, while the patients are kept on a restricted diet and the motions carefully examined daily for the flagellate. Iodine solution (1 : 1,000) by rectal injection has been recommended by Escomel, but is painful.

Thymol, turpentine, etc., have also been recommended, but these various methods of treatment do not induce a complete disappearance of Lamblia infections.

Prophylaxis.—This consists in preventing flies and cockroaches from access to food by keeping kitchens and outhouses, and all the immediate surroundings of a house, in a good sanitary condition. Kitchens may be wire-netted and fly-traps may be provided both inside the kitchen and outside. Balfour says that 'chicken entrails' are the best baits for large fly-traps situate in the open air The flies may be killed after being caught by means of a daisy killer or any other smoke apparatus.

All fly-breeding places should be destroyed by the removal of the dirt and the digging up and disinfection of the ground.

FIG. 760.—SERBIAN SOLDIER SUFFERING FROM THE EFFECT OF FAMINE DIARRHŒA AFTER THE ALBANIAN RETREAT.

FAMINE DIARRHŒA.

Historical and Geographical.—This condition has been observed in India during periods of famine, and recently by us in the Balkans, in Serbian and Montenegrin troops after the retreat through Albania.

Ætiology.—Bad, insufficient food and extreme fatigue play a very important rôle in the causation. No specific germ has been found.

Symptomatology.—The patient is extremely weak and terribly wasted, though the abdomen may at times be prominent and distended. He may feel famished, but when given food can take very little of it, and cannot digest it. He complains of slight abdominal pains and has diarrhœa; the motions may not be very numerous; they are liquid, of fæcaloid or at times greenish colour, with some mucus, but no blood. The condition lasts usually between a couple of weeks and one to two months, and often terminates fatally.

Diagnosis.—This is based on the history of starvation and extreme fatigue, with diarrhœa without blood, while the patient wastes horribly in a short time, and there are no signs of tuberculosis. It may be differentiated from dysentery by the stools not containing blood, and by the absence of dysenteric germs; from cholera by the longer course and absence of cholera and para-cholera germs.

Prognosis.—This is serious, many cases terminating fatally.

Treatment.—This is very unsatisfactory. Astringents such as bismuth subnitrate, etc., even when given in massive doses, may not stop the diarrhœa; at times they may check it, but the patient continues to become weaker and weaker, and often dies.

CŒLIAC DISEASE.

Gee described in England, in 1888, an infantile affection characterized by its long course, anæmia, great wasting, and pale greyish abundant stools. Cases are not very rare in Great Britain, and have been reported also from other countries. The ætiology is unknown, though various germs have been found. In three cases Nabarro has carried out a very complete investigation, and has isolated from the fæces a dysenteric bacillus of the Flexner type. This result would suggest that the condition might perhaps be ætiologically related to the so-called pseudo sprue of the tropics, described by one of us.

In cœliac disease the tongue apparently does not become affected, and this and also the fact that it is found in children rather than in adults differentiates the malady from tropical sprue.

The treatment consists in very careful dieting. Fresh cow milk should be prohibited, and dried milk given instead, using one of the preparations on the market which contain only a very low proportion of fat. Condensed milk may also be used, but is generally less successful than dried milk. A fruit diet, in contrast to what one sees in true sprue, is badly tolerated, and should never be ordered. As regards drugs, Still's mixture is often found useful:

Ol. ricini	♏v.
Salol	gr. 1½.
Spir. chlorof.	♏i.
Muc. acaciæ	♏xv.
Aq. anethi	ad ℥i.

Ter die.

Occasionally silver nitrate is valuable when the diarrhœa is very marked, and Still recommends it to be given thus:—

Arg. nitratis	gr. ⅛.
Glycerini	♏v.
Aq. dest.	ad ℥i.

Ter die.

Bismuth preparations are practically useless, but tannalbin has at times a favourable action.

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CHAPTER LXXVII

THE CHOLERAS

Cholera —Synonyms—Definition—History, Geography, and Epidemiology—Ætiology—Pathology—Symptomatology—Diagnosis—Prognosis—Treatment—Prophylaxis—*Paracholera*—*Pseudocholera*—References.

CHOLERA.

Synonyms.—Cholera Asiatica. *Hindustani:* Haiza. *Tamil:* Enerum Vandec. *Chinese*. Ho-louan. *Arabic:* Duba.

Definition.—Cholera is an acute specific endemic or epidemic disease caused by *Vibrio choleræ* Koch, 1883, and characterized by violent purging, vomiting, muscular cramps, suppression of urine, and collapse.

Remarks.—There is little doubt that in the past the term 'cholera'—in analogy to other diseases—has been used to cover a group of clinically similar affections caused by closely allied germs. See remarks on paracholera, p. 1819.

History, Geography, and Epidemiology.—Cholera appears to have been known in India from the most ancient times, for Charaka and Susruta describe symptoms which most probably refer to this disease. The name is of Greek origin, being perhaps derived from χολέρα, a spout, which may have been applied with the idea that the violent purging resembled the water rushing out of a spout. Apart from the two authors mentioned above, the earliest record of the disease is found in 1438, when Ahmed Shah's army is said to have been decimated by it. After this date there are several references, for it is mentioned by Vasco da Gama in 1490; an account is given of an outbreak in Goa in 1543, another in Pondicherry in 1768, and another in Calcutta in 1781-82, the last of which appears to have spread to Madras, Ceylon, and Burma in 1782-83. Outbreaks occurred in Travancore in 1792, and in the Mahratta country in 1794. But these are only a few of the recorded outbreaks, for, according to Macnamara, no less than sixty-six separate observers mention the disease between the years 1438 and 1817.

With regard to Europe, cholera was recorded at Nismes in 1564, but it and the sporadic outbursts in the seventeenth century may not have been true cholera. It also appears to have been endemic in Java as far back as 1629, and occurs yearly in Southern China and the Philippine Islands.

In 1817 began an epidemic which may have originated in Calcutta or in Jessore, and which lasted till 1823. During this time it spread to the west coast of India, Arabia, Ceylon, Burma, Malacca, Penang, Singapore, and Manilla, reaching Mauritius in 1819 and China in 1820. This is certainly the first extensive epidemic ever recorded outside India. In 1826 the first pandemic, which lasted till 1837, and spread into Europe, Africa, and America, began in India, through which it spread slowly, and then passed to Europe and Africa by three routes, the first and earliest via Kabul, Bokhara, and Khiva to the Russian province of Orenburg, which was reached in 1829. The second route was through Persia, Tabriz, and Tiflis, to Astrakhan in 1830. In this year the two routes met at Nijni-Novgorod, where there is an annual peasant gathering. These peasants, on returning home, infected Moscow, and as there were military operations proceeding in Poland, the disease rapidly spread through Western Russia into Poland, and on to Germany, Austria, Sweden, and England. In 1831 France became infected, and from 1832-33 the whole of Europe was ravaged, and the disease spread to the United States, Mexico, Cuba, and Guiana, and even to Australia. In the meanwhile the epidemic had spread by the third route from Bombay to Arabia in 1826, and then to Syria, Turkey, Egypt, and finally to North Africa in 1834, after which it died down.

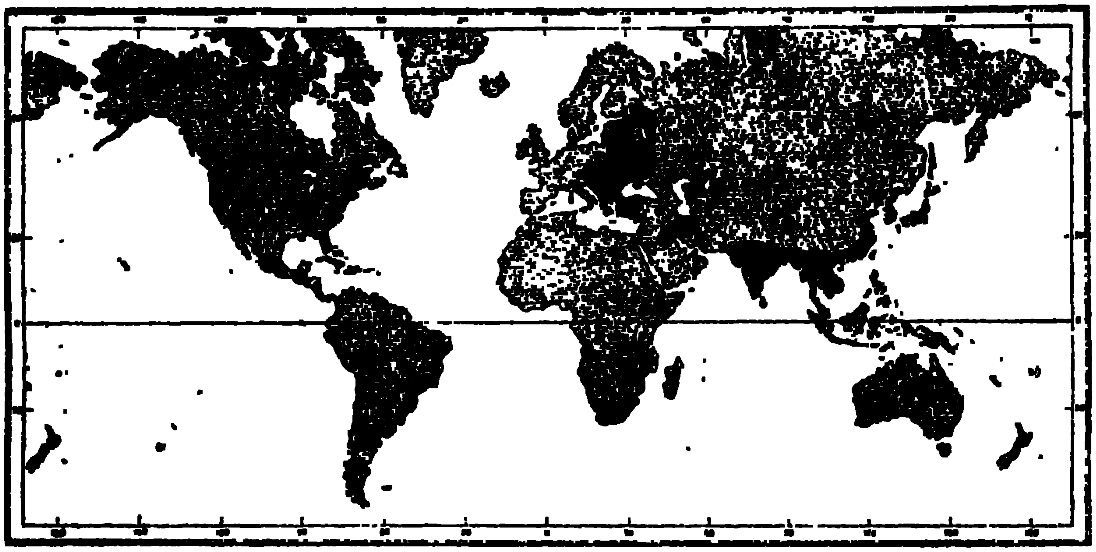

FIG. 761.—DISTRIBUTION OF CHOLERA IN 1915.

In 1840 troops were collected together in India for service in China, and as they travelled eastwards they carried the cholera, which was present in Bengal and Madras, to Malacca and China, in which country it was very prevalent in 1841, and through which it spread, reaching Northern Burma in 1842. It now proceeded north of the Himalayas, reaching Yarkand, from whence it passed to Bokhara and Afghanistan, and spread into the Punjaub and the North-West Provinces in 1844, and into Persia in 1845, when it again travelled via Tabriz and Derbend to Orenburg in 1847, and so to Europe and America in 1848. In this year it was very prevalent in India, spreading again from Bombay to Arabia in 1851, and to Turkey in 1853; while it also again travelled via Persia to Russia in 1852, and so over Europe. This epidemic lasted till 1857, and affected the troops engaged in the Crimean War.

The fourth extensive epidemic began in 1863, and spread to Europe by the two usual routes—viz., via Persia and Arabia—and lasted till 1875, extending as usual to America.

The fifth epidemic began in 1879, when the disease passed from Mecca to Egypt, and so to Europe. It was during this epidemic that Koch discovered the *Vibrio choleræ* in Egypt in 1883.

The sixth epidemic (1891-96) appears to owe its origin in India to the great bathing festival at Karagola, on the Ganges, which, being only held once in thirty years, came as a surprise to the officials, who were not prepared for it. Cholera broke out among the pilgrims on February 8, 1891, and spread rapidly, reaching Europe in 1892.

The seventh epidemic began in 1900, and may be said to be continuing at the present time. It started in 1900 in India after a severe famine, and spread extensively through that country, and then began to travel, reaching Japan in 1901; Arabia, Mecca and Jeddah, Egypt and Erythræa, Syria, Persia, and the Philippines in 1902; Palestine, Asia Minor, and Mesopotamia in 1903; Persia, Russia, and Turkey in Asia in 1904; Russia, Germany, and the Philippine Islands in 1905; Russia (few cases), Burma, Siam, Singapore, Japan, China, and the Philippine Islands in 1906; Ceylon, Peshawar, Singapore, Philippines, Japan, Korea, Manchuria, China, Russia, Turkey, and Persia in 1907; China, Russia, Mecca, and Medina in 1908; and Russia in the beginning of 1909. In 1910 it was present in Russia and Italy. In 1911 it was recognized in Turkey, Roumania, Hungary, Austria, Italy, and Russia, and in 1912 in Turkey, Italy, and Russia.

In 1914 the Dutch East Indies were attacked, and during the war the Austrian Army and civil population were attacked, especially in Galicia, as well as Bulgaria and Greece, while Turkey has also suffered. In 1915 Brčka, in Northern Bosnia, was infected.

Some places have always so far escaped the visitation of cholera. These are either situated in the colder regions, of which the climatic conditions are unsuitable for the propagation of the disease, or are islands to which the disease is less likely to be brought, or where precautions are taken. As examples of these islands may be mentioned the Andaman and Pacific Islands, Réunion, the Azores, etc. Tropical and Southern Africa have not yet been infected.

The climatic influences which appear to favour the development of the disease are low-lying areas, and soils easily permeable to water, especially if they are polluted with decomposing matter. It would, however, appear that the most inimical climatic conditions can be overcome if there is lack of cleanliness, especially with regard to drinking-water and food, together with bad sanitation, and the disease may spread where every climatic influence is opposed to it. With regard to the use of permanganate of potash in cholera, it was recommended in 1866 by Everest, who treated seventeen cases with Condy's fluid, with only one death. Dr. Mackie in the same year treated six cases similarly without a death. In 1884 J. W. Fry stated that the only thing he found of remedial use was an enema of diluted Condy's fluid. In 1910 Rogers reported favourably of the use of the permanganates given liberally in cholera. In 1913 Castellani definitely separated the condition which he called paracholera, from cholera.

Ætiology---*The Vibrio.*- The cause of the disease is undoubtedly Koch's vibrio (p. 962); still, this alone may not produce illness, for, as Dunbar showed in 1892 in Hamburg, people who had never suffered from the disease, and who were in good health, might still be passing quantities of the virulent micro-organisms in their fæces. It is evident, therefore, that these persons lacked some predisposing condition, and, further, that they must have been a fruitful source of infection. What this condition may be we do not definitely know, but it would appear that such factors, as mental worry, underfeeding, and any slight disorder, but specially any derangement of the alimentary canal producing diarrhœa, are predisposing causes. With regard to these causes, it may be mentioned that unripe fruit, and especially melons, are regarded with suspicion in times of epidemics, probably because ey cause diarrhœa, and thus predispose to the disease.

It may be that the vibrio merely live in the en of the bowel in the cases in which it causes no symptoms, d only gains access to the epithelial cells and mucosa in cases of wered vitality, and perhaps is only toxic in this situation: but if th is so it still remains to be proved.

This lowered vitality would explain the apparently extraordinary cases which at times appear in gaols when the town is apparently free. The reason may be that short-sentence prisoners are generally on a very low diet, while long-sentence prisoners often have such hard manual labour to perform that they are exhausted at night. Therefore, if a carrier is introduced into a gaol, the disease may easily start apparently *de novo* among incarcerated inmates.

The disease is communicable directly from man to man by contamination. As an example from our own experience, a medical man examines a patient suffering from cholera, and then proceeds to have his lunch, with the result that both patient and doctor were dead within twenty-four hours of cholera. Again, there is the chance of infection from dead bodies in performing autopsies, but graveyards are not important means of dissemination of the disease, because the germ rapidly disappears from the dead body. Fomites may also spread the contamination, but these are not the usual method of infection, which is generally by water. The vibrios pass out with the fæces, in which they are capable of living a long time (163 days); hence the great danger of fæcally contaminated fields, rubbish-heaps, gardens, etc.; for if there is a poor sanitary system in the place, and if fæcal pollution of the drinking-water is possible, the disease may easily become epidemic, for it has been shown that the vibrios can not merely live, but multiply, in water, though the conditions under which they do this are not perfectly understood.

Two classical instances are usually quoted as evidence of the spread of the disease by water. The first of these is the infection in 1854 of a lady and her servant in Hampstead, where there was no cholera, by drinking the water of the Broad Street well, which was infected, the water being carried all the way from Broad Street to Hampstead because the lady in question had a special liking for it. The second is the infection of Hamburg in 1892 from the waters of the Elbe, in which cholera vibrios were found in the river-water and that of the hydrants.

As water is a method of infection, it is quite easy to understand that milk is specially dangerous, for it is often diluted with water, and, moreover, forms an excellent medium in which the germs can grow. Thus Haffkine and Simpson found that an outbreak of cholera in the Gaya Gaol was due to the contamination of the milk, from which they obtained the vibrio.

The Carrier.—Of great importance in the dissemination of the malady are the so-called vibrio-carriers—viz., persons who, though themselves in good health, still harbour the germ in their intestines, or individuals who continue to harbour the germ for months and years after an attack is over.

Greig has demonstrated that carriers can show an increased titre for the agglutination of the vibrio. His researches also show that the vibrio can live for long in the gall-bladder of animals, and he has also demonstrated it in the human gall-bladder.

The fact that the germs can live for a long time in fæcal matter enables them to infect insects such as flies, and perhaps ants. With regard to flies, the germs have been found not merely on the exterior of the body, but also in the alimentary canal, in which they are believed to multiply. The habits of flies make them, therefore, an important possible means of dissemination of the disease.

Barber, in 1914, brought forward experimental evidence showing that the germ could live for a time in the alimentary canals of *Periplaneta americana* (the cockroach) and *Monomorium latinode* Mayr (the red ant).

Fæcal matter may also pollute green vegetables, for in the East vegetable-gardens are often contaminated with human fæcal matter. The most dangerous vegetables are those which are eaten raw, such as lettuces, watercress, and tomatoes. While, however, the above methods explain many points in the epidemiology of cholera, they do not afford a full explanation of the spread of the disease. As we have already said, the principal endemic centre is Lower Bengal, whence it can spread through India, and, indeed, over the greater part of the world, by human agency and along lines of human intercommunication, but in so doing it may miss places on the direct route of its march. The reason of this is not clear. Certainly climatic conditions may be of importance, and perhaps a low level of the subsoil water and a high earth temperature, together with an imperfect sewage disposal and contaminated source of the drinking-water of the place, may have something to do with this anomaly.

Another point which is by no means understood is the fact that the disease remains for years in the endemic region, and then suddenly spreads in epidemic and pandemic form, extending at times over the whole world.

The ætiology may, therefore, be summarized by saying that the disease is caused by Koch's *Vibrio choleræ* acting in the presence of some unknown bodily condition or conditions, and spread directly from man to man by fomites, water, insects, and food, but the reasons for its endemicity and epidemicity are unknown.

When travelling from one place to another, it always adopts channels of human intercommunication, which may be ships, rivers, roads, or railways. When introduced into a locality, it will give rise to a widespread epidemic if the sanitation is so defective that the germs gain access to the drinking-water, but will be far less extensively spread if due to food or insects, and will be merely sporadic if spread from man to man.

Pathology.—The vibrio grows in the lumen, the glands, the epithelial cells, and the mucosa of the small intestine, probably producing an endocellular toxin, which is set free and causes the symptoms.

The question of toxin formation has, however, been much debated. Thus, in 1905, Brau and Denier considered that they had obtained a soluble toxin. In 1906 Kraus said that he had obtained a soluble toxin which caused the disease, and in the same year MacFadyen obtained a virulent endotoxin. In 1907 Strong carefully investigated the subject, and concluded that he was unable to find a soluble toxin as described above, but that MacFadyen's endotoxin was the true toxin which caused the symptoms in man. This endotoxin causes great gastro-intestinal disturbance, leading to the passage of fluid from the blood to the bowel in the following order: First water, and then inorganic salts, especially sodium chloride; later, phosphates and potassium salts; and still later organic substances. This endosmosis causes a great concentration of the blood, producing a high specific gravity, which may reach 1073 to 1078, which is associated with a great increase in the erythrocytes—8,000,000 per cubic millimetre, according to Rogers and Megaw—with a corresponding increase of the hæmoglobin and of the leucocytes, which may number from 14,000 to 60,000 per cubic millimetre. At the same time the alkalinity of the blood is decreased and its coagulative power altered, while the oxygen contained therein is decreased.

The decrease of the alkalinity of the blood may be very marked in severe cases, and Rogers, Sellards and Shaklu give great importance to this so-called cholera acidosis.

The concentration of the blood causes a fall in the blood-pressure, which is indicated by the feeble compressible pulse, but which, to be studied properly, requires investigation by means of a Riva-Rocci's instrument, as has been done by Rogers and Megaw, who found that in typical collapse the blood-pressure might be only 60 to 50 millimetres of mercury, when the patient is markedly cyanosed and restless. If the case is not so serious, the pressure may be higher—70 to 80 millimetres of mercury—and if the patient is on the road to recovery it may reach to 90 millimetres. As a result of this low blood-pressure, the urine may be suppressed or scanty, with a high specific gravity, albumen, casts, and a large quantity of indican.

The body appears to react to the disease by the pouring out of substances from the blood which are probably bactericidal, though Edwards's attempt to prove this failed because of decomposition and the admixture of other micro-organisms. Agglutinins are absent in fatal cases, but, according to Greig, in non-fatal cases they begin to rise after the sixth day, but drop after the twentieth day.

When recovery is about to take place, the specific gravity of the blood decreases, the blood-pressure rises, and the urine becomes abundant. As convalescence continues, the great danger is secondary infection of the body by other micro-organisms, which may cause serious illness and even death.

It is important to note that Greig has found the germ in the gall-bladder (40-70 per cent. of cases)—where it causes cholecystitis, and in animals may give rise to gall-stones—in the lung, kidney, and urine. According to Violle's researches, bile *in vivo* tends, however, to hinder the development of the cholera vibrio. According to the same author a small dose of cholera toxin excites the secretion of bile while a large dose stops it. It is suggested that a septicæmia takes place, but this has not been demonstrated. Manson suggests that it may pass by the lymph channels.

Danysz regards the disease as of anaphylactic origin.

Morbid Anatomy.—Usually post-mortem rigidity is very well marked, and the body keeps warm for some time after death. On cutting into the tissues, it is noticed that they are very dry, and that the blood is often thick and tarry. On opening the peritoneal cavity, the hand experiences a peculiar sticky sensation not felt in any other disease with which we are acquainted.

The stomach is usually empty, and the bowels are reddish in appearance, with injected vessels. When a piece of small bowel is opened, the contents are usually found to be whitish or greyish grumous material; more rarely will the contents be blood-stained. These contents consist of food particles, epithelial cells, red and white corpuscles, and micro-organisms. When allowed to stand, they separate into liquid and solid portions, the former containing albumen, and having a specific gravity varying from 1005 to 1015. The mucosa of the stomach and bowels is hyperæmic and swollen, and may be marked by ecchymoses. There is usually some enlargement of the solitary and agminated glands, as well as of the mesenteric glands.

The liver is generally congested, and the ducts full of bile; the spleen is shrunken; the kidneys are swollen, and often ecchymotic, with tubules blocked with granular débris and cells in a state of cloudy swelling. The right heart is often dilated, and the whole venous system full of blood, while the arterial system and the left heart is empty. The lungs are collapsed, dry, and anæmic, and the brain may be congested.

Microscopically, the vibrios may be seen in Lieberkühn's follicles in the epithelial cells, and in the mucosa of the intestine and the stomach. The kidney shows vascular congestion and destruction of the epithelium. Usually the vibrios do not penetrate into the blood-stream, and therefore the disease is mainly a general intoxication: but Rebowski records cases in which they have been found in the liver, the kidney, and the heart, thus producing a general infection.

If the post mortem is held on a case which has died during the state of reaction, pneumonia and the signs of other secondary infections may be found.

Symptomatology.—A typical case of cholera has an incubation period which varies from a few hours to a few days (three to six). The onset is usually sudden, but there may be prodromata in the form of diarrhœa, or merely a feeling of illness and malaise. The attack begins with diarrhœa, with or without colicky pains in the abdomen. The motions are at first fæculent, and contain bile, but soon assume the typical rice-water appearance, in which they are fluid and acholic, containing numerous white flakes, which, when examined, are found to be composed of mucus containing vibrios and epithelial cells, while exceptionally the motions contain blood. Vomiting generally appears early, food being first expelled, followed later by a watery fluid, with which bile and occasionally blood may be mixed. The patient complains of thirst, and at times of hiccough. As the purging and vomiting proceed the urine diminishes, and may stop, and fluid departs from the subcutaneous tissues, which therefore contract, so that the facies alters, the nose becoming sharp, the cheek-bones prominent, the eyes sunken, and the skin of the fingers becomes wrinkled like that of a washerwoman. Whilst this is taking place, the circulation becomes profoundly affected, the blood-pressure falls, the pulse becomes weak and rapid, the heart-sounds diminish, and the lips, face, and nails become bluish. The patient now has difficulty with his breathing, and his voice becomes weak and husky. Painful cramps appear in various muscles, but especially in the calf, arm, and abdominal muscles, while the reflexes are diminished. The mind is quite clear, but the patient is apathetic, except when agonized by the cramps. The skin feels cold, and the axillary temperature falls below normal, but that of the rectum may be considerably raised. If no change for the better takes place, the patient passes into the algide stage, in which the failure of the circulation becomes more marked, the pulse almost disappearing at the wrist, the heart becoming weak and irregular, the respirations laboured, the skin cold and deeply cyanosed, the urine suppressed, while the diarrhœa may or may not cease, and the temperature falls far below normal. The first heart-sound becomes impure, or a hæmic systolic murmur may be present, and the second may be faint, and friction-sounds may be heard over both the pericardium and pleura. The patient may now become comatose, and death supervenes in from twelve to thirty-six hours after the onset of the attack. If recovery is to take place, the diarrhœa diminishes, the skin becomes warmer, the pulse and blood-pressure improve, and after a time bile appears in the motions, and the skin fills out with fluid again.

Sometimes convalescence is rapid. In some a secondary febrile condition ensues, which may last for several days, or even for a couple of weeks.

The patient may at times pass into a *status typhosus*, with flushed face, raised temperature, dry brown tongue, low muttering delirium, with subsultus and toxic tremblings and toxic rashes, which may be erythematous, papular, or hæmorrhagic. The urine is diminished in quantity, has a high specific gravity, and contains albumen and casts. The motions are somewhat like those of typhoid, or may be bloody.

Death may take place during this stage from complications, or recovery may ensue after a long convalescence. The infection of the convalescent may be said to have ceased when on three separate days the bacteriological examination of the motions is negative.

The typical course of the disease, as described above, is often arbitrarily subdivided into three stages: (1) The stage of evacuation; (2) the algide stage; and (3) the stage of reaction, when the patient is about to recover.

Varieties.—Cholera cases at times present many varied features, which are usually classified into:—

1. *Ambulatory Cases.*—There are cases in which, without any signs of disease, the vibrio may be obtained from the fæces. These people are genuine carriers of the disease.

2. *Choleraic Diarrhœa.*—Choleraic diarrhœa is characterized by severe purgation, associated with the passage of yellowish motions, which contain the specific vibrio. This condition may be recovered from, or may pass into a typical attack of the disease.

3. *Cholerine.*—The patient is suddenly seized with abdominal pains, and passes numerous fæculent motions, followed by typical rice-water motions, which speedily cease, and the patient quickly recovers without further symptoms.

4. *Cholera Gravis.*—This is the typical form already described.

5. *Cholera Sicca.*—In this type the patient becomes rapidly collapsed, and dies before the typical symptoms of diarrhœa and vomiting can appear. The post-mortem and the bacteriological

examination of the bowel contents reveal the true nature of the disorder.

Complications.—In rare cases hyperpyrexia has been noted during the attack, but usually all the complications occur during the stage of reaction, and are due to secondary infections. The most common are pneumonia, enteritis, and inflammation of the kidney. Pregnant women always abort, and the fœtus may show signs of the disease. The reason of this abortive tendency is, according to Schütz, because cholera has a powerful effect upon even the non-pregnant uterus, causing hæmorrhage during the stage characterized by muscular cramps.

Sequelæ.—After such a severe illness, it is usual to find more or less permanent damage to the health of the victim. Thus anæmia, inflammation of the parotid, gangrene, ulceration of the cornea, astigmatism, or other errors of refraction, a tendency to diarrhœa, and digestive disturbances, may persist for a long time.

Diagnosis.—The diagnosis is easy during an epidemic, but it may be very difficult in the period when there are only a few sporadic cases preceding the outbreak.

So closely may cholera be simulated by ptomaine poisoning as regards the collapse, and by infections with germs of the Aertrycke-Gärtner group, which we have seen produce typical rice-water motions, that it is perfectly useless in a sporadic case to attempt to make an accurate diagnosis without a bacteriological examination, and even this has to be performed with the greatest care, as there are many vibrios which are undistinguishable without special tests from the *Vibrio choleræ* Koch. We recommend the following method:—

1. Make films from the rice-like flakes, and stain with diluted Ziehl carbolic fuchsin (1 in 5 for ten minutes, or with Löffler's blue, five minutes. If a large number of curved rods be present, cholera may be suspected: but a definite diagnosis should never be based on the simple microscopical examination, as comma-like germs are found in many cases of ordinary diarrhœa, and even in normal stools.

2. Inoculate four tubes of peptone water with the suspected stools, the first with ¼ c.c., the second with ½ c.c., the third with 1 c.c., and the fourth with 2 c.c.; or inoculate each of two Erlenmeyer flasks, capped with sterile filter-paper without wool-plugs, with 1 c.c. of the stools. The formation of a scum on the surface of the medium within eight to ten hours is suspicious of cholera. The pellicle and the upper portions of the medium should be examined microscopically for the presence of vibrios, and a microscopical agglutination test carried out, mixing one loopful of the culture with one loopful of diluted cholera serum (1 in 1,000). The peptone water should be tested for the presence of indol, adding a few drops of pure sulphuric acid. In true cholera the indol reaction is generally present eight to ten hours after inoculation. From the pellicle and upper portion of the peptone-water tubes ordinary agar and MacConkey agar plates should be made, and any suspicious

colony developing should be further examined and the germ investigated as regards the following characters:—

(*a*) *Motility.*—The cholera vibrio is very actively motile.

(*b*) *Morphology.*—The cholera organism is often bent, comma-like, but may be straight, bacillus-like.

(*c*) *Agglutination.*—A strong anticholera serum obtained from some well-known laboratory should be used. Any vibrio found in stools which is agglutinated by this serum in a dilution not less than 1 in 2,000 can safely be considered, as a rule, to be the true germ of cholera. In doubtful cases, all the cultural characters should be studied, and Pfeiffer's test and Castellani's absorption test should be carried out.

Dunbar has recommended a special agglutinative test, which consists in mixing directly a drop of the stools with diluted immune serum. The cholera vibrios become agglutinated. This process is practicable only when the stools contain many vibrios.

3. Take a rice-like flake, and smear it direct on to the surface of MacConkey's lactose-agar plate, using a sterile bent glass rod or Kruse's platinum pencil. Inoculate with the same rod or pencil without recharging the surface of two more plates, and incubate at 35° C. The colonies of the cholera and cholera-like vibrios develop on MacConkey's medium as delicate, small, yellowish, roundish dots within twelve to eighteen hours. Any suspicious yellowish colony should be examined, and the germ investigated as regards motility, morphology, and agglutination, as already mentioned.

4. Inoculate the surface of three ordinary serum-tubes with the suspected stools, and incubate at 35° C. If within sixteen hours there is no zone of liquefaction in the medium, cholera may be practically excluded. If there is liquefaction, this may be due to the presence of the cholera or other serum liquefying germs, or to the stools containing an amount of proteolytic substances. The liquefied serum may be plated on MacConkey or ordinary agar plates, and any suspicious colony further investigated.

5. Dieudonné's special strongly alkaline blood agar may be used for the isolation of the cholera vibrio in faeces. On this medium the cholera germ grows well, forming pearl-like colonies, while the coli and coli-like organisms scarcely vegetate. Of course, the colonies which grow must be carefully investigated, as already described.

6. *Bandi's Method.*—The suspected faecal matter is inoculated into a sedimentative tube containing peptone water and a certain amount of immune serum. After incubation at 37° C. for three to seven hours this tube shows, if the case is one of cholera, numerous small flocculi, which at first are in suspension, and later sink to the bottom. These flocculi consist of agglutinated vibrios.

7. *Ottolenghi's Method.*—The suspected stools are inoculated in a medium consisting of pure bile mixed with 3 per cent. of a 10 per cent. solution of sodium carbonate, which after incubation at 37° C. for some hours is plated and further investigated.

8. *Aronson's Method.*—This is an alkaline agar medium containing cane sugar and dextrin, with fuchsin and sodium sulphite as indicator. Good results have been recorded by several observers.

9. *Castellani's Method.*—Inoculate peptone water tubes (it is of advantage to use centrifuge tubes) with the fæcal matter in the usual way, but before or immediately after making the inoculation add to each tube 3 to 5 drops polyvalent lactose fermenting fæcal bacteria serum (*B. coli*, *B. pseudo-coli*, *B. coli tropicalis*, etc.), or the respective mono-serums may be used; 3 to 5 drops polyvalent non-lactose fermenting fæcal bacteria serum (*B. proteus* group, etc.); 3 to 5 drops paratyphoid B serum. The addition of the last-named serum is made with the object of agglutinating and delaying the growth of the bacilli of the paratyphoid B and *aertrycke* type, which, in the tropics at least, are not very rarely found in the intestinal fluid. Care should be taken, of course, to use serums containing no coagglutinin for the cholera vibrio, or only in very small amount. Or serums can be used from which the cholera coagglutinin—which is always in very much smaller amount than the other coagglutinins—has been removed by absorption. The tubes are placed in the incubator, and the further steps in the investigation are carried out in exactly the same manner as with the ordinary methods. For details see *British Medical Journal*, October 13, 1917.

A modification of the method consists in inoculating ordinary peptone-water tubes with the fæcal matter, and, after four to six hours, from the upper portions of these tubes inoculations are made in peptone-water tubes containing a few drops of intestinal bacteria polyserums.

If material has to be sent to a central depot for bacteriological examination, certain precautions must be carried out. The fæces must be carefully collected, if possible into a bed-pan which has been scalded or boiled, or a loop of small intestine carefully removed post mortem. These specimens must be forwarded in a glass bottle, which, as well as the cork, has been boiled. It is, perhaps, hardly necessary to state that no antiseptic must be mixed with the specimens.

Prognosis.—The prognosis is usually bad at the beginning of the epidemic, but improves as the epidemic continues. The case-mortality may be stated to be on the average about 50 per cent.

Treatment.—The treatment of cholera must aim at the destruction and removal of the vibrios, the neutralization of the toxins, the prevention of secondary infection through the damaged intestinal mucosa, the healing of which must be assisted, and the relief of symptoms.

To promote these objects, the patient must at once be sent to bed, no matter how slight the attack may seem to be. His room should be airy, and he should not be allowed to leave the horizontal position. The bed-pan and urine bottle must be used, and the former should be slightly warmed.

The best treatment is that devised by Rogers, which is as follows:—

The patient is given as much calcium permanganate water (1 to 6 grains to the pint) as he can drink, and permanganate pills every quarter of an hour for two hours, and then one pill every half hour (any pill rejected by vomiting being immediately replaced). These pills are continued until the stools become green and less copious, which may occur in twelve to twenty-four hours. At the beginning of the second twenty-four hours eight pills are administered within four hours, and in severe cases this is repeated at the beginning of the third twenty-four hours. In mild cases after the first twenty-four hours the pills are only administered every four hours.

The composition of the pills is:—

Potassium permanganate	2 grains.
Kaolin and vaseline as may be required to make a pill.	

This pill is coated with a varnish composed of 1 part of salol and 5 parts of sandarach varnish, or with keratin. Pills kept for any length of time are apt to become hard and useless.

The patient must be kept warm, and supplied with plenty of water to drink, which preferably should be taken in sips, and sinapisms or turpentine stupes should be applied to the abdomen.

When collapse has set in, hot bottles must be applied to the extremities and round the body, and when the pulse fails, the median cephalic vein should be opened at the elbow, and Rogers's special silver cannula, made by Messrs. Down and Company, inserted, and through this injections of hypertonic saline solution should be injected until the blood-pressure returns as tested by the pulse, or more preferably by a Riva-Rocci's instrument. If the blood-pressure sinks below 70 millimetres, Rogers considers this to indicate the presence of a dangerous degree of collapse and an indication for an immediate intravenous injection. He takes the specific gravity of the blood by the simple method of placing a drop of blood in the centre of a small vial containing a mixture of glycerine and water of known specific gravity (at the mean temperature of the air), and if the droplet rises or falls, trying another vial of lesser or greater density until the right specific gravity is reached.

He concludes that, if the specific gravity is over 1060, while the blood-pressure is low, a copious intravenous injection may be safely administered. If the specific gravity is over 1065, even if the blood-pressure is over 70 millimetres, it is advisable to give an intravenous injection, as the blood is dangerously concentrated, and a single evacuation may lead to a rapidly fatal collapse.

Restlessness, cyanosis, and cramps are also taken as indications for intravenous injection, especially if the blood from the pricked finger is black, and may be obviously thicker in consistency than normal.

The hypertonic saline solution recommended by Rogers is:—

Sodium chloride	120 grains (8 grammes).
Calcium chloride	4 ,, (0·25 gramme).
Potassium chloride	6 ,, (0·4 ,,).
Water	To 1 pint (568 c.c.).

The temperature of the sterilized solution (in an emergency pure water filtered through cotton-wool, and boiled for fifteen minutes will suffice) has to be judged by the rectal temperature. If this is 99° F. or over, Rogers injects the fluid at about the normal temperature of the body (98·4° F.)—*i.e.*, the flask temperature is about 100° F. If the rectal temperature is a degree or so below 99° F., the temperature of the solution in the flask should vary from 102° to 104° F. If the rectal temperature is high—*i.e.*, over 100° F.—the solution should be run in below 98·4° F.: if the temperature is over 102° F. the solution should not be warmed. About 4 pints of fluid are required for an adult male, but the case must be carefully watched, and the injection stopped if any distress of increased frequency of respiration is noted. These injections may have to be repeated several times, and therefore the cannula must be left *in situ*. At the same time, hypodermic injections of strychnine, provided there are no severe cramps, with or without atropine, should also be given, and warm rectal injections.

During this treatment the bladder must be carefully watched to see whether urine is being passed or not, and if suppression occurs, dry-cupping should be performed over each loin.

In some cases, especially when anuria has developed, an alkaline solution acts better, and Rogers recommends the following: Sodium chloride, 4 grammes; sodium bicarbonate, 10 grammes; water, 500 c.c. Bayliss' solution (6 per cent. gum acacia in 0·9 per cent. sodium chloride solution) may be used.

When the stage of reaction sets in, a mixture containing salicylate of bismuth gr. xv., bicarbonate of soda gr. v., liquor opii sedativus min. v., mucilage q.s., and chloroform water 1 ounce, should be given, and later one containing alkalis and digitalis is useful.

With regard to symptoms, the persistent vomiting may be relieved by small pieces of ice or by $\frac{1}{4}$ grain of cocaine dissolved in a teaspoonful of water, or by a dose of 10 minims of mistura pepsini composita et bismutho every half-hour until four doses have been given, or by one or two drops of tincture of iodine in water. Cramps are treated by massage, assisted by rubbing with dry powdered ginger, by hypodermic injections of morphia, or by inhalations of a mixture of chloroform and oxygen. Prostration must be combated by hypodermic injections of strychnine or of camphor in ether. Delirium must be relieved by bromides with tincture of hyoscyamus.

The treatment of complications, such as pneumonia, etc., must be conducted on the lines laid down in textbooks on general medicine.

Other methods of treatment may be briefly mentioned. Many disinfectants are recommended by different authors—*e.g.*, a mixture of sulphocarbolates of zinc, 2 grains, soda, 2 grains, calcium, 3 grains, dissolved in peppermint. Acetozone, alphazone, and medical cyllin are recommended by O'Gorman, and both he and Waters advise the administration of 15 minims of medical izal dissolved in 1 ounce of water every two hours. Salol has been strongly recommended by some writers, and Brown and Banerji praise an emulsion of eucalyptus oil with mucilage and syrup of lemons, of which 5 minims are given for a dose. O'Gorman advises copper arsenite for infants, while Duke recommends red iodide of mercury in the algide stage, and Choksy cyanide of mercury in $\frac{1}{16}$-grain doses in syrup and water every two or three hours, but says this is apt to cause stomatitis during convalescence, which can be avoided by regulating the doses. Cantani long ago advised slow intestinal injections of 3 to 4 pints of a 1 per cent. solution of tannin, with or without 20 to 40 drops of tincture of opium, and warmed to 100° F. and given every three to ur hours. Denier's serum treatment has been found useless by Strong, ut Kolle's serum promises to be more useful. Berdnikoff gave 30 to 50 c.c. f Schurupon's serum intravenously and subcutaneously with success. Salim-ni used 100 to 350 c.c. Pasteur Institute serum together with saline ected subcutaneously and intravenously. Macfadyen and Hewlett have

prepared an endotoxic serum, and Violle has prepared a serum by inoculating the cholera vibrio in the gall-bladder of rabbits. Several authors recommend treatment by repeated hypodermic injections of morphia, and others adrenalin and pituitary extract. Kuhne recommends massive doses of bolus alba (kaolin).

With regard to diet, no food should be given during the acute attack, but merely liquids, which should consist of water, iced water, iced soda-water. Stimulants should only be given with great moderation, and carefully by the mouth, as at times they are apt to do more harm than good. In the algide state the liquids given should be warmed, and hot black coffee may be used as a cardiac stimulant.

When reaction sets in, only the mildest foods must be allowed, and then only with care. Begin with thin arrowroot, and continue with milk mixed with soda-water, and then with milk, barley-water, rice-water, etc. Sanatogen, plasmon, and somatose are also recommended. Meat-extracts should be avoided. As improvement continues, the diet may be slowly and carefully increased, but the greatest care must be taken for a long time.

Prophylaxis.—The prophylaxis must be based upon the knowledge that the disease is carried by man, and is spread from one man to another by water, milk, contaminated food, especially green vegetables, and insects, especially flies and perhaps ants.

The methods which may be adopted are classifiable into private and public.

Private Methods.—At the beginning of an epidemic it is as well to circulate a printed notice in English and in the vernacular telling the householder what he should do to prevent the disease attacking his household. It is the duty of the head of every household to personally inspect twice a week at least his kitchen and go-downs, and especially his servants' latrines, and to see that the house and compound are kept in a clean, sanitary condition. He must also see that the filters are properly cleaned, and should flies abound in the house, their source should be diligently sought for, or, if it cannot be found and dealt with, the Sanitary Authority should be informed. He should also see that the whole household keep themselves strictly clean, especially the cooks.

With regard to food and drink, care should be taken that all cooking and serving vessels are thoroughly cleansed with boiling water, and that kitchen cloths are washed in a solution of cyllin or carbolic acid. Especial care should be taken with regard to the ice-safe, which is apt to become coated internally with green slime, which may cause diarrhœa. This ice-safe must be thoroughly cleaned with hot soda and water, and exposed to the sun at least once a week. Food must not be stored near latrines, and must be protected from flies and ants, and the rooms and cupboards in which it is placed must be thoroughly cleansed with soda and hot water at least once a week.

All water must be boiled and filtered, and stored in covered vessels, and all milk must be boiled and carefully protected from flies and other insects. Care should be taken that good milk is procured. No uncooked vegetables or salads should be used; fruit must be sparingly indulged in, and unripe fruit, especially melons, must be avoided. Balfour advises that jellies in particular should not be used during a dangerous season. Weak tea and lime drinks made with boiling water should be used as beverages.

All cases of illness, but especially diarrhœa, must be promptly treated by a medical man.

With regard to prophylactics, eucalyptus oil in 10-minim doses twice daily has been strongly recommended by some authors, but the most usual prophylactic is a protective inoculation, which was first introduced by Ferran in Spain, and has been studied and improved by Haffkine and Gamaleia; by Tamancheff, who added 0·5 per cent. carbolic acid to the sterilized prophylactic; and by Strong and others.

Vaccines.—Haffkine originally used two prophylactics—a weak and a strong—with the idea that the strong would produce too violent a local reaction: but this proving to be wrong, only the strong is now used. This prophylactic is prepared by intensifying the virulence of the vibrios by passing them through a series of rabbits, and then growing on agar, from which the growth is washed off by sterile broth which is made up to 8 c.c., of which one is injected hypodermically into the flank as a dose. There is some local reaction in the form of redness, swelling, and pain, and some general febrile reaction. The result is that after an initial diminution of the resistance against the disease this becomes considerably increased after the fifth day. Haffkine's statistics show that it diminishes by one-tenth the liability to the disease, and increases the chance of surviving if attacked. Thus, according to Powell, in 6,549 non-vaccinated there were 198 cases and 124 deaths, and in 5,778 vaccinated there were 27 cases and 14 deaths. Vaccination confers a partial immunity, which is said to last about fourteen months, after which it diminishes, and finally disappears. Re-vaccination is, therefore, necessary after this period.

Strong's method is to spray agar which is contained in large flat-sided flasks with a twenty-four-hour-old culture of the vibrio in broth, and then to incubate the flasks at 37° C. for twenty hours, and to suspend the subsequent growth in sterile water, which is first heated to 60° C. for one to twenty-four hours, then incubated at 37° C. for two to five days, and then filtered through a Reichel candle. Two c.c. (the equivalent of 10,000 units of immunity in a rabbit) of the filtrate, which must be sterile, are inoculated. This prophylactic, which is said to be capable of being kept for a year, produces no local reaction, and but slight general reaction, and increases the bactericidal and agglutinative powers of the serum considerably. Strong considers that it contains receptors separated from the vibrios, and that it probably acts by increasing the bactericidal and antitoxic powers of the epithelial cells of the mucosa of the alimentary canal.

One of us has prepared an attenuated live vaccine by heating emulsions of agar cultures to 45° C. or 48° C. for one hour.

A nucleo-proteid vaccine, according to Lustig and Galeotti's method, can also be prepared.

Tetravaccine (T.A.B.C.)—This is a vaccine prepared and used by Castellani since 1909, and now frequently employed in various countries as a prophylactic measure against cholera as well as typhoid and the paratyphoid fevers. It has been adopted in the Serbian Army since 1915. It is prepared as follows:—

The growth of typhoid cultures is washed off with sterile 0·85 per cent. salt solution, to which 0·5 per cent. carbolic acid has been added; the emulsion so obtained is stored at room temperature (18° to 20° C.) for twenty-four hours, and then standardized. To standardize it the germs are counted by using a Thoma-Zeiss apparatus, and sufficient carbolic salt solution is added to bring the number of germs down to 2,000 millions per cubic centimetre. The standardized emulsion is tested for sterility. The same procedure is carried out with paratyphoid A and paratyphoid B cultures, these two emulsions being also standardized to contain 1,000 million germs per cubic centimetre. The above procedure is also carried out with cholera, the emulsion of which, however, is standardized to contain 4,000 million germs per cubic centimetre. The four standardized emulsions when found sterile are mixed together in equal proportions, and the vaccine will therefore contain per cubic centimetre:—

Typhoid .	500 millions
Paratyphoid A	250 ,,
Paratyphoid B	
Cholera .	

Of this mixture, 0·5 to 0·6 c.cm. are given under the skin of the arm, or better into the loose tissue below the angle of the scapula, the first time, and double the amount a week later. A third dose, also ½ c.cm., given two weeks after the first, is of advantage, but not essential for practical purposes. The amount of agglutinins for each germ is about the same as if monovalent vaccine had been injected. The protection for cholera seems to last for about six months.

Castellani has prepared also a glycero-tetravaccine containing 2 per cent. pure glycerine and standardized as to contain per c c. typhoid 2,000 millions, paratyphoid A 100 millions, paratyphoid B 1,000 millions, cholera 4,000 millions. Of this vaccine only one inoculation of 1 c.c. is given.

A *pentavaccine* having in addition 300 millions of *B. pestis* may also be prepared. The effect of the vaccine in man lasts for several months (six to seven).

Public Prophylaxis.—It is the duty of the State to attempt to ward off cholera by preventing human beings introducing the germ. This involves the careful watching of the frontiers, especially along the lines of intercommunication, whether roads, railways, or waterways. Under the last heading must be included ships, boats, and rafts, for it must be remembered that cholera is very apt to be introduced by persons travelling along rivers.

Any suspicious case must be detained for five days in quarantine in suitable isolation hospitals erected near the frontiers, while the sick must be tended in special hospitals with all the precautions to be mentioned later.

Merchandise does not, as a rule, require any disinfection, unless there is reason to suspect that some of it has been fæcally contaminated from a case.

When an epidemic begins, the first duty is to form a special Cholera Board to deal with the outbreak, and this Board should be composed of financial and legal authorities, as well as of doctors and bacteriologists. This Board will form the central authority for the control of the epidemic. All suspicious cases must be reported to this central authority at once.

Then central and outlying bacteriological stations must be provided, and special hospitals and isolation hospitals built, and, if possible, nurses and medical men obtained who have some practical knowledge of the disease. If time permits, it is as well to have these vaccinated against the disease, but it should be remembered that five days must elapse before the immunity is effective.

Arrangements must then be made for the prompt bacteriological diagnosis of cases, for the prompt treatment of all disorders, especially intestinal, and extra dispensaries must be opened, and the public informed of the necessity of availing themselves of these medical arrangements. If necessary, a house-to-house inspection should be made, in order to find out if there are mild concealed cases, and nobody should be buried without a proper medical certificate.

All patients must be removed to the hospitals, and the houses disinfected with the Clayton gas apparatus, in order to kill not merely the germs, but also the flies and ants. If this is not available, formalin sprays, together with burning sulphur, may be used. Fomites should be carefully disinfected, and persons attending the sick must avoid infection by careful disinfection of the hands and by wearing overalls.

The dejecta of patients should be carefully disinfected with cyllin or carbolic acid, and no patient should be liberated from the hospital until bacteriological examinations of his fæces on three successive days are negative. This is a most necessary precaution, because otherwise he may spread the germs broadcast for a period of about six weeks at least.

Care must be taken to disinfect and bury the dead with least chance of the infection spreading. Cremation should be encouraged in preference to burial.

A systematic search must be made for the origin of the infection, and drinking-water, well-water, etc., must be regularly examined bacteriologically. Dangerous wells must be closed, and all wells may be Hankenized—*i.e.*, disinfected with permanganate of potash.

The milk, ice, and aerated waters should be taken under the municipal control, and not merely must care be taken that they are pure, but they must be tested bacteriologically from time to time.

Vegetables must be inspected, and the place where they are grown ascertained and inspected, in order to find whether there is fæcal pollution. A crusade must be made against flies and dirt in general. The disposal of sewage should, of course, have been dealt with before the epidemic has occurred; but if it is defective, attempts should be made to remedy this as far as possible, and a scheme at once started for proper collection and disposal.

Bathing-places must be carefully inspected, and bad places closed, and only pure water allowed to be used. No washing must be allowed near wells. Drugs must be given free, and means for inoculation of the prophylactic provided on a large scale.

When the epidemic is past, the sanitary defects found out during its course should be remedied, and not forgotten until another outbreak occurs.

Summary of Prophylactic Measures.

Public Prophylaxis :—

1. Protection of the frontiers by regular inspection posts and quarantine stations.
2. A central Cholera Board, with full staff and apparatus for bacteriological disinfection and hospital work.
3. Instruction of the populace by means of pamphlets.
4. House-to-house search for cases.
5. Search for carriers and sources of infection.
6. Distribution of medicines and disinfectants.
7. Provision of medical aid which can be readily obtained by anyone.
8. Crusade against house flies.

Private Prophylaxis :—

1. Personal cleanliness.
2. Avoidance of foods liable to be contaminated or to cause diarrhœa.
3. Avoidance of pollution of foods, especially by flies.
4. Filtration and boiling of all water used for cooking, drinking, etc. Filters to be kept strictly clean.
5. Boiling of milk and protection against flies.
6. Clean, sanitary dwelling free from flies.
7. Anti-cholera vaccination, repeated yearly in endemic centres.
8. Immediate application for medical aid in case of diarrhœal illness of any description.

PARACHOLERA.

Synonym.—N'diank (Senegal).

Definition.—Paracholera, a term first introduced by Castellani, indicates an acute attack of colic and diarrhœa, with or without rice-water motions, which resembles cholera in the severity of the symptoms, but differs therefrom in that its causal organism is a vibrio different from *Vibrio choleræ* Koch.

Remarks.—The work of Castellani, Thiroux, Lamas, Greig, Orticoni, Chalmers and Waterfield, and many others, has demonstrated

the existence of a clinical entity differing from true cholera mainly in the fact that the causal organism is not the cholera vibrio.

Ætiology.—The organisms which have been isolated from cases of paracholera are:—

Vibrio kegallensis vel paracholeræ Castellani in Ceylon.

Vibrio freseris Lamas in Spain.

Vibrio gindha Pfeiffer, by Chalmers and Waterfield, in 1916, in the Anglo-Egyptian Sudan.

Orticoni's vibrio in Marseilles in 1911.

Symptomatology.—Clinically the symptoms resemble those of Asiatic cholera, and as such the cases are generally diagnosed. The motions are generally of the rice-water type, but are sometimes slightly greenish, therein differing from true cholera.

Treatment.—This is the same as for cholera.

PSEUDOCHOLERA.

Synonyms.—Choleraic diarrhœa, called ptomaine poisoning, Serous diarrhœa, Trench diarrhœa.

Definition.—Pseudocholera is an acute attack of serous diarrhœa which resembles cholera and paracholera in its symptoms, but differs therefrom in being due to various causes, none of which is a vibrio.

Remarks.—Cases of profuse serous diarrhœa associated with algidity, muscular cramps, and in general showing symptoms resembling cholera or paracholera, are not rare, in our experience, in tropical and subtropical lands and war zones.

Ætiology.—The causal agents are very various—*e.g.*, food poisoning, generally caused by bacilli of the *aertrycke* type; serous diarrhœa, caused by bacilli of the *dysentery* group: atypical subtertian *malaria*; certain *poisons*. We will now consider the symptomatology of these varieties.

Food-Poisoning Pseudocholera.

This form of pseudocholera is generally due to *B. aertrycke.* The cases are of mild or moderate severity, and are often termed 'ptomaine poisoning.' The onset is acute, with severe abdominal pain, furred tongue, and diarrhœa. The motions do not contain blood or mucus, nor are they usually of the nature of rice-water, but in the more severe cases the stools are choleraic and there may be algidity and cramp.

Bacillus aertrycke can be differentiated from *B. paratyphosus B* by means of Castellani's absorption test. Broughton Alcock has described several varieties of *B. aertrycke* which can be distinguished by this method. For its biochemical characters see table of intestinal bacteria, p. 944.

Dysenteric Pseudocholera.

Castellani some years ago showed that the type of choleraic diarrhœa, called serous diarrhœa, was often due to bacilli of the dysentery group, and therefore of dysenteric origin. Recently Besredka in cases of so-called *trench choleraic diarrhœa* has also found bacilli of the dysentery group. The onset is sudden, and at times the symptoms may be mild, but more commonly they are severe. The patient passes a number of serous motions resembling those of cholera. There may be algidity, cramps, and the illness may terminate in death. In most cases, however, the motions are now and then tinged with blood, which arouses suspicion as to its dysenteric nature. Microscopical examination of a fresh preparation of the fæces may show a few red cells and leucocytes, instead of the epithelial desquamation found in true cholera. Bacteriological examination demonstrates the presence of dysentery bacilli and the absence of cholera and paracholera vibrios.

Malarial Pseudocholera.

This type is not rare in the tropics. The onset is sudden, with profuse serous diarrhœa, algidity, and other symptoms closely resembling true cholera (see p. 1177)..

If the spleen is enlarged the diagnosis is facilitated, though true cholera may develop in cases of malarial infection. Microscopical examination of the blood and bacteriological investigation of the fæces are also useful in demonstrating the presence of malarial parasites and the absence of cholera and paracholera vibrios. Intramuscular injections of quinine quickly cures this type of choleraic diarrhœa.

Pseudocholera caused by Poisons.

This is most usually caused by *arsenic*, which is commonly in use in the tropics, especially in Ceylon, where it can be bought in the local markets. The diagnosis may be established by the history and by chemical analysis of the vomit and fæces and negative bacteriological examination.

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CHAPTER LXXVIII

THE DYSENTERIES

The term ‘dysentery’—Dysentery and dysenteric diarrhœa—Dysenteries caused by animal parasites—Protozoal dysenteries—Amœbic dysentery—Laveranic dysentery—Leishmanic dysentery—Ciliar dysenteries—Balantidic dysentery—Spirochætic dysentery—Entoplasmic dysentery—Platyhelminthic dysenteries—Nemathelminthic dysenteries—Arthropodic dysenteries—Dysenteries caused by bacteria—Pseudo-dysenteries—References.

The Term ‘Dysentery.’—The term ‘dysentery’ is derived from *δυσεντερία*, signifying a bowel trouble, and was first employed by Hippocrates. As used at present, it covers a large number of distinct affections, induced by various species of animal and vegetal parasites. In England it used to be called the *Bloody flux*, in France *Ténesme*, and in Italy *Flusso sanguigno*. The Latin equivalent is *Tormina*, the German *Ruhr*; while the native terms applied to it are too numerous to be considered here, but we may mention the Sinhalese term *Lehedanpachanai* (*Leh* = blood, *hedan* = mucus, *pachanai* = diarrhœa), and the Indian term, *Rattam-seedam-banthala-porado* or *Wayatholechell*.

Dysentery and Dysenteric Diarrhœa.—The occurrence of a bowel disease in which blood appeared in the motions was well known to the ancients, for descriptions of such a condition can be found in the works of the old authors Charaka and Susruta, in which dysentery was called ‘Atisar,’ and acute dysentery ‘Ama-apaka,’ while the chronic variety was called ‘Pakitsar.’

Hippocrates recognized two distinct types of disease of the bowels—one characterized by the number and fluidity of the motions, which he called *διαῤῥοία*, and the other, by the presence of blood in the motions, which he termed *δυσεντερία*.

At first the term ‘dysentery’ included any disease in which there was a discharge of blood *per anum*, but Aretæus, Celsus, Archigenes, Galen, and other ancient physicians, soon differentiated the disease more clearly by emphasizing the fact that there should be mucus as well as blood in the motions, and that the symptoms of tormina and tenesmus must be present. They further stated that the disease was due to an ulcerated condition of the bowels, and the contagious nature of the malady was early recognized and it was thought that its epidemics were due to miasmata. According to these ancient writers, in order to make the diagnosis of dysentery, it was necessary to have blood and mucus in the motions. Recent investigations have, however, shown that certain cases of diarrhœa and dysentery are brought about by the same organism, and that a form of diarrhœa which may be called dysenteric diarrhœa is only one phase of the clinical appearances of a dysentery, and is ætiologically in no way different from what might be termed a true dysentery, except in the severity of the symptoms and the post-mortem appearances. Briefly, dysenteric diarrhœas are dysentery under a somewhat different clinical aspect—viz., the stools do not contain blood and mucus, although the complaint is due to the same organisms as true dysentery. Hence it is not expedient to attempt to classify dysenteries by their clinical symptoms or by their post-mortem appearances, and any rational classification and description of the complaint must be based on the causation.

We therefore classify dysenteries and dysenteric diarrhœas into:—

A. Dysenteries caused by Animal Parasites:—
  I. The Protozoal Dysenteries.
  II. The Platyhelminthic Dysenteries.
  III. The Nemathelminthic Dysenteries.
  IV. The Arthropodic Dysenteries.
B. Dysenteries caused by Bacteria.
C. Pseudo-dysenteries.

By the last expression we mean such forms of the complaint as may be due to the irritation of fish-bones, glass, cancer, or inflammations of organs adjoining the alimentary canal.

A. DYSENTERIES CAUSED BY ANIMAL PARASITES.

I. THE PROTOZOAL DYSENTERIES.

The protozoal dysenteries are classified into:—

(*a*) Amœbic Dysentery.
(*b*) Laveranic Dysentery.
(*c*) Leishmanic Dysentery.
(*d*) Ciliar Dysenteries.
(*e*) Balantidic Dysentery.
(*f*) Spirochætic Dysentery.
(*g*) Entoplasmic Dysentery.

With regard to the term 'amœbic dysentery,' we prefer this term as less likely to be altered rather than the more correct nomenclature Loeschial dysentery or Loeschiasis.

(*a*) Amœbic Dysentery.

Synonyms.—*Loeschiasis*, *Loeschial dysentery*, Entamœbiasis, Amœbiasis, Entamœbic dysentery, Amœbic enteritis, Amœbic colitis. *French:* Dysenterie Amibienne, Dysenterie à Amibes. *Italian:* Dissenteria Amebica. *German:* Amöbenruhr.

Definition.—Amœbic dysentery is an acute or chronic specific disease of the intestine, caused most commonly by *Loeschia histolytica* Schaudinn, 1903, and possibly by other species. These amœbæ enter the body with food or water, and produce colitis, rectitis, and enteritis, characterized by the passage of frequent motions, which generally contain blood and mucus, and are associated with abdominal pain and tenesmus. At times they also produce abscesses in the liver and other parts of the body.

History.—In 1860 Lambl noticed amœbæ in the motions of a child suffering from diarrhœa, and in 1870 Lewis found the same organisms in the motions of cholera patients; while Loesch, in 1875, gave a careful description of certain amœbæ which he found in the motions of a man suffering from chronic diarrhœa. Loesch's drawing signifies that he saw the organism which we call now *Loeschia histolytica*. Further, he found that solutions of quinine of a strength of 1 in 5,000, when injected *per rectum*, temporarily benefited his patient, who, however, subsequently died of pneumonia, when a post-mortem revealed that the bowels were ulcerated. Loesch was able to infect dogs; but, on the other hand, Grassi, and later Cunningham and Lewis, showed that the motions of healthy people also contained amœbæ. Koch, in 1883, found amœbæ in the ulcers in cases of dysentery in Egypt, and Kartulis began a series of investigations, which finally ended by his defining the types of dysentery as 'endemic,' due to amœbæ, and 'epidemic,' due to bacteria. In 1891 Councilman and Lafleur introduced the term 'amœbic dysentery,' and Quincke, Roos, Vivaldi, and many others published experimental researches on the infection of animals by amœbæ and the production of dysentery.

In the meanwhile a prolonged discussion took place, some observers denying, and others asserting, the pathogenicity of the amœbæ. Kruse and Pasquale were the first to throw light upon this difference of opinion by suggesting that both theories might be correct, and that there might be two species of amœbæ, one pathogenic and the other harmless; but this was not finally settled until the researches of Casagrandi and Barbagallo, together with those of Jürgens, were confirmed and greatly extended by Schaudinn, who showed that there were two forms of amœbæ quite distinct from one another—viz., a *Loeschia coli* Loesch, which was harmless, and another, *L. histolytica* Schaudinn, which was the true cause of entamœbic dysentery.

During recent years the labours of Hartmann, Whitmore, Wenyon, Fantham and Porter, Dobell and others, have proved that the amœba which most commonly causes dysentery is *L. histolytica*, and that the other forms of amœbæ described in dysentery by Viereck (*L. tetragena*) and other observers are different stages of this amœba, the cysts of which can be carried by domestic flies.

Climatology.—Amœbic dysentery is found throughout the tropical world, and also occurs in the Temperate Zone. In general terms it may be stated that amœbic dysentery is common in tropical and subtropical Africa, especially in Senegambia, Algeria, and Egypt. It is common in Mauritius and Ceylon, and is possibly not as rare in India as it is alleged to be. It is common in China, Indo-China, and the Philippines, and not infrequent in North America, but is said to be rare in Central America, in the West Indies, and the Guianas, while common in Brazil and Chili. In Europe it is endemic in Russia and Germany, and fairly frequently met with in the south, especially in Italy and in the Balkans. Sporadic indigenous cases have been reported also from Great Britain, where carriers of *Loeschia histolytica* cysts are not very rare especially among miners.

Our observations do not lend support to the theory that amœbic dysentery is more common in the hills than in the plains of the tropics, as we have frequently met with it in persons residing in the low country. We have noted the disease all the year round, but it would appear to be more prevalent towards the end of the dry and the beginning of the wet seasons, which probably merely means that the chance of drinking polluted water is greater at that time, for though the climatological characters are not well understood, the disease appears to bear a relationship to contaminated water, though flies are also very important.

Amœbic dysentery is generally endemic, and does not spread in epidemic, still less in pandemic, form. Probably, as medical science advances, it will be found to be of more frequent occurrence and of wide distribution.

Ætiology.—The prevalent opinion at the present time is that amœbic dysentery is generally caused by *Loeschia histolytica* Schaudinn, 1903, but the possibility is not excluded of there being other pathogenic *Loeschiæ*. The life-histories of the various species, as far as they are known, have already been described in Chapter XVII., p. 285. The most common source of infection is the drinking-water, which has been contaminated by fæces, and contaminated food, and especially green vegetables, which may be infected principally by the agency of flies carrying the cysts in their intestine and depositing them upon the food, and less frequently by actual human fæcal contamination.

Woodcock has called attention to the importance of a hot, damp climate as a factor in the spread of amœbic dysentery, as cysts survive much longer in a hot, damp climate than in a dry climate. Cysts cannot withstand drying; while the experiments of Penfold, Woodcock and Drew have shown that cysts of *Loeschia histolytica* can retain their vitality for more than a fortnight in water.

There does not appear to be any well-established racial or age predisposition, but the disease is less common in women than in men, perhaps because they are in some way less exposed to infection.

Pathology.—The spores of the amœbæ enter the body by the drinking-water, and by food contaminated with cysts, often deposited by flies, and produce the young amœbæ on arrival in the large bowel. These young forms enter the mucosa, probably by passing between the cells lining Lieberkühn's follicles, and then, entering the lymphatics, make their way through the muscularis mucosæ into the submucosa, where they live and feed upon the tissue cells, red cells, and perhaps leucocytes. They, however, invade not merely the tissue of the submucosa, but also the radicles of the portal vein, and at times the branches of the mesenteric arteries, in which they may cause thrombosis. From the radicles of the portal vein they may be carried to the liver, and cause hepatitis and hepatic abscess.

In the submucosa they induce cellular and œdematous infiltrations, which cause the mucosa to project in the form of small elevations, which generally show a minute blackish point or slough at the summit. This slough is cast off, and a small ulcer is formed, which rapidly deepens until it extends into the submucosa. These ulcers become infected with bacteria, and quickly extend by the joint action of the bacteria and the amœbæ, forming roundish or oval ulcers with undermined edges: in the latter case the long axis of the ulcer lies transverse to the direction of the bowel. These ulcers may deepen until the muscular and the peritoneal coats are exposed, and even perforated, which, of course, leads to peritonitis or abscess formation, according to the position of the perforation.

Amœbic dysentery would appear to undergo in many cases no spontaneous cure, but may at times remain quiescent, forming a type of latent amœbic dysentery, which may be found accidentally while performing an autopsy. When the ulcers heal, which they do by the formation of connective tissue, a distinct scar is formed, which is often black in colour from the action of the sulphuretted hydrogen of the bowel upon the iron of the blood. When cicatrization takes place, the lumen of the bowel may be constricted, causing stenosis and obstinate constipation. Peritonitic adhesions are also very common, binding the large bowel to the viscera or walls of the abdomen and pelvis.

Sometimes, when the infection is severe, the bowel becomes gangrenous; at other times the amœbæ may be carried to the liver or other parts of the body, and form abscesses, which, though most commonly met with in the liver, may still occur in the spleen, the salivary glands, and elsewhere.

Morbid Anatomy.—Usually the body of a person dying from amœbic dysentery is emaciated, and the abdomen is sunken. Rigor mortis begins, and passes off early, and decomposition sets in quickly. On opening the abdomen, it is noticed that the tissues are dry, and that a peculiar odour is perceived; the omentum may be normal or congested, and may or may not be adherent. The coils of the small intestines are usually normal, but may be congested. The large intestine is generally contracted and thickened, but may be gangrenous in places or along its entire length. There may be perforation and purulent peritonitis. The mesocolon may be congested and œdematous, or thin and fibrous, and adhesions to various organs may be noted. The mesocolic glands are usually enlarged and hyperæmic. The colon may be found adherent to the liver, the spleen, or the wall of the pelvis, while internally the mucosa will be found to be reddened and inflamed, and to show more or less numerous areas of ulceration and infiltration. These areas are most commonly found in the cæcum, the hepatic flexure, and the sigmoid colon, but may occur anywhere along the course of the large intestine. In places small nodules surrounded by a ring of dilated vessels may be observed, between which the mucosa may or may not be normal, while the nodules may show superficial or deep ulceration. Deeper circular or oval ulcers may be noted with their surface covered with a dark reddish slough, their edges undermined, and their base formed by the muscular coats. In the case of the oval ulcers, the longer diameter lies transverse to the long diameter of the bowel, as a rule. The peritoneal coat may be normal, inflamed, or softened and gangrenous. Usually the muscular coat is thickened, as are the remains of the submucosa. Scrapings from these ulcers reveal blood cells, leucocytes, bacteria, and amœbæ. The small intestine may show small bright red nodules, and the Peyer's patches may be enlarged. The vermiform appendix is usually normal, but occasionally may be ulcerated.

FIG. 762.—THE COLON IN A CASE OF AMŒBIC DYSENTERY.

The liver is often fatty, but may be congested and inflamed, or may show one or more abscesses. The pancreas is generally normal, but may be cirrhotic in chronic cases. The spleen is also usually normal, but may contain an abscess; the kidneys often show signs of parenchymatous inflammation. The heart and lungs are generally normal, but the former may be fatty or show brown atrophy, and the latter, especially the right lung, may show a hepato-pulmonary abscess.

Symptomatology.—The symptomatology of amœbic dysentery may be classified into:—

1. Acute Type.
2. Chronic Type.
3. Latent Type.
4. Mixed Type.

1. *Acute Type.*—The onset is abrupt, but may occasionally be preceded for a few days by slight diarrhœa, alternating with constipation. Pain is felt in the lower part of the abdomen, which may become very severe, while the motions are attended with much griping and straining. These motions, which rarely exceed thirty per diem, contain blood and mucus, and occasionally greenish material, and when examined by the microscope reveal leucocytes, mucus, Charcot-Leyden crystals, amœbæ, bacteria, and at times shreds of tissue.

The tongue is moist, and often coated with a white fur, and there is usually anorexia, and there may be nausea and vomiting, while digestion is usually much impaired. The abdomen is sunken, the liver and spleen normal, but tenderness is felt on pressure along the whole or a part of the large bowel.

The examination of the heart and lungs reveals, as a rule, no abnormality, but the pulse and respirations are quickened. The microscopical examination of the blood usually shows that the red cells are diminished, and sometimes that there is leucocytosis (upwards of 20,000 per cubic millimetre), and at times, as first pointed out by Billet, the number of eosinophiles is distinctly increased, even when there is no concomitant helminthiasis.

The urine is diminished in quantity, and sometimes contains albumen and casts; but the skin is generally normal, though there is often some fever of a remittent type, which, however, may be entirely absent.

When the temperature falls to normal, and the pain and tenderness abate, these may be favourable signs, or may be merely a prelude to a gangrenous complication or a hæmorrhage. If recovery is to take place, the motions become less frequent and more fæculent, and contain less blood and mucus, and gradually improve until normal motions are passed. If death takes place, which usually happens about the end of the first week, and ten days from the commencement, it is generally caused by exhaustion, or much more rarely by perforation and peritonitis or hæmorrhage.

2. *Chronic Type.*—This may follow an acute attack, or, in many cases, may begin quite insidiously, the symptoms being merely

those of diarrhœa, associated at times with abdominal pain and the passage of fæculent motions mixed with mucus and sometimes streaked with blood, while in the intervals between these exacerbations there may be constipation. An exacerbation is usually ushered in by pain in the abdomen, slight fever, griping, and tenesmus, and passage of blood and mucus in the motions, while the fæces contain small greyish masses, in which the amœbæ may be found. The number of motions per diem is not excessive, and may be only twelve to fourteen. Usually they are passed somewhat more frequently at night than in the day. Gangrenous complications may, however, occur at any time in the course of an exacerbation, or, indeed, during any stage of this type, when large sloughs, smelling offensively, may be passed with the motions. Chronic dysentery may persist for years, and cause the patient to slowly emaciate. The blood, as shown by Chalmers and Archibald, often shows an increase in the large mononuclears.

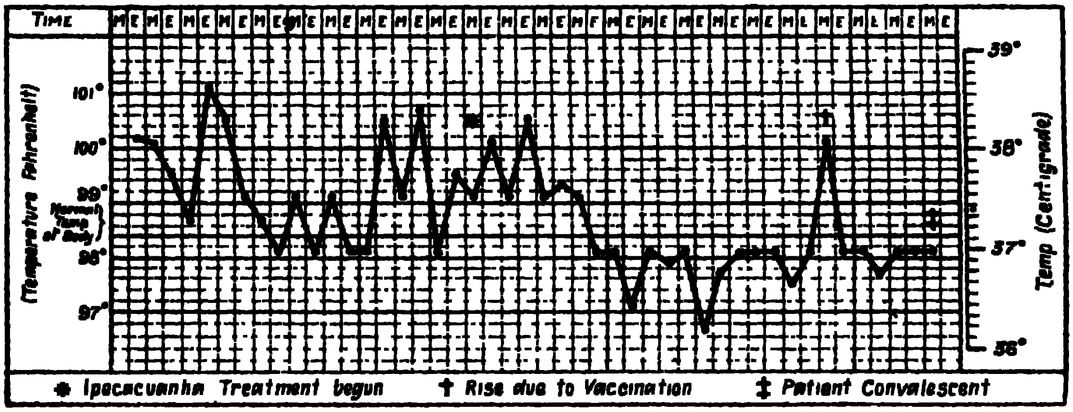

FIG. 763.—TEMPERATURE CHART OF A CASE OF AMŒBIC DYSENTERY COMPLICATED BY HEPATITIS.

3. *Latent Type.*—We have several times met with cases in which, though dysenteric symptoms were absent, still, amœbæ were present in the motions, and others in which dysenteric ulcers were only discovered accidentally on post-mortem examination, the death being due to other causes. This latent condition is important, as it can easily lead to an acute attack or to liver abscess, and no doubt these 'entamœbic carriers,' as has been noted by Martini, Vincent, and others, are a source of the dissemination of the infection.

4. *Mixed Type.*—These are cases in which there is a mixed infection of *Loeschia histolytica* and the Shiga-Kruse bacillus. Usually in these cases the motions are numerous from the first, and there is considerable fever, nausea, vomiting, and great constitutional disturbance. The motions are apt to be very offensive, and to contain sloughs, indicating a gangrenous condition of the bowel. Exhaustion may come on early, and the patient may die delirious or comatose, or, more rarely, from peritonitis, with or without perforation. More rarely improvement sets in, and the disease becomes chronic.

Amœbic Fever or General Amœbiasis.—This term has been applied to certain cases of *L. histolytica* infections in which there is fever, but no dysenteric symptoms and no sign of hepatitis. A few cysts are generally found in the stools, and emetine induces a prompt disappearance of the fever.

Complications.—The most usual complication is hepatitis and hepatic abscess; more rarely gangrene of the bowel and peritonitis may supervene during an attack; while hæmorrhage is a most unusual complication. The hepatitis is recognized by the tenderness in the right hypochondrium and by the rise in the temperature, but it and the hepatic abscess will be discussed in a subsequent chapter. In Ceylon we have observed cases of mixed infection, dysentery and enteric, the two infections developing apparently contemporaneously.

Sequelæ.—The important sequel to an attack of amœbic dysentery is liver abscess, but abscesses in other parts of the body such as the spleen may be met with. Stenosis of the sigmoid colon, due to cicatrization of the healing ulcers, is well known, and will be dealt with under the heading of Bacterial Dysentery. Sprue is often said to be a sequel of dysentery, but this must be considered to be doubtful. Certain authors have described a persistent bradycardia.

Diagnosis.—The diagnosis between bacterial and amœbic dysentery by clinical phenomena only is, in our opinion, impossible in most cases, though several observers have attempted to define some differential points. These authors state that amœbic dysentery is to be distinguished from bacillary dysentery by its chronic course, its rare pyrexia, and the absence of toxic symptoms, while it is often followed by liver abscess. Apart from the last feature, the other so-called differential signs have, in our experience, no importance, as we have come across extremely acute cases of amœbic dysentery with fever and toxic symptoms.

The only certain method of diagnosis is by the discovery of *Loeschia histolytica* in the stools, and this should be done by picking out and examining any mucus which may be seen. It is of practical importance to distinguish between *L. histolytica* and the harmless *L. coli*, and this differentiation may at times be difficult. The former is often larger, and possesses an ectoplasm, which is easily differentiated from the endoplasm; it is more actively motile than *L. coli*, and often contains erythrocytes, which is the most important character. The nucleus of *L. histolytica* is eccentric, small, and generally indistinct, does not stain deeply, and has very little chromatin (see p. 313).

In order to expedite the diagnosis the French method is to add a drop of a 1 per cent. solution of methylene blue to the mucus before placing on the coverslip, when the pus and epithelial cells will be stained, and the amœbæ more easily recognized as unstained, clear objects.

The diagnosis of latent cases and of carriers is based on the finding of the characteristic histolytica cysts containing four nuclei. It is important to note that cysts are not often seen during the acute attacks with blood and muco-pus.

In the search for cysts, only a small quantity of material should be used well diluted with saline. The addition of a little iodine solution is useful, as it makes the nuclei more visible. Dead cysts are easily stained by eosin, while live ones are not.

Cysts of *Loeschia histolytica* have to be differentiated principally from cysts of *L. coli*, *Vahlkamfia nana*, amœbæ of *Limax* type, *Chilomastix*, *Lamblia*, and from the structures known as *Blastocystis hominis*. The characters of all these cysts have been given in detail in Chapters XVII. and XVIII. For diagnostic purposes it is sufficient to remember the following:—

I. Cysts of *L. histolytica* in fresh preparations from stools mixed with salt solution appear as spherical, greenish, very refractile bodies 10-14 microns in diameter, containing four nuclei (at times two) and one or two highly refractile homogeneous rods known as chromidial bodies. Several vacuoles may be present. Dobell and others have called attention to the fact that the size may vary a great deal, there being races of *histolytica* (*minuta* type) giving rise to much smaller cysts, 7 to 9 microns, and others to much larger ones, 12 to 20 microns.

II. Cysts of *L. coli* vary between 15 and 20 microns, are rarely larger, occasionally smaller. They are clear spherical bodies of sharp outline, less refractile than those of *L. histolytica*. They contain 8 *nuclei*, which appear as faint granular rings with a central dot (karyosome). Often only one vacuole.

III. Cysts of *Vahlkampia nana* are oval or spherical structures 7 to 9 microns in diameter, with one, two, or four nuclei, very rarely eight; in addition, a variable number of highly refringent granules and sometimes a large dull inclusion (glycogen). There is absence of chromidial bodies, and this distinguishes the cyst at once from the small ones of *L. histolytica*.

IV. Cysts of amœbæ of *Limax* type are found in stale stools, are always small, uninucleated, and often have a thick wall of brownish colour.

V. Cysts of *Chilomastix mesnili* are often lemon-shaped, and are characterized by the presence of the chromatic rod (parabasal).

VI. Cysts of *Giardia intestinalis* are easily recognized by their egg-shaped appearance; they are about 14 microns in length and very transparent, so that the lamblia can be seen within it with the characteristic central paired rod-like structure in which originate the four pairs of flagelli.

VII. Cysts of *Oicomonas*, *Bodo*, *Prowazekia* are very small, spherical, 6-8 microns in diameter, uninucleated, very similar to those of *Amœba limax*, but the wall is not so thick nor of brownish colour, and the outline is more regular. Sometimes, however, it is impossible to distinguish these cysts from those of *Amœba limax*. They can always be differentiated, however, from those of *L. histolytica*, as they are very small and uninucleated.

VIII. The structures known as *Blastocystis hominis*—considered by some authors to be vegetal organisms—are more or less spherical, 5 to 15 microns in diameter, with a more delicate capsule than the cysts of Loeschiæ, and contain a very large vacuole, which reduces the cytoplasm to a narrow rim at one pole or both poles of the cyst.

IX. *Iodine cysts* (I-cysts). These structures, described by Wenyon and O'Connor, are generally roundish or oval, varying between 6 and 16 microns in diameter, and show frequently a iodophilic body, which tends to be rounded or lobed.

To facilitate the detection of cysts when these are in very small numbers various methods have been suggested, though in practice, as shown by Miss Porter, such methods take a great deal of time, and the results are not much better than those obtained by the simple immediate microscopical examination of several preparations. It is of advantage to give the patient a saline purge, and then one of the so-called enrichment methods of Cropper and others may be used: about 1 gramme of fæcal matter is mixed with 30 c.c. of salt solution in a conical glass, and ether added in the amount of about 10 to 20 per cent. The cysts are generally found in the supernatant fluid, and may be collected by centrifuging it.

Cysts maintain all their morphological characters for a very long period in fæcal matter mixed with a formalin solution (2 per cent.).

The presence in dysenteric stools of Charcot-Leyden crystals, as emphasized by Acton, points to the condition being of amœbic origin rather than bacterial, especially if there is scanty cellular exudate with preponderance of mononuclears.

Prognosis.—The prognosis in a case of amœbic dysentery must always be guarded, as there is the possibility of hepatic abscess as sequela of the mildest case, and the cure induced by emetine and ipecacuanha, though striking, is often merely clinical, complete sterilization not being attained. The prognosis is worst in the gangrenous cases, better in the acute, and still better in the mild chronic cases, but the danger of latency after an apparent cure must be remembered. In the acute type hiccough is an unfavourable sign, often indicating the approach of exhaustion and death.

Treatment.—It is of the utmost importance that the patient should be placed at rest in bed. For the same purpose the urine bottle and the bed-pan must be used. It is advisable to relieve the severe griping and straining by either a hypodermic injection of morphia or by small enemata of 40 minims of laudanum in 1 ounce of mucilage of starch, or by using a morphia (gr. ¼), or codeine (gr. ¼) suppository.

At first the bowels should be swept clean by a dose of castor oil (ʒiv. to ʒvi.), with or without a few minims of liquor opii sedativus, or a few doses of saline may be given during the first twenty-four hours (see Bacillary Dysentery). After the castor oil has acted, or simultaneously, the emetine treatment should be begun. One-third to half a grain of emetine hydrochloride, dissolved in sterile normal saline solution, should be administered as a hypodermic injection two or three times a day for several days. Emetine hydrobromide may also be used in the same dosage, but it is not quite so soluble. These drugs may be obtained in sterile tubes ready for injection. We have never seen any bad effects on the heart from the administration of emetine, but we have met with cases of dermatitis probably due thereto, while Dale and Low have noted diarrhœa after prolonged administration.

A combined subcutaneous and oral administration of emetine as recommended by Wenyon and O'Connor (one grain emetin by injection in the morning and a ½ grain emetine tablet at night) answers well, especially in subacute and chronic cases, and in carriers.

If emetine cannot be obtained, then ipecacuanha should be administered in 5-grain doses every three or six hours, or in larger doses (gr. x. to xx.) twice daily, given either in the form of 'membroids' or as pills coated with salol varnish or keratin. Our experiments *in vitro* tend to show that membroids and salol varnish do not dissolve freely in peptic juice, while they do so in pancreatic juice. The salol varnish was very efficient, but care must be taken that too thick a coating is not used, as it may not dissolve in pancreatic juice. Martindale's method of stearin-coated pills is good. In this way the nauseating effects of the ipecacuanha are often avoided without diminishing its efficiency, which is the result of using the de-emetized drug. Rarely the membroids and salol varnished pills may be passed unaltered in the motions, and in such cases ipecacuanha may be given in suspension in mucilage and chloroform water or in cachets or pills (gr. x. to xx. twice a day), and should be preceded a quarter of an hour by a dose of 15 minims of tincture of opium, in order to prevent the possible vomiting.

With regard to ipecacuanha, it is of great importance to use the best Brazilian, which should contain 72 per cent. of emetine (methyl-cephaeline) in its total alkaloids, the other alkaloids being cephaeline 26 per cent., and psychotrine 2 per cent.; on the other hand, Carthagena ipecacuanha contains cephaeline 57 per cent. and emetine only 40 per cent The powdered ipecacuanha should have an alkaloidal strength of 2 per cent.

Emetine and bismuth iodide has been introduced by Dale, and its efficacy has been confirmed by Low and Dobell and numerous other observers, including ourselves. It is especially useful in the treatment of carriers, inducing at times a complete disappearance of the cysts. It is useful also in amœbic hepatitis and general amœbiasis. It is given in gelatine capsules, one capsule containing gr. iii., at night for two or three weeks, or salol-coated tablets may be used. A shorter course seldom induces a cure. Not rarely the drug produces nausea and at times actual vomiting; in such cases the same precautions may be taken as when giving ipecacuanha.

When the acute symptoms have passed away, intestinal irrigations are useful, and should be administered every other day, or once or twice daily. We generally use a solution of tannic acid (3 to 5 in 1,000), or a solution of the bihydrochloride of quinine in varying strength from 1 in 5,000 to 1 in 750. About ½ to 3 pints should be very slowly injected by gravity from a glass douche vessel by means of a long soft rectal tube well greased with boric vaseline. This injection may be preceded by a cocaine or morphine (gr. ¼) suppository introduced half an hour previously.

Other substances used for rectal irrigations are:- Acetozone (1 in 2,000); alphozone (1 in 2,000); argentum nitras (1 in 2,000 or 1 in 1,000), useful in some very chronic cases; protargol (1 in 500). Creosote is recommended by Zanardini, and may be used by injecting 2 pints of 1 in 300 or 1 pint of 1 in 100. The injection, however, may be followed by symptoms of absorption—*e.g.*, dyspnœa and faintness. A solution of sodium hypochlorite may be used, 2 pints of 8 to 12 in 1,000 being recommended by Vincent once or twice a day, which is also useful for amœbic carriers.

In gangrenous dysentery the only chance of saving the life of the patient is to perform the operation of appendicostomy, and irrigate the whole lower bowel with quinine lotion (1 in 1,000) or collargol (1 in 500). The details of this operation are given under the heading Bacterial Dysenteries.

With regard to the treatment of symptoms, the most important is the relief of pain by hypodermic injections of morphia or by fomentations sprinkled with opium and applied to the abdomen. As the case progresses favourably, a bismuth mixture or tannalbin in cachets (gr. xx. every two to four hours) may be given, while the irrigation may be diminished and stopped, and finally a tonic may be prescribed.

We are strongly of opinion that the ipecacuanha or the emetine should continue to be given in smaller doses long after the dysenteric symptoms have disappeared, in order to prevent relapses, and possibly also the development of a liver abscess, which is the most dangerous sequel. Among the other drugs which have been recommended in the treatment of amœbic dysentery are *Simaruba officinalis* and the so-called *Kho-sam* powder.

The former is recommended by Manson to be used as a decoction which is prepared by taking simaruba bark, pomegranate fruit-rind, and gum arabic, 15 grammes of each, and placing in a litre of warm water, which is boiled till reduced to half its bulk, and of this decoction 1 ounce is taken three or four times a day. Shepherd and Lillie have cured, using preparations of chaparro or simaruba, 34 cases out of 80 cases of Loeschial carriers, refractory to emetine.

Nixon and Sellards and McIver have had good results by using preparations of Castela, a genus of the Simarubaceæ.

The Kho-sam powder is derived from the berries of *Brucia antidysenterica* and *B. sumatrana*, which grow in Indo-China. It is administered in pill form, 1 grain being given two to four times a day. Cinnamon has been often used in the past, and the compound extract of garcinia known also by the trade name of ambiasine is praised by several authors.

If cicatrization of the colon results with stenosis, then sigmoidoscopy must be performed, and the condition treated as described under Bacterial Dysentery. Liver abscess is considered separately. Abscesses in other parts of the body—*e.g.*, the spleen—are rarely met with, though it is possible that some of the inexplicable deep-seated abscesses may have their causation in amœbæ.

The *diet* should be the same as that to be described presently under the heading Bacterial Dysentery. During convalescence the food must be slowly and carefully increased, no acid or very warm substances being allowed.

Prophylaxis.—The prophylaxis consists in the drinking of only boiled and filtered water, and the avoidance of salads and uncooked vegetables and the prevention of fly infestation of food.

Stools of dysentery patients and carriers should be disinfected with cresol, 1 in 10.

Amœbæ, probably non-parasitic, were shown to exist in the drinking-water in Manila, and it was found that copper sulphate and filter-beds were useless. The only safeguard was to sterilize the water by boiling.

(*b*) Laveranic Dysentery.

Definition.—An acute enteritis and colitis caused by *Laverania malariæ* Laveran, and characterized by high fever, associated with the passage of frequent motions containing blood and mucus.

Symptomatology.—The attack usually begins suddenly, with high fever, great distress, and prostration. The tongue is coated, the abdomen tender, and many motions are passed containing blood and mucus. The spleen may or may not be palpable. Unless correctly treated, the condition becomes serious, and rapidly leads to the death of the patient.

Diagnosis.—The routine examination of the blood in all cases of tropical disease will prevent mistakes being made, as the presence of numerous subtertian parasites in the blood, with absence of amœbæ and dysenteric bacilli in the stools, will reveal the nature of the complaint. It should be kept in mind, however, that most cases of dysenteric colitis in malarial patients are, in reality, of amœbic and bacillary origin, and not of Laveranic origin.

Treatment.—Quinine should be given in large doses, best by intramuscular injection, and the intestinal symptoms first treated with castor oil or salines, and then with astringents, such as bismuth subnitrate, tannalbin, and salol.

(c) Leishmanic Dysentery.

Definition.—An acute enteritis and colitis caused by *Leishmania donovani* Laveran and Mesnil, and characterized by the passage of blood and mucus in the motions.

Symptomatology and Treatment.—As already mentioned in the chapter on Kala-Azar, dysenteric symptoms closely allied to true dysentery may appear during the course of that disease, and must be treated on the same lines as those laid down for the treatment of kala-azar, together with symptomatic treatment as indicated above. The diagnosis is based on the presence of Leishmanic bodies in the spleen or liver and absence of amœbæ and dysentery bacilli in the stools. True bacterial or amœbic dysentery is far from rare in cases of kala-azar.

(d) Ciliar Dysenteries.

One variety of the ciliar dysenteries may be briefly described—viz., that caused by *Balantidium coli* Malmsten. Other less known causes are *Colpoda cucullus* Schutz, *Balantidium minutum* Schaudinn, *Nyctotherus faba* Schaudinn, *Nyctotherus giganteus* P. Krause. Other possible causes are *Uronema caudatum* Dujardin, *Balantidium italicum* Sangiorgi and Ugdulena, and *Nyctotherus africanus* Castellani. For description of these parasites see p. 544.

(e) Balantidic Dysentery.

Definition.—An acute or chronic ulceration of the large intestine caused by *Balantidium coli* Malmsten, 1857.

History.—Leeuwenhoek originally discovered the parasite *Balantidium coli*, but Malmsten described and named it. The latter observer found it in the motions of a man suffering alternately from diarrhœa and constipation. Other cases have been recorded by Stieda, Henschen, Treille, Graziadei, Railliet, Blanchard, Collmann, Strong, Bowman, Manlove, Mason, and others.

FIG. 763A.- BALANTIDIUM COLI IN HUMAN FÆCES (× 520 DIAMETERS).

(Photomicrograph.)

Climatology.—The disease is known to occur in man in the Philippine Islands, Japan, and Europe, while the parasite is said to be constantly found in pigs. We have seen a case in Ceylon.

Ætiology.—The cause of the disease is *Balantidium coli* Malmsten, which may be different from the parasite found in pigs (for description of the parasite see Chapter XVIII., p. 547).

Pathology.—The method of infection is unknown. The parasite appears to enter the mucosa, in which it wanders, causing an inflammatory reaction and ulceration.

Morbid Anatomy.—This has been investigated principally by Strong. The intestine may show a diphtheritic false membrane, with often deep burrowing ulcers in the rectum and colon indistinguishable from those of amœbic dysentery. On microscopical examination the parasites can be found in the mucosa surrounded by a round-celled infiltration, and several observers have noted a marked eosinophilia of the intestinal wall.

Symptomatology.—The disease is insidious in its onset, being marked by attacks of diarrhœa, alternating with constipation and vomiting, with anorexia and at times the passage of blood and muco-pus in the motions. Œdema of the face and limbs may set in, and death result from exhaustion.

In our patient, a little native girl, there was rather high fever, with persistent diarrhœa, great wasting, and severe anæmia. No blood in the motions. The *Balantidia*, which were abundant, were associated with numerous *Trichomonata* and *Oicomonas;* moreover, the patient harboured various worms, ova of *Ancylostoma duodenale, Ascaris lumbricoides*, and *Trichuris trichiura* being present. Some of the symptoms may have been caused by these parasites.

Complications.—The parasite may enter the liver and form cysts. It may be associated with other parasites—*Amœbæ, Trichomonata, Oicomonata*, etc.

Treatment.—The symptomatic treatment laid down for amœbic dysentery may be tried, beginning with castor oil or salines, and followed by intestinal irrigations of tannic and boric acids or quinine. Ipecacuanha and emetine may be administered as described for amœbic dysentery. Large rectal injections of a solution of methylene blue (1 in 3,000), combined with the internal administration of the same drug in 1 or 2 grain doses in cachets or pills, may also be tried. Oil of chenopodium has been recommended.

Some authorities give Salvarsan by intravenous injection.

Prophylaxis.—It is not certain that the parasite found in the pig is the same as the human parasite, and, further, the method of infection being quite unknown, no useful remarks can be made with regard to prophylaxis.

(*f*) Spirochætic Dysentery.

This type of dysentery was first described by Le Dantec. It has not been generally accepted, as spirochætes may be found in cases of typical bacterial and amœbic dysentery and even in normal stools in which *Spiroschaudinnia eugyrata* Werner, *emendavit* Fantham, is commonly met with. It is very probable, however, in our opinion, that there may be pathogenic intestinal spirochætes capable of giving rise to dysenteric symptoms. In a case observed by one of us preparations from the muco-pus were teeming with spirochætes, while amœbæ and ciliates were absent, and the further bacteriological examination showed absence of dysentery bacilli. Emetine and serum treatment had no effect, and the patient made a very slow recovery.

Remarks.—A mistake not rarely made is to recognize as spirochætes the undulating forms of a germ found by Castellani in Ceylon, and described by him in 1910, under the term of *Spirillum* (*Vibrio, Vibriothrix, Spirobacillus*) *zeylanicum*, in the *Philippine Journal of Science*, vol. v., No. 2, Section B, 'Medical Sciences,' July, 1910.

The generic classification of this germ is most difficult, as it is extremely polymorphic, the same preparation showing bacillary, vibrionic, undulating forms.

At times coccus-like and also fairly large spherical bodies are seen and claviform swellings, and Castellani has recently created a new genus for it, *vibriothrix*, the name of the organism becoming, therefore, *Vibriothrix zeylanica* Castellani, 1910. This germ is found also in Europe, as recently shown by Castellani, Spagnuolo and Russo, by Taylor, Ghiron, and by Douglas.

Morphology.—The best way to see the characteristics of the germ is to make a preparation from the water of condensation of a glucose agar tube inoculated with it. In the same preparation forms so different in shape may be met with, that one might think one had to deal with two or more organisms living in symbiosis, but by plating and replating one never succeeds in separating the various forms. Long undulating forms may be present 20 to 40 microns in length, and also numerous short vibrio-like and bacillary forms, and in preparations from the pellicle which forms in certain media, curved filaments may be found with claviform swellings, and also globular small bodies.

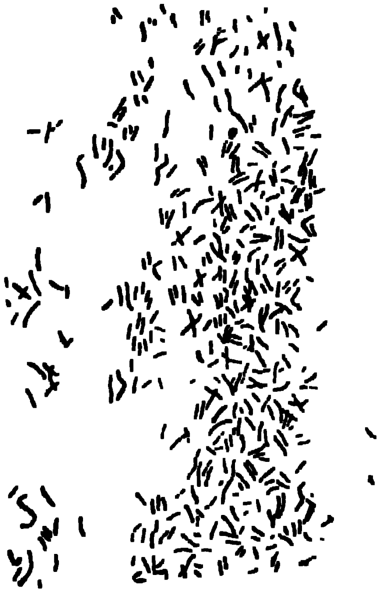
FIG. 764.—*Vibriothrix zeylanica* (CASTELLANI, 1910).
(Vibrio-like forms from a culture.)

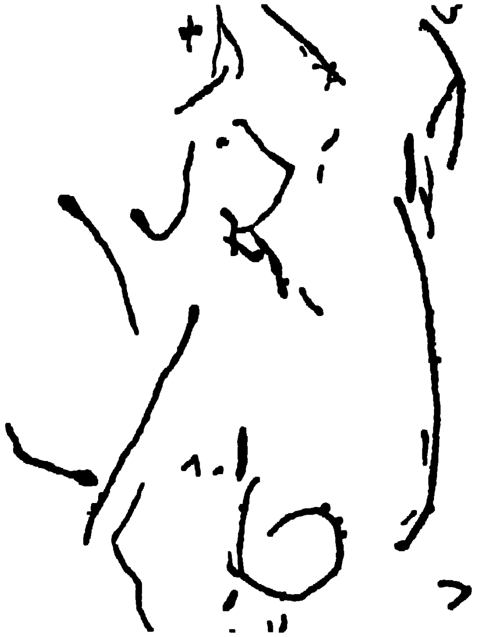
FIG. 765.—*Vibriothrix zeylanica* (CASTELLANI, 1910).
(Forms from the pellicle in a culture.)

The germ is easily stained by the usual aniline dyes. It is Gram-negative.

Motility.—The germ is motile.

Cultural and Biochemical Characters.—On MacConkey, Endo, and Drigalski-Conradi plates the colonies are similar to those of the germs of the typhoid dysentery group, the organism being a non-lactose fermenter. The micro-organism grows well on all the usual laboratory media, in the water of condensation of glucose agar tubes producing a rather characteristic pellicle. It often produces a pellicle also in broth and several sugar media. It produces neither acidity nor gas in any of the usual carbohydrates—lactose, glucose, levulose, galactose, saccharose, dulcite, mannite, maltose, dextrin, raffinose, arabinose, adonite, inulin; on the contrary, there is often production of alkalinity.

Most strains are non-pathogenic to rabbits and guinea-pigs when inoculated subcutaneously, but there are exceptions.

(g) Entoplasmic Dysentery.

In two cases of dysentery contracted apparently in Burma, Castellani observed peculiar protozoal bodies, while amœbæ and dysentery bacilli were absent. In fresh preparations one sees large rather elongated or oval bodies with one extremity, the one which in stained preparations appears mammillary, shaken, so to speak, by an extremely frequent vibrating movement, which makes one suspect the presence of flagella or cilia, or an undulating membrane. No such structures, however, can be detected either in fresh preparations or in slides stained with the usual methods, such as Giemsa, iron—hæmatoxylin, etc.

The protoplasm presents numerous roundish vacuoles, none of which is contractile. No distinct nucleus is evident in fresh preparations. The parasite does not emit true pseudopodia, but changes in the shape of the body take place.

Stained Preparations.—The typical forms have a peculiar flask-like appearance, but round forms are also found, the maximum diameter varying between 45 and 80 microns. In preparations stained with Leishman the protoplasm is stained blue and presents numerous non-stained roundish vacuoles regularly distributed all over. In certain individuals a large mass of chromatoid roundish coccoid granules are present, which represent, according to Mesnil, a diffuse nucleus. In one specimen the granules were bacillary in shape. In none of the bodies were flagella, cilia, or evidence of any undulating membrane seen by Castellani, Mesnil or any protozoologist to whom the specimens were submitted. It may be, of course, that such organs were of such extremely delicate nature that they required the use of special methods to put them in evidence.

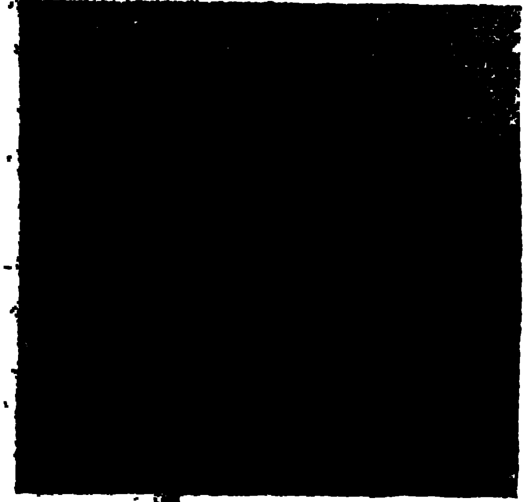

FIG. 766.—*Entoplasma castellani* PAUL, 1914.

Zoological Position of the Parasite.—It is impossible to classify this parasite, which, for convenience' sake, might be maintained in the temporary genus *Entoplasma*, until further researches render possible its proper classification. The suggestion has been made that these bodies are probably forms of *Chilomastix mesnili* Wenyon, but the size of the bodies apart from other characters is evidently against this hypothesis.

Symptomatology.—This was identical to what one sees in a case of amœbic or bacterial dysentery of medium gravity, the stools containing blood and mucus.

Treatment.—Salines were administered with good effects. Emetine was also given, but it is difficult to say whether it had any part in inducing the cure of the condition.

II. THE PLATYHELMINTHIC DYSENTERIES.

Fasciolopsis buski, *Schistosoma japonicum*, and *S. mansoni* cause dysenteric symptoms, which can only be diagnosed by the discovery of the eggs in the motions. The symptoms produced by the latter worms are described in detail in Chapter LXXIX. (p. 1864), while those of the former still require detailed investigation.

III. THE NEMATHELMINTHIC DYSENTERIES.

Nemathelminthic dysentery is due to the sclerostome (*Œsophagostomum brumpti* Railliet and Henry, 1905), immature females of which were found by Brumpt in cyst-like nodules in the cæcum and colon of a negro in West Africa. Similar symptoms are caused by *Œs. stephanostomum* var. *thomasi* Railliet and Henry, 1909, discovered in South America by Thomas (see p. 661).

IV. THE ARTHROPODIC DYSENTERIES.

We have already drawn attention to the fact that diarrhœas and dysenteries may be caused by the presence of species of the Chilopoda and Diplopoda, and by the larvæ of flies in the intestine, but these are rare, and are sufficiently described in Chapters XXVIII. and LXVII.

B. DYSENTERIES CAUSED BY BACTERIA:

The Bacillary Dysenteries.

Synonyms.—*French* : Dysenterie Bacillaire. *Italian* : Dissenteria Bacterica. *German* : Bacillenruhr.

Definition.—The bacillary dysenteries are acute or chronic, endemic or epidemic, specific intestinal disorders caused by several varieties of bacteria, which are disseminated largely by means of the fæcal matter of dysentery carriers, as well as by that of persons suffering from these disorders. From the sources of infection the germs are conveyed to food or drink by the agency of flies, dust, surface water, and by direct contact with any contaminated substance. Infection usually takes place by the consumption of contaminated food or drink, more rarely by direct contact with contaminated substances. In the body the micro-organisms cause a specific inflammation of the large, and occasionally also of the small, intestine, which is characterized by diarrhœa, usually accompanied by pain, tenesmus, and the passage of blood and mucus in the motions. More rarely the bacilli cause a general septicæmia.

History.—For years the theory of a bacterial causation for dysentery found many supporters, among whom may be mentioned Klebs, Prior, Ziegler, Hlava, Chantemesse, Widal, and Grigoriew, all of whom attempted to isolate a specific organism.

Maggiora, Laveran, Arnaud, and Escherich believed that the *Bacillus coli communis* was the true cause, while Celli described as the cause of the disease a bacillus fermenting glucose and clotting milk, which he called the *Bacillus coli dysentericus* ; but according to his more recent description some strains produce very little or no gas in glucose media, and may not clot milk, and closely resemble Flexner's bacillus.

During an epidemic in the province of Oita, in Japan, Ogata isolated a bacillus which liquefied gelatine, stained by Gram's method, and produced intestinal ulcers in guinea-pigs and cats, a discovery which was confirmed by Vivaldi of Padua, but not by other observers.

In the same year Calmette announced that the *Bacillus pyocyaneus* was a cause of dysentery in Cochin China, an observation since confirmed by Lartigan in the United States, Adami in Canada, and others, but not generally accepted.

The elucidation of the ætiology of bacillary dysentery is due to the investigations of Shiga in Japan and Kruse in Germany during the years 1898-1900. They described as the cause of the malady a short bacillus, not decolourized by Gram, not clotting milk, not producing gas in any sugar media. There was at first some difference of opinion as regards motility, but Kruse's statement that the bacillus was always non-motile has been proved to be correct. Kruse was also the first observer to state that there was more than one variety of dysenteric bacilli.

In 1900 Flexner reported that he had isolated a moderately motile bacillus from cases of dysentery in Manila identical with Shiga's bacillus, and producing a severe muco-hæmorrhagic diarrhœa in a human being who was the victim of an accidental laboratory infection. This bacillus was later demonstrated to be non-motile, and to differ in several respects from Shiga's bacillus, notably in fermenting certain sugar media, and could be distinguished therefrom by the different biological tests. These results have been frequently confirmed by observers in different parts of the world. Strong isolated a bacillus slightly different from that of Flexner, also from cases in Manila.

In 1903 Hiss and Russell separated a bacillus which closely resembles Flexner's bacillus, but fails to ferment maltose. This bacillus is often called the Y bacillus. In 1904 Castellani isolated a bacillus from cases in Ceylon which he named the 'paradysenteric bacillus,' and later he described the group of metadysentery bacilli. Several other germs have been described by various authorities, while Kruse, Flexner, Strong, Lucet, Conradi, and others have made a detailed study of the pathogenesis of the disease.

Climatology.—Bacillary dysentery is found all over the world, in cold, temperate, and warm climates, but especially in the latter. In temperate climates the germs probably cause a type of the infantile diarrhœas which are such potent factors in the infantile mortality of those regions, while they are also responsible for the endemic and epidemic cases so frequently met with in Europe and America.

In the tropics they are also extremely common, occurring more frequently at the end of the dry and the beginning of the wet seasons. In certain regions and at certain times the virulence of the complaint appears to be increased, the reason of which is not at present apparent. Probably it depends upon the greater possibility of infection, owing to the drinking-water being highly contaminated in warm weather, or perhaps to the presence of multitudes of flies. The agency of these or other factors has not been completely inquired into. Whatever the cause may be, it is well known that at times the disease may spread in epidemic form over larger or smaller areas. These epidemics may be institutional, urban, or rural, or they may attack a district, a country, or a continent. Thus, celebrated epidemics are known to have occurred in Europe in 1538, 1717-19, 1779-83, and 1834-36.

Dysentery is particularly prone to occur whenever sanitation is defective, and hence is found prevalent in lunatic asylums and in armies in times of active service, as is clearly shown by the present war; and this factor appears to be more potent than any climatological cause, and, indeed, may be the principal reason why the disease is so prevalent in the tropics, though the high atmospheric temperature of these regions must assist the growth of the organisms.

Ætiology.—Bacillary dysentery is brought about by a group of closely allied bacilli which may be separated into several principal types according to their fermentative action on glucose, mannite, maltose, saccharose, lactose.

I. *Shiga-Kruse Type.*—Glucose fermented (acid only); mannite, maltose, saccharose, lactose not fermented. Agglutinated only by homologous serum. Not agglutinated by normal horse serum. Very toxic to rabbits.

II. *Flexner Type.*—Glucose, mannite, maltose fermented (acid only); saccharose not fermented, but there are exceptions; lactose not fermented. Agglutinated by homologous serum and Y serum, and not unfrequently by Shiga serum and, as shown by M. Nicolle, normal horse serum. Non-toxic to the rabbits.

III. *Strong Type.*—Glucose, mannite, and saccharose fermented (acid only); maltose not fermented. Agglutinated by homologous serum only. Most authorities consider it non-toxic, but the original Strong strain was very toxic to rabbits.

IV. *Hiss and Russell Type.*- Glucose and mannite fermented (acid only); maltose, saccharose, lactose not fermented. Agglutinated by homologous and Flexner serums, at times by Shiga serum and normal horse serum.

V. *Metadysentery (Castellani) Type.*—Differs from all above groups in fermenting (slowly and acidity only) lactose in addition to glucose. Well agglutinated by homologous serum; not agglutinated by Flexner and Shiga serum. Non-toxic to rabbits.

For more details on bacteria of the dysentery group the reader is referred to Chapter XXXVI., p. 936. Less important types are Rüffer and Willmore's *Bacillus El Tor* No. 1, Baerthlein's *Bacillus dysenteriæ*, Shiga's *B. dysenteriæ Tokio*, Castellani's *Bacillus paradysentericus*, etc.

Hiss divides the dysentery bacilli into four principal groups:—

Group 1: Ferments glucose only (Shiga-Kruse bacillus).

Group 2: Ferments glucose and mannite (*Bacillus Y*).

Group 3: Ferments glucose, mannite, and saccharose (Flexner - Manila bacillus).

Group 4: Ferments glucose, mannite, saccharose, maltose, and dextrine (Harris's bacillus, Wollstein's bacillus).

Leitz, Kruse, and Shiga have called attention to the fact that while the fermentation of mannite is a reliable means of differentiation, not so much importance can be given to the fermentation of maltose, saccharose, and dextrine.

Lehman and Neumann give the following classification:—

1. Shiga-Kruse: No fermentation of mannite, maltose, saccharose.
2. Flexner: Ferments mannite and maltose.
3. Strong: Ferments mannite and saccharose.
4. B.Y.: Ferments mannite; has no action on maltose and saccharose.

Bahr has noted that the various strains may vary their fermentative character when passing through flies.

Under the term *B. pseudo-dysentericus*, Kruse described a non-lactose fermenting bacillus which is the cause of many outbreaks of asylum-dysentery in Germany. Later he used the term 'pseudo-dysentery' to denote every variety of dysentery caused by bacilli other than those of the Shiga-Kruse type.

Celli's *B. coli dysentericus*, according to the original description, is motile, clots milk, and produces gas in some sugar media, and therefore cannot be considered to belong to the dysentery group. According, however, to more recent descriptions by De Blasi and others, some strains of the *B. coli dysentericus* may not produce gas, and may not clot milk, and closely resemble Flexner's bacillus.

The true dysenteric bacilli may be differentiated from one another by their varying fermentative actions upon carbohydrates, by agglutination, Pfeiffer's reaction, and Castellani's absorption method. A table showing the characters of the more important dysentery germs as well as other intestinal bacteria will be found in Chapter XXXVI., p. 944. We wish to emphasise, however, the fact that the biological reactions of the bacilli are much more reliable than the fermentative changes.

The dysenteric bacilli are distributed mainly by the fæces of persons suffering from the disease, but there are also 'dysentery carriers' in the true sense of the word, who are perhaps not merely an important source of infection, but possibly *the important factor* in the dissemination of dysentery.

Strong and Musgrave have proved that infection takes place by the mouth by feeding a man with pure cultures of the dysentery bacillus, which quickly produced an attack of dysentery, characterized by motions containing blood and mucus, from which the typical bacilli were grown.

The most prevalent method of infection is direct contact with a patient or a carrier, or with articles or more especially food contaminated by them. The bacilli are conveyed from fæcal matter to the mouth by the contamination of food or drink, or the utensils for preparing or serving the same. This method of infection is probably common in hospitals and asylums, cooks and all persons engaged in handling food being possible disseminators. Another method of dissemination would appear to be the dust, especially in places with badly polluted soils. Flies, as has been experimentally demonstrated by one of us, are capable of carrying the bacilli, and are therefore probably a prolific source of infection in tropical countries. Luckily the water-supply is very rarely infected. With regard to lower animals, Kruse and Bowman have recorded spontaneous bacillary dysentery in monkeys, due to bacilli of the Flexner group, and Messerschmidt has found a bacillus of Type Y in the fæces of apparently healthy rabbits, so that there may be a possibility that lower animals are of importance in the spread of the disease.

It would, however, appear that the bacilli are capable of living in the alimentary canal without causing the symptoms of the disease until the vitality of the host is lowered by some agency, such as a chill, an attack of diarrhœa, or some intercurrent disorder, when they are capable of producing their ill-effects.

This carrier problem in the ætiology of dysentery is of great importance, and though as yet it has never been *conclusively* proved that an outbreak has been due to a carrier, still it is known that the bacilli can be excreted in an intermittent manner by people suffering from mild relapses. The dysentery carriers are classified into—(1) healthy, (2) precocious, (3) convalescent, (4) relapsing, and (5) chronic carriers. The healthy carrier is rare, but May has found 22 out of 573 persons examined during an epidemic. The precocious are believed to be very rare. The convalescent and relapsing carriers are well known, of which the latter are of the greatest importance in spreading the disease. The chronic carrier excretes but few bacilli, but may be of importance in the spread of the disease. With regard to the geographical distribution of the principal forms of bacilli, it may be stated that practically all of them seem to have a cosmopolitan distribution.

Ætiological Classification of Bacterial Dysenteries.—An ætiological classification of bacterial dysenteries has been suggested as follows:—

I. Due to *B. dysenteriæ* Shiga-Kruse—*Bacterial dysentery sensu stricto.*

II. Due to mannite fermenting dysentery bacilli (Flexner, Hiss and Russell, Strong)—*Paradysentery.*

III. Due to germs having the general character of the dysentery bacilli; but slowly fermenting (acidity only) lactose and not agglutinated by Shiga-Kruse, and paradysenteric serums—*Metadysentery.*

Pathology. The bacilli taken into the body with food and drink pass to the intestine, in which they grow and multiply, and along the whole length of which they can be found. The researches of Flexner and Sweet have proved that the bacilli can abound in the small intestine, where no pathological lesion may be found. In the bowel they give rise to the toxins, of which two are known—one which acts upon the lower bowel, and the other on the nervous system. Both these toxins are absorbed into the blood, but the first, being excreted by the large bowel, causes the lesions well known to be associated with dysentery, and explains the localization of these lesions. In the process of excretion this toxin first causes an exudation of lymph into the submucosa, and later into the mucosa. This lymph coagulates, and is invaded by a cellular exudate, and in due course the glands and the tissue of the mucosa and the muscularis mucosæ are destroyed by coagulative necrosis, with thrombosis of the vessels. This fibrinous or diphtheroid membrane is at first most marked on the summits of the ridges, and may not be found at the bottom between the ridges. It contains large numbers of micro-organisms of varying characters, while the depths of the submucosa may reveal accumulations of leucocytes, and the peritoneal coat may be œdematous. The micro-organisms destroy the fibrinous false membrane, which may separate off in flakes, thus causing ulcers, which are at first superficial, but later become deep and extensive. After treatment these ulcers heal with the formation of connective tissue, thus producing a scar in the mucous membrane, which in due course becomes pigmented from the sulphuretted hydrogen of the bowel acting on the iron of the blood. The other toxin may attack the nervous system, causing peripheral neuritis.

Very rarely do the bacilli enter the blood stream, and cause true septicæmia, though such cases have been recorded by Rosenthal and Markwald, the latter observer stating that he found the bacilli in the blood and intestinal contents of a fœtus which had been prematurely expelled from the uterus of a mother who was suffering from bacillary dysentery. Darling has actually grown the bacillus from the blood of cases of bacterial dysentery. Occasionally the bacilli affect the joints and very rarely the conjunctiva.

Morbid Anatomy.—On opening the abdomen, the peritoneum is found in general to be normal, but the bloodvessels of the large bowel are seen to be injected, and the mesocolons may be infiltrated with lymph, or firm and fibrinous. There may be adhesions of the sigmoid colon to the omentum, pelvis, bladder, or small intestines, while the splenic flexure may be adherent to the spleen and surrounding parts, and the hepatic lexure to the liver. The cæcum may show adhesions to the omentum, and more rarely there may be pericæcal abscess. Signs of a general peritonitis may be met with, and will generally be associated with a gangrenous or perforated condition of the intestine.

The small bowel is usually normal, but may be hyperæmic or, much more rarely, ecchymotic. The walls of the large intestine are usually considerably thickened and hyperæmic, and may at times be found to be gangrenous along a great or lesser extent of their course. On opening the large bowel, the mucosa will be seen to be covered with a coagulated exudate in the form of a false membrane, which is more evident on the summits of the folds, and is especially well marked in the sigmoid colon, the cæcum, and the ampulla of the rectum. Around the areas covered by the false membrane the mucosa is seen to be hyperæmic and œdematous. As a rule, numerous ulcers are also to be seen, with clean surfaces, elevated edges, and a base formed by the submucosa. These ulcers may be very extensive, leading to the separation of large sloughs, or may extend deeply into the coats of the bowel, causing perforation and peritonitis, or in less serious cases induce the exudation of much lymph into the peritoneum coat, which subsequently causes adhesions.

In post-mortem examinations of cases which have died from some other complaint it is not unusual to find the intestines matted together in the pelvis, the omentum adherent to the colon, and the colon to the bladder, etc. On opening such a colon it will be found scarred by old dark-coloured cicatrices, indicating the position of the healed ulcers of a previous dysentery. More rarely the cicatrization may have proceeded to such an extent as to cause narrowing of the lumen of the gut, and still more rarely may the process lead to abscess formation in the adherent omentum, the pus of this abscess slowly working its way into the anterior abdominal wall, and so to the exterior. The cæcum and other parts of the bowel may show polypi protruding from the mucous membrane, a condition often called 'colitis polyposa.'

In the epidemic diarrhœa of infants, the lesions which may be found are classifiable into hyperplasia of the agminated and solitary glands, superficial ulcers, lesions resembling those described above, or invisible lesions.

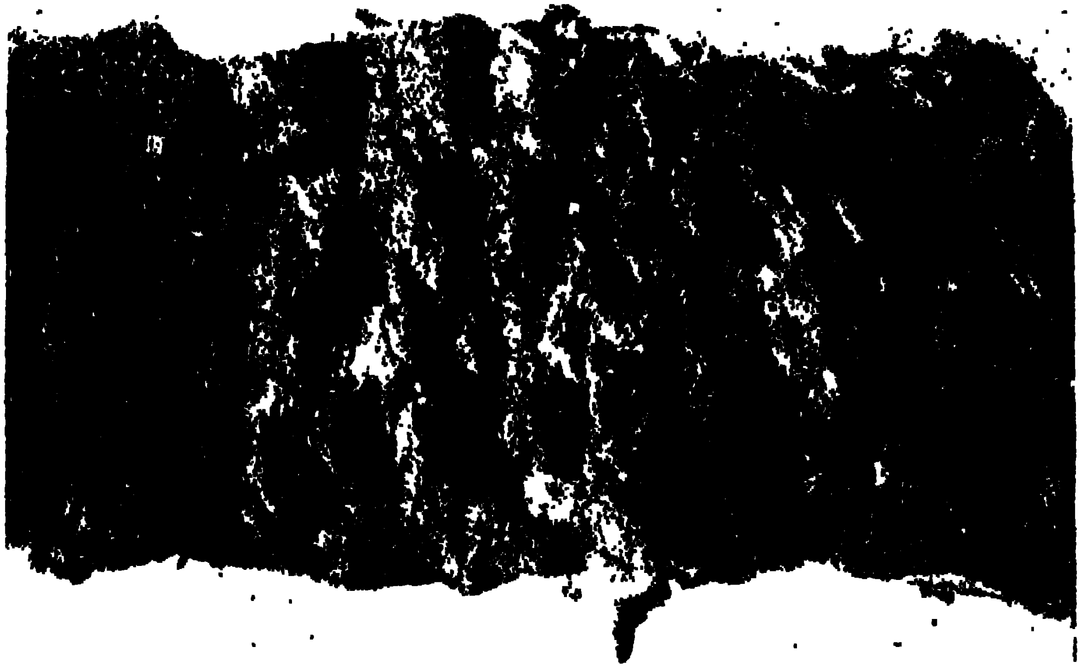

FIG. 767.—THE COLON IN A CASE OF BACILLARY DYSENTERY.

Microscopically, there is at first an exudation of fluid containing but few cells into the submucosa, while the mucosa is congested, but the glands are seen to be quite normal. A little later the exudate into the submucosa is seen to have formed fibrin, and the vessels of this coat are noted to be dilated, to contain numerous polymorphonuclear leucocytes, which may be seen undergoing diapedesis into the surrounding tissue. In this stage the exudate has also affected the mucosa, the glands and tissue of which may be seen to be undergoing coagulative necrosis. In a still later stage nothing is to be seen of the mucosa, and in bad cases of the submucosa, except fibrinous exudate, mixed with cells and blood-vessels. Often, however, the submucosa shows dense collections of leucocytes. Where ulcers occur, the amount of exudate covering the muscular coat may be thin, while in other places it may be thick. The peritoneum is also generally infiltrated by a coagulated exudate.

Symptomatology.—The different appearances presented by the bacillary dysenteries may be grouped into:—

1. The acute type.
2. The gangrenous type.
3. The entero-dysenteric type.
4. Choleraic dysentery.
5. Chronic dysentery.
6. Dysenteric diarrhœa.
7. Dysenteric infantile diarrhœa.

1. *Acute Bacterial Dysentery.* -The incubation varies from twenty-four hours to three or four days, and is not well known in natural infections. Usually after an incubation of a few days, during which the patient may not feel quite well, and may complain of constipation or diarrhœa, with loss of appetite and malaise, the disease begins with an attack of pain in the lower part of the abdomen, and an urgent desire to defæcate, which results in the passage of perhaps an ordinary formed fæculent motion, which temporarily relieves the pain. Soon, however, another attack of pain is felt, generally in the region of the umbilicus, from which it radiates to any part of the large intestine, and this is again associated with a desire to defæcate and the passage of a motion which is composed of fæcal matter, but may now be soft. The pain increases, and the desire to defæcate becomes more and more frequent, until almost constantly present, while any nourishment, however bland and unirritating, at once produces a desire to defæcate. After a time the patient sits almost continuously upon the commode, straining violently, and passing at first motions of fæculent matter mixed with blood and mucus, and then blood and mucus mixed with a little fæculent matter, and finally nothing but a little blood and mucus. As a result of the straining and the passage of numerous motions, the anus becomes inflamed and very painful, and prolapse of the bowel is not uncommon, and adds greatly to the distress of the patient. The urine diminishes in quantity, and therefore may show an increased quantity of urea, and at times may contain a trace of albumen. Pain is often complained of in the region of the bladder during and after straining at the commode. In slight cases the number of motions may be only about one every hour, but in more severe cases they number from fifty upwards, until they are passed almost continuously. This constant pain and desire to defæcate naturally weakens and exhausts the patient very quickly, for it prevents sleep and rest.

In ordinary cases the tongue is moist and coated with a white fur, and usually the patient is thirsty, but not markedly so, except in bad cases. Nausea is often present, and there is no desire for food, which is badly digested. There is often epigastric pain. Vomiting occurs, but is relatively unusual in cases which are taken in hand early and properly treated. The abdomen soon becomes sunken and tender, especially along the course of the large bowel, but this tenderness may be restricted to certain areas only of that bowel. On careful palpation the thickened bowel may at times be felt, but usually it is too tender to allow such manipulation. With the numerous motions, it may be imagined that constipation would not occur; but this is not so, for the disease may be limited to the lower bowel, and as it is the involvement of the rectum which causes the tenesmus and constant desire to defæcate, fæces may be accumulating in the higher region of the large bowel —a condition which may be recognized by the distension. Shiga, indeed, describes an ascending variety of acute dysentery, which, beginning in the rectum, spreads upwards along the large bowel, as well as a descending variety, which usually starts in the small intestine. The typical motions are composed of blood and mucus only, but in bad cases they may consist of a reddish albuminous fluid containing white shreds. The typical dysenteric motions have no fæcal smell, and microscopically show numerous micro-organisms, leucocytes, and red cells, and epithelial débris and cells. Usually there is some fever, ranging from 99° to 103° F. The pulse is quickened, and in bad cases may be not merely rapid, but irregular, when the heart will be found to be dilated, and perhaps hæmic murmurs may be heard; but these symptoms are unusual, except in grave cases. The blood usually shows a diminution in the red cells, and a slight polymorphonuclear leucocytosis. The lungs are usually normal. Delirium is unusual.

If the patient is to die, the motions assume the serous character mentioned above, the pulse becomes rapid and irregular, the temperature drops to subnormal, the motions diminish in number, hiccough appears, and exhaustion ushers in death generally during the second or third week.

If the patient is to recover, the motions become more fæculent, and the blood and mucus generally disappear, while the pain and tenesmus subside, the pulse returns to normal, the tongue cleans, and convalescence begins about the end of one week in mild, or of one month in more severe cases.

2. *Gangrenous Dysentery.*—This most severe type of the disease may begin insidiously with some slight fæculent diarrhœa, which may not attract attention until suddenly the patient becomes collapsed and dies within a few hours without the passage of the typical motions. Thus a prisoner may stand in the dock throughout the whole day, and then die in the night from gangrenous dysentery, while his sudden death may awake suspicions of suicide.

The more usual history is that, during an attack of acute dysentery, the abdominal pain and tenesmus become very severe, while the motions alter their characters, becoming exceedingly offensive, and containing gangrenous sloughs composed of the mucosa and the submucosa. These sloughs may be small or large, and even at times may be tubular. The motions are now exceedingly numerous, and sometimes hæmorrhage *per anum* may take place. The patient becomes extremely exhausted, the pulse small and frequent, the temperature falls to subnormal, and the extremities become cold up to the knees and elbows, while the motions are passed involuntarily, and death takes place in some two or three days from exhaustion. Recovery from an attack of gangrenous dysentery is extremely unusual, but when it does occur the pulse slows, the temperature rises, the motions become fæculent again, and the urine, which has been suppressed, reappears.

3. *Entero-Dysentery*.- This variety begins with one or more rigors, and a rise of temperature to 103° F. or more. The temperature keeps high, assuming either a continuous or a high remittent type, and is associated with a dry tongue, and a mouth covered with sordes, fœtid breath, headache, malaise, pains in various parts of the body, marked epigastric disturbance, and occasionally with ecchymoses under the skin in various parts of the body. The characteristic signs of abdominal pain and tenesmus are absent, and the motions, though containing blood and mucus, are mixed with considerable quantities of fæculent matter. The mind is clouded, the patient becoming very stupid, sleepless, and at times delirious. Abscesses may now appear in varying parts of the body, but especially in the parotid or the ischio-rectal fossæ, while carbuncles, bedsores, and peritonitis may also occur. Death usually ensues after a few days' illness from exhaustion, toxæmia, or hyperpyrexia.

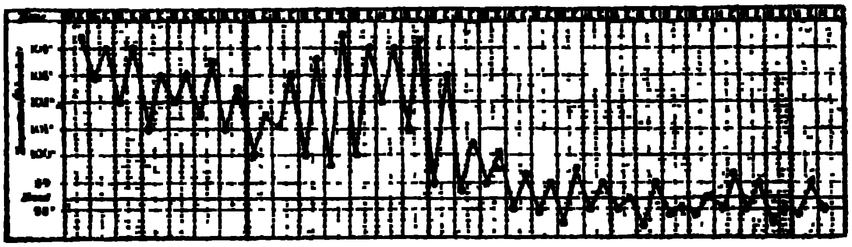

FIG. 768.—TEMPERATURE CHART OF A CASE OF BACILLARY DYSENTERY, SHOWING THE EFFECT OF SERUM TREATMENT.

Chart by Archibald.

4. *Choleraic Dysentery*. Castellani called attention some years ago in the tropics, and again recently in various war zones, to a type of dysentery or serous diarrhœa which is often mistaken for cholera. The onset is sudden, with rice-water-like or serous motions; there may be vomiting, and the condition of the patient becomes rapidly very grave. In most cases, however, a motion is passed now and then tinged with blood, and this clears the diagnosis.

5. *Chronic Bacterial Dysentery*.—Chronic dysentery appears after an attack of acute dysentery which has apparently been cured, but in which, after a period of quiescence, diarrhœa appears. About five or six motions, composed of watery, evil-smelling, fæcu-

lent matter, are passed per diem, and may at times contain blood and mucus, or simply mucus. After a time these symptoms disappear, and the motions become normal, or there may be slight constipation. In due course, however, the diarrhœa returns, and these exacerbations recur for months and years, and seriously affect the patient's general health. The appetite becomes bad; the tongue red and smooth, or flabby and coated; digestion is impaired, and fermentative changes cause the bowels to be distended with gas; while hæmorrhage, slight or severe, may take place from the nose or under the skin. Profuse sweats may occur at night, and tend to exhaust the patient. Recovery may take place spontaneously, or after treatment, or the diarrhœa, continuing fitfully, may gradually wear out the patient, who may die of exhaustion or some intercurrent disease. Some authorities believe that chronic dysentery may become sprue. We do not agree with them, although, of course, sprue may develop in a case of chronic dysentery.

6. *Dysenteric Diarrhœa.*- The term 'dysenteric diarrhœa' may be applied to the non-bloody diarrhœa of chronic dysentery, and to those cases of diarrhœa which occur during an epidemic of dysentery, and in which the bacillus is either proved to be present in the motions, or the patient's blood agglutinates in high dilution one of the dysenteric bacilli. The attack may in no way differ from an ordinary attack of diarrhœa due to other causes, but is apt to recur and to turn into chronic dysentery.

7. *Dysenteric Infantile Diarrhœa.* -Diarrhœa is an extremely common disease among infants in the tropics, but has not yet received the attention which it has in the United States, in Europe, and in Japan, where it is called 'ekiri.' It is believed to be due to Flexner's bacillus, or more rarely to Shiga-Kruse's bacillus; while the symptoms resemble entero-dysentery, being characterized by beginning with vomiting, and a rise of temperature from 103° to 104° F., a dry mouth, coated tongue, distended and tender abdomen, and the passage of motions containing fæculent matter, often green in colour, generally mixed with blood and mucus. The fever is of the remittent type, and as the disease progresses the child wastes, and may become convulsed or comatose and die, or may live for weeks, suffering from repeated attacks of diarrhœa, and finally die from exhaustion. If recovery is to take place, the temperature declines and the diarrhœa ceases, but the child is left in a pale and emaciated condition, from which it takes months to recover.

Complications.—Peripheral neuritis is not uncommonly met with, generally in a mild form, and often confined to one nerve. Arthritis and polyarthritis are also not uncommon, while inflammation of the tendon-sheaths may also take place. In entero-dysentery parotid buboes are not uncommon, while abscesses in other parts of the body and peritonitis may develop. In gangrenous dysentery hæmorrhage may be a serious complication. Typhoid fever may occur at the same time as a dysenteric attack, and is a serious complication. We have met with several cases of appenditicis developing in people convalescent from dysentery. Conjunctivitis and iritis have been recorded.

Sequelæ.—One of the most important sequels of dysentery, to which Cantlie has drawn attention, is stenosis of the large bowel, and more particularly of the sigmoid flexure, due to cicatricial contraction of the healing ulcers. The symptoms are the onset of an insidious constipation, associated in due course with a sensation of distension in the abdomen, loss of appetite, and nausea. The constipation is apt to alternate with attacks of diarrhœa. In due course the constipation becomes severe, and is accompanied with recurrent attacks of colic, in which the pain may be localized or radiating, and sooner or later vomiting occurs. On inspecting the abdomen a swollen region may be observed, and the attacks of colic may be seen to be associated with visible peristaltic movements, while more or less meteorism occurs. Succussion sounds may be heard over the dilated bowel. This condition is serious, and must be energetically treated.

According to some authors, 'sprue' is a sequel to dysentery, and we have, in fact, seen several cases of sprue developing in patients who have been suffering from chronic dysentery. We believe, however, the two diseases to be of different ætiology.

Diagnosis.—It may be of advantage to say a few words, first, on the diagnosis of dysentery in general. In presence of a patient suffering from abdominal pains, with frequent stools containing blood and mucus, the practitioner is, as a rule, justified in making the generic diagnosis 'dysentery.'

Next the specific diagnosis must be made—viz., what type of dysentery is the patient suffering from. For practical purposes it is sufficient in the enormous majority of cases to keep in mind the following types: amœbic dysentery, ciliar dysentery, bacterial dysentery. A particle of the muco-pus, immediately after evacuation, should be examined microscopically, and this examination can be carried out with great advantage at the bedside by means of a portable microscope. If the microscopical examination shows presence of amœbæ of the histolytica type, especially if containing red blood cells, the diagnosis will be *amœbic dysentery*. If amœbæ of the histolytica type are absent, and ciliates of the balantidium type are present, the diagnosis will be *ciliar dysentery*. If on prolonged and repeated examination, amœbæ and ciliates are absent, the diagnosis of probability will be *bacterial dysentery*. A probable diagnosis of bacterial dysentery can be made also by the practitioner who is not in position to carry out microscopical examinations, if emetine does not make the dysenteric symptoms disappear within three days.

The diagnosis of bacillary dysentery has to be made with special reference to pseudo-dysentery and amœbic dysentery, especially when there is blood and mucus in the motions, and from the various forms of diarrhœa when these signs are absent.

With regard to pseudo-dysentery, cancer and syphilis of the rectum and inflamed hæmorrhoids may give rise to tenesmus and the passage of blood and mucus, but can be differentiated by the history and by an examination of the rectum. Cancer of the colon and intussusception may also cause the passage of blood, with or without mucus and with or without tenesmus, but the history and a careful abdominal examination, together with the discovery of a localized swelling, should serve to distinguish these affections. Parametritis on the left side may cause diarrhœa, and more rarely the passage of blood and mucus, but the absence of tenesmus, the presence of pain more at the side of the uterus than in the sigmoid colon, should indicate the necessity of an examination *per vaginam* or *per rectum*, when the nature of the case will be cleared up. A careful examination of the fæces should exclude such causes as fish-bones injuring the rectum. Mercurial poisoning can be distinguished by the history, the presence of salivation, etc. The diagnosis from amœbic, balantidic, and the other dysenteries of animal origin can only be made by the careful microscopical examination of the fæces, when the absence of these parasites will be made certain. The absence in dysenteric stools of Charcot-Leyden crystals and presence of very abundant cellular exudate with macrophages and preponderance of polymorphonuclears points to the condition being bacterial rather than amœbic.

Positive diagnosis can, however, only be made by a bacteriological examination of the fæces and the determination of the specific bacillus. Agglutination tests with the patient's blood are not of much use in acute cases, as agglutinins are not present in the blood the first few days of the disease.

For the bacteriological diagnosis a shred of mucus or pus is smeared over a plate of MacConkie's bile-salt-lactose-neutral-red agar, by means of a bent glass rod or Kruse's platinum pencil.

Two more plates of the same medium are prepared in a similar manner without recharging the rod or pencil.

Any white colonies which develop are further investigated as to their sugar reactions, and by using the agglutination and absorption methods.

The following method will be found useful: - Twenty white colonies are selected; in this way we discard all lactose rapid fermenters. From each colony one glucose peptone water (or glucose agar) and a litmus milk are inoculated. After sixteen to twenty-four hours at 35° C. to 37 C. the glucose and milk tubes so inoculated are examined: all the strains which have produced gas or clotted milk are discarded. In this way we discard all germs of the genus Salmonella, Lankoides (p. 938), etc., and we retain only the strains which do not produce gas in glucose and do not clot milk. If a germ does not produce gas in glucose, as a rule it does not produce it in any other carbohydrate, and therefore we may say that we are left with strains which do not produce gas in any sugar and do not rapidly clot milk, and which, therefore, if they are bacilli, must belong to one of the following groups:— (*a*) Eberthus (p. 930), (*b*) Alcaligenes (p. 930), (*c*) Vibriothrix (p. 1068), (*d*) dysentery-metalkaligenes group *sensu lato*. From the glucose tubes hanging-drops are made; all germs which are not bacilli are discarded, and similarly all motile germs. In this way we shall retain only germs which are non-motile bacilli, which do not produce gas in any sugar, and do not clot milk—bacilli, therefore, which belong to the dysentery (glucose acid) and metalkaligenes group (glucose not acid). Those which ferment glucose (acidity only) are further investigated, and agglutination reactions are carried out, using Shiga, Flexner, and other dysenteric sera.

At times it will be found of advantage to use the so-called *Castellani's contemporary gas-agglutination test*. Tubes of glucose peptone water with Durham's fermentation small tubes are prepared, and two or three drops of a mixed serum, Shiga-Flexner, Hiss, etc., added. Twenty white colonies are inoculated in twenty such tubes. If any of these tubes, after twelve hours in the incubator, shows absence of gas and presence of agglutination, a diagnosis of bacterial dysentery can be made, though not of what variety of bacterial dysentery. It must be remembered also that there are rare strains of dysenteric bacilli which are not agglutinated by any of the usual antidysentery sera.

We wish to emphasize the fact that simple agglutination is not sufficient to diagnose that a certain bacillus is a dysentery bacillus. As shown by Levi della Vida, by one of us, and other observers, it is not at all rare to isolate from dysentery patients bacilli which are extremely well agglutinated, say, by Shiga serum, but which produce gas in glucose. Notwithstanding the opinion of a few authorities, such germs cannot be considered to be true dysentery bacilli, they are nosoparasites or secondary invaders. Hence the importance of carrying out fermentation tests in addition to serological tests.

To the bacteriological diagnosis of bacterial dysentery may be applied also *Castellani's polyserum method* as used for the diagnosis of cholera. A large number of the white colonies from MacConkey plates are inoculated in a tube of peptone water containing a few drops of lactose non-fermenters agglutinating polyserum (excepting the dysentery group) In theory all non-lactose fermenters, apart from the dysentery bacilli, will be agglutinated, while the dysentery bacilli will grow diffusely; in practice, however, many difficulties are met with owing to the great difficulty in producing an efficient polyserum.

Finally, we wish to call attention to the necessity of carrying out the bacteriological examination for dysentery on stools absolutely fresh, as soon as evacuated, plates being made at the bedside and then sent to the laboratory. If this precaution is not carried out, a very large number of cases will give negative results.

Prognosis.—In the milder forms of acute dysentery, the prognosis is good, recovery being the rule, but the death-rate of severe acute dysentery is high, while the prognosis in gangrenous dysentery is very bad. As an average, the mortality of the various forms may perhaps range from 12 to 25 per cent., for there is no doubt that in Ceylon and other tropical countries dysentery is a more potent factor in the death-rate than malaria, though the latter may cause more illness.

The site of the disease is also a factor in determining the prognosis, being as a rule better if it is situate low down, and worse if high up in the bowel. According to Kruse, Shiga, Duval, Dopter, and our own experience, early serum treatment lessens the mortality and therefore improves the prognosis.

As regards age and sex, the prognosis is better for adults than for children, and for men than for women. The European or new-comer into the tropics suffers more severely than the native resident race, but this racial difference is merely relative.

Treatment.—In all cases, however mild, the patient should be kept at rest in bed, and the urine-bottle and bed-pan must be used. The latter should preferably be slightly warmed before being used, especially in cool climates. Damp cotton-wool should be substituted for sanitary paper, in order to prevent irritation of the region of the anus.

All motions should be disinfected, after having been seen by the physician, with Jeyes' fluid or carbolic acid, and they should also be protected from flies. It is, however, most necessary that the motions should be saved for the physician to see, because they are extremely important in judging the progress of the case.

In very mild cases the bowels should be cleansed by an initial dose of one tablespoonful of castor oil, which may be administered in neat brandy, with or without a few drops of liquor opii sedativus or tincture of opium, and this should be followed a few hours later by the administration of astringents, such as bismuth salicylate 5 grains, and salol 5 grains, made into cachets, and taken every two or four hours at first, and less frequently when the character of the motions improves. In these mild cases tenesmus rarely requires any special treatment, and rectal injections are well borne, and may be administered twice daily, though in most cases they are unnecessary. These injections should consist of either boric acid (1 in 100), which is probably the best, salicylic acid (1 in 500), tannic acid (1 in 500), normal saline solution, or borax and bicarbonate of soda (5 grains of each to the ounce). In administering these enemata, the patient should lie on the left side, with the buttocks elevated on a pillow and the head placed low. A soft rectal tube should be smeared with vaseline and passed as high up the bowel as possible. Two pints of the enema are now run in by gravity from a glass irrigation vessel, and should be warmed to a temperature of about 99° to 100° F. The enema should be retained as long as possible. This treatment, with an appropriate diet, soon gives relief, the pain disappearing, the motions becoming fæculent. During convalescence a tonic of hydrochloric acid, cinchona bark, and gentian is found to be very serviceable.

In **severe cases** the serum treatment should be used as soon as possible, though at times it is useful to precede it with a dose of castor oil and associate to it the saline treatment. Kruse's serum, Shiga's serum, the Lister Institute serum (Todd), and that of the Pasteur Institute (Vaillard and Dopter), are all good. A polyvalent serum, such as that of Shiga, is preferable in those cases in which a complete ætiological diagnosis of the malady cannot be made.

The serum, in our experience, should be given in large doses; thus that from the Pasteur Institute and the Lister Institute should be given in 20 c.c. to 40 c.c. doses twice daily, and in very severe cases four times daily. The injection should be made under the skin of the abdomen or flank, using the ordinary aseptic precautions. These injections, as a rule, need not be continued after the second or third day. They may be followed by urticarial-like eruptions and pains in the joints. Calcium chloride or, better, calcium lactate in doses of gr. x. may be administered if these symptoms are severe three or four times daily. When the blood and mucus have disappeared from the stools, salol (gr. x. every four hours) or the ordinary astringents, such as bismuth subnitrate, or tannalbin (gr. x. to xv. every two hours), should be prescribed.

Our rules for the administration of the polyvalent serum are:—

I. In mild cases inject one dose of 20 c.c.

II. In cases of medium severity inject two doses daily of 20 c.c. for two days.

III. In severe cases inject 40 c.c. twice or thrice a day for two or three or four consecutive days.

As a rule the serum treatment should not be continued for more than four or five days, and it should not be repeated later on, or symptoms of anaphylaxis may develop.

The serum has often a marked effect upon the disease, hastening the cure, ameliorating the symptoms, and reducing the mortality, but it must be admitted that in certain cases it has practically no action whatever.

When the serum treatment cannot be carried out, the *saline treatment* is, in our experience, the most useful. Two drachms of magnesium sulphate and 2 drachms of sodium sulphate, dissolved in an ounce of water, chloroform water, or peppermint water, should be administered, and then 1 drachm of each should be given every two hours, or half doses every hour, until the motions become fæculent.

There is generally considerable pain in these more acute cases, and therefore a fomentation sprinkled with laudanum should be applied to the abdomen, and the tenesmus should be relieved by suppositories of morphia or of cocaine. If these remedies fail, then hypodermic injections of morphia or opium (gr. ½) by the mouth must be given, for it is a most important factor in the treatment that the patient should not suffer more than can possibly be avoided from this distressing symptom. If prolapse of the anus or rectum occurs, it is important that this should be reduced and relieved by an astringent ointment, such as hazeline or gall and opium.

Rectal injections may be given, as described above, but in sensitive cases it is as well to pass in a second tube alongside the enema-tube, so that, instead of the inflamed bowel being distended by the injection, it may be simply washed by the irrigation of the boric lotion.

During the treatment of the severe acute forms a great danger is to stop the saline treatment too quickly, and to allow constipation to occur, by which is meant that, though the patient may be having fifty to a hundred motions per diem, still fæculent matter is being retained. On the other hand, there is danger in continuing the saline treatment too long, for in our experience this should be stopped on the third day if there is no improvement, and also when the motions become serous.

After the acute stage is over it may be found useful to employ some astringent drugs, such as tannalbin, 15 grains every two hours, or large doses of bismuth subnitrate (gr. xv. to xxx., with or without salol (gr. v. to x.), every two hours, in cachets or emulsion, and an enema of boracic or tannic acid (½ to 1 per cent.) *per rectum* may be administered.

If there is a tendency to chronicity, fresh Bael fruit may be given. It must, however, be both fresh and ripe, and should be prepared by being boiled, and then shredded with a fork into warm milk, pressed and strained, and then a little sugar added. A tumblerful of the milk extract of Bael fruit may be taken twice daily.

Tincture of *Mansonia ovata* in 1-drachm doses is also recommended. Other remedies resembling the above are the roots of *Pelargonium tuberosum* and *P. flabellifolium*.

With regard to individual symptoms, *collapse* should be treated by the hypodermic injection of saline, *hæmorrhage* by calcium lactate.

Very severe cases, involving the whole of the large bowel, and gangrenous cases may be treated by appendicostomy and washing out of the bowel with a weak permanganate or boric acid solution.

The simple operation is performed as follows: -The patient is placed under chloroform, after the usual antiseptic preparation of the area of the operation. An incision of about 3 inches in length is made in the usual site for the operation of appendectomy, and, the layers of the abdominal wall having been incised, the peritoneum is carefully opened, and the appendix is searched for and brought forward into the wound, so that about 1 inch protrudes. Here it is stitched by four stitches to the muscles. The wound is now closed, the appendix being fixed to the skin by a couple of stitches The wound is now dressed aseptically with a thin layer of wool and covered with collodion. The tip of the appendix is now removed and a No 8 or No. 6 catheter inserted. The wound is now dressed antiseptically and left for twenty-four hours, at the end of which time a large tube is placed in the rectum, and the whole bowel is irrigated with 1 per cent solution of bicarbonate of soda to remove the mucus, and then with a boracic acid lotion, 1 drachm to the pint. This is repeated daily, but if the case tends to become chronic a solution of silver nitrate (5 to 20 grains to the pint) is u

When the cure is effected, the small nd is easily closed.

Other methods of treatment include th lomel treatment much praised by Scheube and Kartulis, and begun lon go by the Indian physicians, and among the various forms in which it has n applied, Twining's pill of calomel, blue pill, and ipecacuanha used to be y celebrated. Plehn recommends that, after a preliminary dose of castor oil, ½ grain of lomel be administered hourly until twelve doses have been ta en during the day The treatment is discontinued during the night, and repeated in the same manner during the second and third days, after which b smuth sul trate is given in 6-grain doses hourly during the day for a long period of time.

Yellow santonin, 0·3 gramme in 8 gr mmes of olive oil, administered three times a day, has been recommended by Drake. Musgrave recommends that acetozone (strength 1 in 5,000; aerated if necessary) should be freely drunk, so as to prevent fermentation in the stomach and bowels. In all cases a mouth-wash—*e g.*, glyco-thymoline - should be ordered. During convalescence the great point is to prevent chills and indiscretions in diet, which may induce attacks of diarrhœa. Turpentine diotal and styracol, especially in combination with castor oil, have been recommended by some.

Cyllin and other similar disinfectants have been advised, but hav not given any very good results in our experience. Bolus alba has been ad ocated

Various colloidal silver preparations have been recommended

The sour-milk treatment may be tried in subacute or chronic ses, with sauerin, lacto-bacillin, fermenlactyn, or any other preparation on the market, or by using the ferment as prepared by the natives of the country. Constipation is counteracted by small doses of castor oil, liquid paraffin, Carlsbad salts, Hunyádi János, Apenta water, or enemata, but if of a marked nature should arouse suspicions of stenosis, especially if the ordinary laxative remedies do not ameliorate the condition. Under these circumstances sigmoidoscopy should be performed, and the stricture dilated by bougies or catheters.

Treatment of Dysenteric Infantile Diarrhœa.—The treatment of infantile diarrhœa and of dysentery in children is best conducted by administering a small dose of castor oil (ʒi. to ʒii.), followed by calomel (gr. ⅙) or grey powder (gr. ¼), every hour until six doses are given in a child of two years of age. The dosage may be decreased or increased according to age. Afterwards astringents such as tannigen (gr. iii.) or tannalbin (gr. v.) may be given every two to four hours.

In severe cases, due to the Shiga-Kruse or the Flexner bacillus, serum treatment is the best, 5 to 10 c.c. being injected twice daily. The diet should be altered from milk to albumen water, whey, diluted meat-juice, or clear soup.

Pain must be combated by hot fomentations, and convulsions by bromides given in gr. xv. as enemata, or in small doses by the mouth in albumen water. Chloroform may require to be administered, while some authors recommend minute doses of morphia.

Treatment of Chronic Dysentery.—The treatment of chronic dysentery varies, for sometimes the malady is easily amenable to the treatment laid down for mild cases of acute dysentery, while at other times many remedies may be tried without success. After an initial dose of castor oil, tannigen, in 3 to 8 grain, or tannalbin in 10 to 20 grain doses, in cachets, may be tried three to six times a day. In old-standing cases pilula plumbi cum opio should be given twice a day. Serum treatment should also be tried during the exacerbations, as indicated above. Bael fruit, the rind of the mangosteen, simaruba bark, etc., are all useful in this condition, and the lavage treatment is more useful than in acute cases. Rectal irrigations should always begin with 2 pints of 1 per cent. solution of bicarbonate of soda to remove the adherent mucus, and then the medicated enema may be administered, and may consist of boracic acid (1 per cent.), followed by an enema containing bismuth subnitrate and sodium salicylate suspended in a pint or less of mucilage, silver nitrate (½ to 1 grain to the ounce), copper sulphate (2 grains, with 5 minims of tincture of opium to the ounce of water), tannin (0·2 to 0·5 per cent.), resorcin (1 to 2 per cent.), creolin (1 drachm to the pint), lysol (1 per cent.), or formalin (1 in 5,000), may all be used. Silver nitrate, however, gives the best results, gr. x. to the pint. Albargin (1 in 500, 1 in 1,000) has also been recommended. Perchloride of mercury (1 in 20,000) should not be used as a rectal enema, as it is dangerous, and may increase the symptoms instead of diminishing them. In chronic or subacute obstinate cases the *vaccine treatment* first introduced for dysentery by Castellani and Greig may be tried, using vaccines prepared from the dysenteric bacilli isolated from the stools of the patient. Forster has tried this treatment also in acute cases. In our experience it gives good results in several cases of the chronic type; but in acute dysentery is much inferior to the serum and saline treatment. If all these methods of treatment fail, appendicostomy should be tried.

Diet.—There is no point in the treatment of dysentery of greater importance than the diet. The bowel requires physiological rest, and therefore, in very severe cases, the diet must be restricted to albumen water and whey, and brandy given only if absolutely necessary.

In milder cases the diet should consist of milk, which must be diluted with Perrier, soda, Vichy, or barley water, or may be mixed with powders of sodium bicarbonate (gr. vi.), potassium bicarbonate (gr. vi.), sodium chloride (gr. iii.), or sodium citrate (gr. xl.), to the pint of milk, and less in proportion. Arrowroot made with water or milk, at first thin and later thick and flavoured with a little brandy, is most useful. Benger's food and Horlick's malted milk are also useful. Strong meat-essences and alcohol should be avoided.

In all severe cases the food must be given in small quantities every two hours, about 4 ounces at a time, and must be taken very slowly, and should be neither very warm nor cold. In chronic dysentery this milk diet is of the greatest importance, and may, as already stated, be supplemented by the sour-milk treatment.

When convalescence begins, chicken-broth and milk-puddings may be added to the diet, and then lightly-boiled eggs and toast; then chicken, cream, and fish; but for a long time only white flesh should be allowed, and not much of this, for the diet should for several weeks consist largely of milk foods. Of especial importance in convalescence is the chewing of the food, and care must be taken not merely that the teeth are in good order, but that the patient is directed not to swallow any tough or very fibrous piece of food. Fruit must be avoided for a long time.

Prophylaxis.—One of the important prophylactic measures which is at present but little used, owing to practical difficulties, is the isolation of the convalescent until three bacteriological examinations of the fæces give a negative result. Another is the search for dysentery carriers in a locality in which the disease is endemic or occasionally epidemic. The treatment of a carrier must be the same as for a case of chronic dysentery, but here vaccination will be distinctly useful. The persons to be suspected are those with a history of dysentery, or with a history of having nursed a case of dysentery, and people occupied in the cooking or handling of food materials.

Another very important measure is the destruction by burning or the disinfection of the dysenteric motion by either crude carbolic acid or by Jeyes' fluid, together with its careful protection against flies before its final disposal.

The personal prophylaxis consists in drinking only filtered and boiled water, and using the same for cleaning the teeth, in avoiding salads and fresh vegetables and unripe fruit, and in carefully washing the exterior of any fruit.

With regard to public prophylaxis, a modern method of collecting and disposing of the sewage of towns is necessary everywhere in order to prevent the disease from spreading, and there is no doubt that for this purpose the best method for tropical towns is the Shone or pneumatic system, as introduced into Rangoon, Bombay, and Karachi.

Good scavenging and strict hygienic laws are necessary to prevent the breeding of flies, and if an epidemic of dysentery occurs, a special crusade against the common house-fly, if not begun before, should at once be undertaken, as has been done for other reasons in Liverpool and elsewhere, especially in America.

Dust should be diminished in the warm dry weather by the efficient watering and brushing of the roads of towns, and in this water some cheap disinfectant such as permanganate of potash should be used, especially for the more important streets.

The drinking-water of all large towns should be filtered, though it must be admitted that this alone is not a sufficient safeguard against a water-borne epidemic.

Vaccination.—Owing to bacterial dysentery being due to several different bacilli, and owing to the fact that the Shiga-Kruse bacillus is very toxic the preparation of an efficient vaccine giving a not too severe reaction is difficult.

Broth Cultures Vaccine.—Antidysentery vaccines prepared with broth cultures should never be used, as they give rise to an extremely severe local reaction, with at times abscess formation.

Peptone Water Vaccine.—Castellani, in 1904, prepared a mixed peptone water vaccine which gave fairly satisfactory results. The preparation was as follows:—The Shiga-Kruse bacillus and three other species of dysentery bacilli were grown in peptone water tubes for three days at 35° C. They were kept for an hour at the temperature of 55°-60° C., and then mixed, three parts Shiga-Kruse and one part of each of the others. Of the resulting mixed vaccine 1 c.c. (sometimes ½ c.c.) was injected, the inoculation being repeated after a week or two. The reaction was not severe. Later Castellani prepared the same vaccine without heating, adding simply ½ per cent. carbolic. According to Castellani, the very much less marked reaction noted than when using broth vaccines, is not merely due to the fact that peptone water cultures contain fewer bacilli than broth cultures.

Carbolized Emulsion Mixed Vaccine.—Since 1912 Castellani has used in Ceylon a carbolized mixed vaccine containing *B. dysenteriæ* Shiga-Kruse, Hiss-Russell Y, original Flexner, Ceylon Flexner-like No. 1, Ceylon Flexner-like No. 2. The preparation of this mixed vaccine is as follows: The individual vaccines are prepared by making emulsions from twenty-four hours' old agar cultures in normal salt solution (0·75 per cent.), to which 0·5 per cent. of carbolic acid has been added, and the individual vaccines are standardized in such a way as to contain per c.c. 1,000 million germs. These monovaccines so standardized are mixed in equal parts, so that 1 c.c. of the mixed vaccine will contain 125 millions of each of the organisms used. Of this mixed vaccine 0·5 to 0·6 c.c. is given hypodermically the first time, and the same or double the amount after a week. Agglutinins generally develop for all the inoculated germs, but their amount is not high, and may be inconstant and irregular, but the same may be said of simple monovaccines, Shiga, Flexner, etc.

It is essential to prepare the vaccine with strains which, though rich in antigen, are only slightly virulent. It is extremely rare to come across such a strain of Shiga-Kruse. A large series of strains of this species are inoculated into rabbits, and the least virulent, provided it is rich in antigen, is kept permanently as a stock culture to prepare the vaccine.

Combined Carbolized Dysentery and Typhoid and Para A and Para B Vaccine.—This vaccine has been prepared by Castellani, in 1913, following this technique:—The individual vaccines are prepared by making emulsions from twenty-four hours' old agar cultures in normal salt solution (0·75 per cent.), to which ½ per cent. carbolic has been added. The monovaccines are then standardized as follows:—Typhoid vaccine 4,000 millions per c.c., para A 1,000, para B 1,000, Shiga 1,000, Flexner 1,000, Hiss-Russell Y 1,000, Flexner Ceylon (No. 1) 1,000, Flexner Ceylon (No. 2) 1,000. The monovaccines are mixed in equal parts. The mixed vaccine will therefore contain 200 millions typhoid and 125 millions each of the other organisms used. Of this vaccine 0·5 to 0·6 c.c. is given hypodermically the first time, and the same or double the amount after a week. The reaction is somewhat more severe than after inoculation with the triple typhoid para A and para B vaccine.

In the preparation of the vaccine it is necessary to use a selected strain of Shiga-Kruse, as little virulent as possible.

Sensitized Vaccine.—An emulsion in normal saline is made from twenty-four hours' old agar cultures. To the suspension is added some undiluted dysentery serum, and after twenty-four hours it is centrifuged and the serum and saline pipetted off. The sediment is washed in normal saline, and then a suspension is made in fresh saline containing 1 per cent. carbolic, and standardized to contain 100 million bacilli or more, ½ c.c. is injected the first time, and the same or double the dose a week later.

A sensitized dysentery vaccine was first prepared and used by Broughton Alcock in 1914. It has been used later by other observers, and experiments on it have been carried out recently by Gibson. The reaction is much less severe than using broth vaccines.

Serum-Vaccine. In Japan a vaccine has been given mixed with anti-dysenteric serum, with the object of neutralizing the bacillary endotoxin with the anti-endotoxin present in the serum. The injection of such serum-vaccine does not give rise to any production of agglutinins, and the doubt has arisen, to which Gibson has called attention, that the antiserum might neutralize all the antigenic properties of the vaccine, besides neutralizing the toxin.

Gibson's 'Absorbed-Serum Vaccine.' Gibson mixes the dysentery vaccine with antidysentery serum from which the agglutinins and other antibacterial substances have been removed by means of Castellani's absorption method. Suspensions in normal saline are made from agar cultures of Shiga-Kruse, Flexner, and Y; they are standardized, and then mixed in such proportion that 1 c.c. of the mixture will contain 2,000 millions Shiga-Kruse, 2,000 millions Flexner, 2,000 millions Y.

Trivalent antidysentery serum (Shiga-Flexner-Y) is absorbed with Flexner, then with Y, then with Shiga. It is centrifuged and filtered through a Chamberland. The filtered serum is then so diluted that 1 c.c. of the resulting dilution will contain 0·4 of serum. The diluted serum and the vaccine are filled into twin non-communicating phials, which are joined together. The inoculation is carried out as follows: 0·25 c.c. is aspirated in the syringe from each phial and injected subcutaneously in the usual way. The first dose contains Shiga 500 millions, Flexner 500 millions, Hiss and Russell 500 millions, and 0·10 absorbed serum. A week later double the amount is given. This absorbed serum-vaccine gives only a very moderate reaction, and seems to induce in the blood of the inoculated persons a satisfactory amount of antibacterial substances as well as antitoxin.

Dysbackta.—This is a vaccine prepared according to a special method by Boehncke.

Lipovaccine.—A vaccine consisting of an oil emulsion of dysentery bacilli has been prepared according to Le Moignic's method. The reaction is said to be mild.

C. PSEUDO-DYSENTERIES.

Definition.—Pseudo-dysenteries are diseases other than those defined above, which give rise to diarrhœa, with the passage of blood and mucus in the motions, and are sometimes associated with abdominal pain and tenesmus, and may readily, on superficial examination, be mistaken for true dysentery.

Remarks.—It should, however, be noted that the term 'pseudo-dysentery' has been used by Kruse to signify a form of bacterial dysentery commonly found among inmates of lunatic asylums, and later to denote every variety of the disease not caused by the Shiga-Kruse bacillus.

Ætiology.—The most common causes of the pseudo-dysenteries are cancer of the intestine, especially of the rectum, inflamed piles, gummata in the rectum, cancers of the large bowel other than the rectum, and intussusception. The native habit of eating the small bones of fish along with the flesh is apt to cause irritation of the rectum and a pseudo-dysenteric attack. Inflammations of the broad ligament, especially on the left side, are apt to be confused with a mild attack of dysentery. Poisons, such as mercury, ptomaines, ricin, abrin, etc., may also produce symptoms resembling dysenteric attacks. Prout has described a form of dysentery in the Gambia due to drinking-water containing the excreta of locusts.

Diagnosis.—The diagnosis of these various conditions has already been discussed in the Diagnosis of Bacillary Dysentery, and need not be repeated.

Treatment. - The treatment must be adapted to the specific complaint, while the bowel symptoms may be relieved as indicated under the treatment of Bacillary Dysentery.

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CHAPTER LXXIX

INTESTINAL SCHISTOSOMIASIS

Synonyms — Definition — History — Climatology — Ætiology — Pathology —Symptomatology —Diagnosis —Prognosis — Treatment — Prophylaxis— References.

Synonyms.—Intestinal bilharzi[illegible] Rectal bilharziosis, Hepatic bilharziosis American bilharziosis, Manson's [illegible]harziosis, Manson's disease.

Definition.—Intestinal bilharziosis is infection with *Schistosoma mansoni* Sambon, 1907, the eggs of which invade and irritate the intestines and the liver, and cause inflammation.

History.—It has long been known that the eggs found in cases of intestinal, rectal, and hepatic bilharziosis are laterally spined, as Bilharz pointed out in 1851; and Sonsino once stated that the two worms must belong to different species, but this statement did not attract attention. In 1903 Manson first suggested, on grounds of dissimilar geographical distribution, that these eggs might belong to a new species of *Schistosoma*, and in 1907 Sambon showed that a separate species really did exist, calling this *S. mansoni*, in which he has been supported by Holcomb, Firket, Broden, Grun, and others, though opposed by the great authority, Looss.

A description of the adult worms has been given by Da Silva and by Flu, confirming the differentiation of the two species.

The fact of the existence of a separate disease caused by the lateral-spined eggs of *S. mansoni* is supported by all authors who have studied the disease in America, where the patients are said never to have eggs in the urine, and never to suffer from urinary schistosomiasis. It is further supported by the work of Mathis and Baujeau on a case from Gaudeloupe, and by that of Turner in South Africa. Flu, after examining 1,000 eggs from fifteen cases of intestinal schistosomiasis in Paramaribo, never found one with a terminal spine. Reference may also be made to Letulle's paper on 'Bilharziose Intestinale,' published in 1905, to Madden's work in 1907, and to Symmer's work in 1902 and 1906, from the latter of which we have taken our two illustrations. Reference must also be made to the admirable exposition of the disease by Mathis, Noc, and Léger in 1913. In 1914 and 1915 Leiper thoroughly established the species *S. mansoni*, and worked out its life-history. He has traced the life-cycle of the parasite through the snails to its adult condition in rabbits, guinea-pigs, and man. Lutz has published his extended researches into the disease and its parasite as seen in Bahia and Northern Brazil. It will thus be seen that the recognition of the disease is becoming generally accepted, although this was by no means the case when this chapter was first written.

Climatology.—As far as is known at present, the disease exists in Egypt, Central Africa, Uganda, South Africa, the Belgian Congo, Central, South, and North America, and the West Indies. In Brazil it is confined to the northern districts, being unknown in the South. In Venezuela it is common around Caracas, where its intermediate host is believed to be *Planorbis guadelupensis* Sowerby by Iturbe and González.

Ætiology.—The cause of the disease is *Schistosoma mansoni*. The description and life-history of the parasite is given in Chapter XXIV., p. 587.

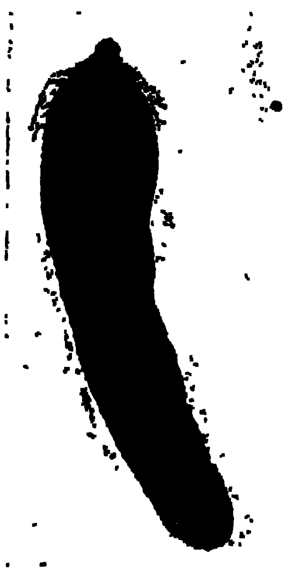

Fig. 768A.—Miracidium of *Schistosomum mansoni*.

(Photomicrograph.)

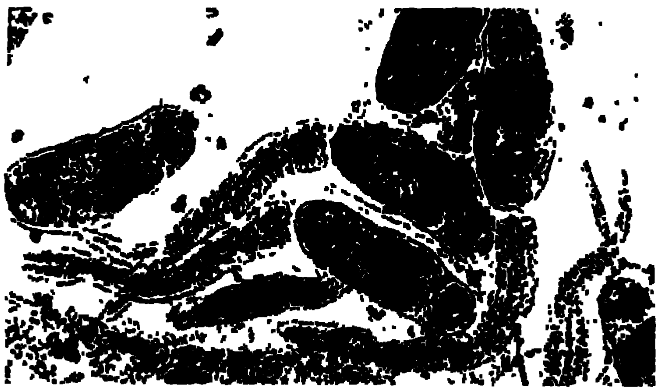

Fig. 768B.—Cercaria of *Schistosoma mansoni* from *Planorbis boissyi*.

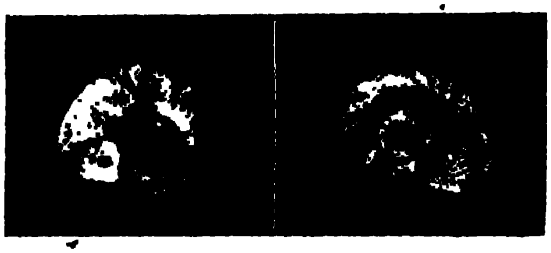

Fig. 768C.—*Planorbis boissyi*.

Pathology.—The worms live in the portal vein, but are especially attracted to the bowels, in the capillaries of which they lay their eggs, which burst those vessels, and escape into the mucosa, causing therein a dense cellular infiltration, which leads to a thickening of the coats of the bowel, and to the formation of papillomata, which may become detached and form ulcers. Dense fibrous infiltration of the peritoneum may also occur, and contain both eggs and worms. The mucosa of the bowel is protected by a quantity of mucus. In the rectum the mucus membrane is apt to become hypertrophied, and to grow, forming large polypoid masses, or adenomata, which may protrude through the anus. The ova may affect the subcutaneous tissue of the sacral and coccygeal regions,

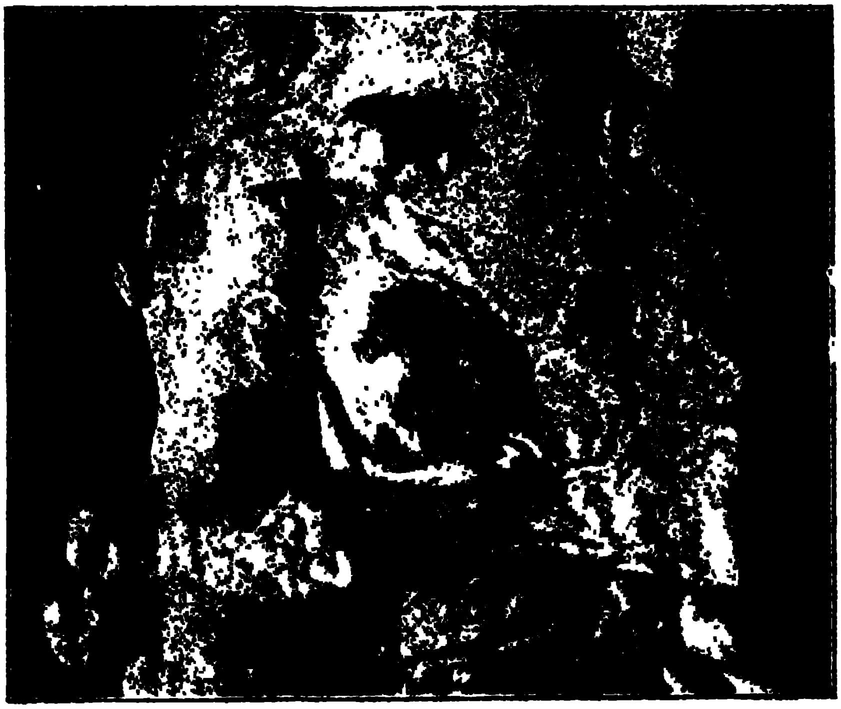

FIG. 769.—INTESTINAL SCHISTOSOMIASIS.
(After Symmers.)
Polypoid growths in descending colon.

FIG. 769A.—BOWEL IN A CASE OF INTESTINAL SCHISTOSOMIASIS.

and cause dense cellular infiltrations, giving rise to fistulæ, which may spread and infect a large cutaneous area.

When the ova reach the liver by the blood-stream, they give rise to fibrous-tissue formation or an abscess. The surface of the liver shows in places a whitish network and also flat, china-white plaques. On section a marked increase in Glisson's capsule may be seen, the portal vessels lying in circular or slightly oval areas of connective tissue. Gall-stones may also form round the ova in the gall-bladder. The pancreas and spleen may also be infected, and the vulva and vagina.

The ova may also reach the lungs, causing a chronic interstitial pneumonia, and, passing through these organs, may enter the heart and the general circulation.

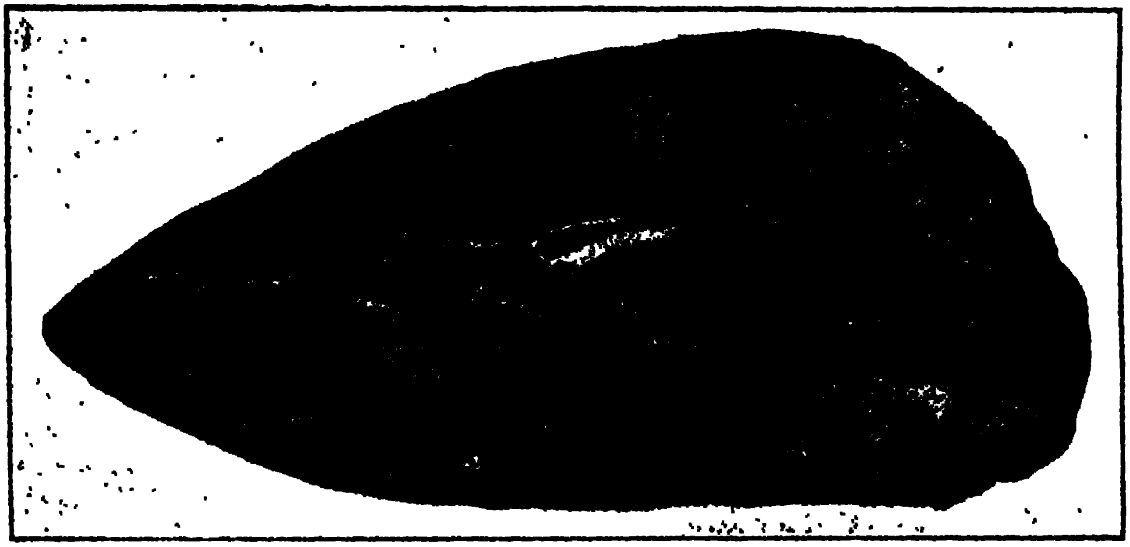

FIG. 770.—LIVER IN INTESTINAL SCHISTOSOMIASIS
(After Symmers)
Shows the increase of fibrous tissue in the portal canals.

Symptomatology.—The incubation period seems to be one to three months. The clinical appearances of the disease may be classified into four varieties:—

1. Slight infections.
2. Schistosomic dysentery.
3. Schistosomic tumours.
4. Schistosomic fever.

Slight Infections.—In these cases there are no symptoms, and the disease is discovered by the examination of the fæces by a microscope.

Schistosomic Dysentery.—The symptoms resemble those of chronic dysentery, consisting of pains in the abdomen and the passage of blood and mucus. The fæces contain the characteristic ova. The attack begins with a hypersecretion of mucus, followed by frequent small motions containing but little fæcal matter and much mucus. The result of these frequent motions is to cause prolapse of the rectum. Papillomatous growths may form in the rectum, and can be distinguished from piles by their large number. They may protrude from the anus, when the removal and microscopical examination of a small portion will clear up the diagnosis. When the lower part of the rectum is involved, much agony from tenesmus and constant desire to defæcate is experienced. The rectal prolapse becomes very distressing, as it has to be constantly replaced by the patient himself, and as both the mucous membrane of the bowel and that of the anus become much inflamed and irritated.

In cases in which there is much sclerosis, with a scarcity or absence of polypi, the dysenteric symptoms are not so marked. On the contrary, the patient complains of constipation, not relievable by ordinary methods, alternating with bouts of diarrhœa.

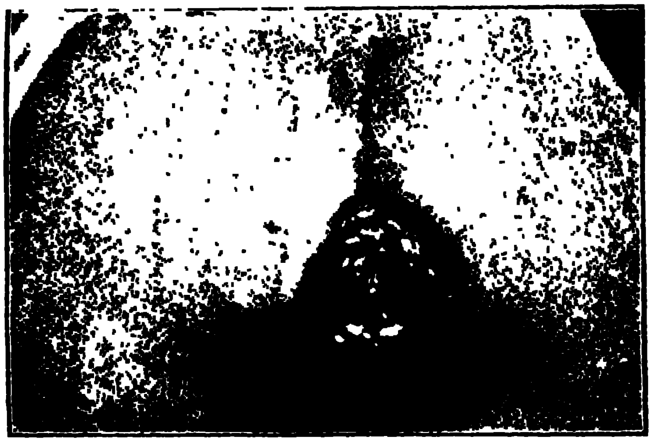

FIG. 771.—PROLAPSE OF THE RECTUM IN INTESTINAL SCHISTOSOMIASIS. (From a photograph by Christopherson.)

Schistosomic Tumours.- When an emaciated patient in one of the endemic regions is examined, one or more abdominal tumours may be found in the region of the cæcum or colon. These tumours, which are fairly hard, are somewhat movable, and are usually elongated, with the long axis corresponding to the direction of the long axis of the bowel in the region in which the tumour is lying. The tumour, accidentally discovered, continues to increase in size for months and years, while the patient becomes very emaciated, and suffers from attacks of colic at times.

Liver and Pancreas.- The liver may be found to be enlarged and cirrhotic, the spleen also be enlarged, and there may be signs of cirrhosis of the pancreas.

If the patient removes from the endemic area, improvement will take place; but if he remains, then no cure appears to be possible, and he dies sooner or later from exhaustion.

Blood.—The blood in intestinal schistosomiasis requires further study, but it would appear that usually there is a marked anæmia, with oligochromæmia, slight leucocytosis, and very slight eosinophilia.

Urine.—In cases uncomplicated with the presence of *S. hæmatobium* there is no albumen, no sugar, and no ova in the urine.

Schistosomic Fever.—Flu in 1911 reported that *Schistosoma mansoni* could give rise to an illness resembling katayama disease. Archibald has also called attention to the fact that intestinal schistosomiasis caused by *S. mansoni* is capable of producing a fever associated with splenomegaly, enlargement of liver, a polymorphonuclear leucocytosis and lymphocytosis, together with a diminution or absence of eosinophiles. The absence of eosinophilia was constantly noted in intestinal schistosomiasis in contrast to urinary schistosomiasis when the reverse holds good. Two cases treated with an autogenous vaccine of the predominant coli organisms present in the stools derived benefit and lessened the symptoms of intestinal toxæmia.

Urticaria has been noted by Lawton, who reports also presence of eosinophilia.

Complications.—A case may be complicated with urinary bilharziosis, ankylostomiasis, and other intestinal parasitic diseases.

Diagnosis.—The diagnosis must be made by finding the characteristic lateral-spined eggs in the fæces.

Prognosis.—The prognosis is unfavourable. It must be noted, however, that in some cases the parasite does not give rise to any distinct pathological symptoms for a long time. One of us has observed in Uganda several natives with eggs of *S. mansoni* in their fæces, although they were apparently in good health. The stools, apart from the eggs of the worm, were normal.

Treatment. Christopherson has recommended the intravenous injection of tartar emetic (antimonium tartaratum). He gives ½ grain dissolved in 2[illegible] of distilled water, and diluted with two volumes of normal saline at the time of use. The dose is increased by ½ grain every other day until 2 grains are reached, and this dose is continued until 30 grains in all have been injected. In children he began with ¼ grain for a boy of ten years. Care has to be taken to avoid acute or chronic antimony poisoning, and the maximum dose for a boy of ten is given as 1 grain, for an adult 2 to 3 grains. The drug appears to have a cumulative action.

Christopherson's results have been confirmed by Low, Taylor and others.

Filix mas may be administered with the purpose of eradicating the worms, and symptomatic treatment may be carried out as mentioned under Urinary Bilharziosis. Madden advises an enterotomy and a cleaning out of the bowel, when a tumour can be felt, and a Whitehead's operation may be done to relieve the rectal symptoms. Vincent has suggested that large intestinal irrigations of a solution of sodium hypochlorite (8 to 10 per 1,000) should be given, and other authorities tannic acid enemata (3 per 1,000). Some authorities recommend the intravenous or intramuscular injections of salvarsan, and others the use of emetine.

Prophylaxis.—This is based principally on Leiper's work. Filtered water should be used for all personal purposes. If this is not possible, tap-water should be stored for forty-eight hours before use, as freshly discharged cercariæ do not usually live in it for more than twenty-four hours. Chemical sterilization may be carried out by using sodium bisulphate tablets, each containing 1 grm. of the chemical. Two tablets are dissolved in a quart water bottle. Leiper has shown that sodium bisulphate in a dilution of 1 in 1,000 is lethal to the cercariæ. For small detachments of troops in outside districts Leiper recommends that the drinking-water should be separated from ablution water, the former being sterilized by boiling or by tablets of acid sulphate of soda, while the ablution water should be rendered safe for immediate use by adding ordinary Cresol in the dilution 1 in 10,000.

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CHAPTER LXXX

EPIDEMIC GANGRENOUS RECTITIS

Synonyms.—Caribi (British Guiana), El bicho (Venezuela).

Definition.—An endemic very contagious disease of South America, and perhaps Fiji and other South Pacific Islands, of unknown causation, and characterized by dysenteric symptoms leading to prolapse and gangrene of the rectum, or at times to disease of the colon.

History.—Chalmers and Archibald, in 1914, drew attention to the fact that an eighteenth-century writer, D. L. F., in his work entitled 'Traité des maladies particulières aux pays orientaux,' had described this disease in Brazil under the name of 'bicho.' His report is similar to the latest information on the subject, which is curious. He wrote as follows:—

> ‘DU MAL QUE LES PORTUGAIS APPELLENT BICHO.’
>
> ‘Les Portugais habituez au Brésil appellent encore Bicho, une inflammation du fondement, qui est également fréquente et dangereuse dans ce pays, elle est toujours suivie du mal de tête, d'épreintes, grande chaleur en la partie malade, et quelquefois de la fièvre. Si l'on la néglige il s'y fait en peu de jours des ulceres venimeux, qui ont donné lieu au nom de Bicho.
>
> ‘Ceux qui se lavent souvent ces parties, sont moins sujets à cette incommodité que ceux qui ne le font pas. D'abord qu'on s'en croit attaqué, il faut étuver plusieurs fois le jour, la partie avec une décoction de limons, à laquelle on ajoutera quelques grains de sel. L'on introduit aussi heureusement dans l'intestin, des petits quartiers de limon, et cela arrete quelques-fois le mal tout court dans son commencement; s'il y a déja une corruption notable, l'on à de coutume de détremper de la poudre à canon dans de l'eau de rose, ou de l'eau de plantain, et de ce liniment l'on en imbibe de petits linges, que l'on met dans le fondement. Après l'avoir bien étuvé avec la décoction de limons, quoy qu'il y ait de la fièvre, il faut bien se donner garde de saigner dans cette occasion, l'expérience ayant fait connoître que ce remède est fort préjudiciable: l'on peut seulement donner fréquemment les lavement anodins ou détersifs, suivant que la corruption ou l'inflammation, sont plus ou moins grandes, et purger doucement sur la fin.’

More than one hundred and fifty years later Ackers of Curaçoa gave Manson an account of the disease as seen in Venezuela. It appears to us that some endeavour should be made to discover the ætiology of this disease and to study it by modern methods, which ought to be easy in an endemic area where animals are attacked.

Climatology.—The disease is apparently known in Brazil, British Guiana, and Venezuela, and with perhaps the addition of Fiji and other islands in the South Pacific.

Ætiology.—This is entirely unknown. The disease occurs in man and animals, fowls, dogs and calves, and is said to be very contagious. The Venezuelan natives say that it arises from children chewing the green tender stalks of unripe maize.

Pathology.—The disease presents two pathological pictures—viz., *a high infection* in the colon, which is rare, and *a low infection* in the rectum.

Symptomatology.—The disease begins as an itching about the anus, followed by symptoms of acute dysentery, which increase in severity until there is a constant discharge of blood-stained or greenish fœtid fluid. Prolapse and gangrene of the rectum may now occur, or convulsions may supervene, but in either case the patient dies.

Diagnosis.—In an endemic area severe dysenteric symptoms in a native child would lead one to suspect the disease.

Prognosis.—This is extremely bad, as the disease appears to be always fatal.

Treatment.—Natives treat the disease by enemata of strong lemon-juice mixed with dilute rum, a dose of castor oil being given at the same time. Enemata and decoctions of *Spigelia anthelmia* are also prescribed. In children a portion of a lemon is roasted and inserted *per anum*. According to local medical men, this native treatment is more efficacious than boric acid and similar enemata.

Prophylaxis.—Nothing can be said with regard to this until the disease is scientifically investigated and its ætiology discovered.

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DIVISION II.: DISEASES OF THE SYSTEMS.

Respiratory System.
Circulatory System.
Liver and Pancreas.
Ductless Glands and Metabolism.
Urinary System.
Generative System.
Lymphatic System.
Connective Tissues, Muscles, Bones, and Joints.
Nervous System.
Organs of Special Sense.

CHAPTER LXXXI

DISEASES OF THE RESPIRATORY ORGANS

General remarks—Rhinitis spastica vasomotoria—Gangosa—Hirudiniasis—Rhinal chilopodiasis—Linguatuliasis—Rhino-pharyngitis spirochætica—Bronchial spirochætosis—Tropical bronchomycoses—Pulmonary nocardiasis—References.

GENERAL REMARKS.

DISEASES of the respiratory organs are of common occurrence in the tropics, in the form of acute or chronic inflammation of the nose, throat, larynx, bronchi, or lungs. *Pneumonia* is less common than in Europe, and must be carefully diagnosed from pneumonic plague, liver abscess, and malaria, by careful physical examination, as well as by microscopical examination of the sputum and blood. Liver abscess may burst into the lung or pleural cavity, and may cause the expectoration of a peculiarly brown and viscid sputum. *Emphysema* and *asthma* are fairly common, and all types of bronchitis are met with, though more rarely than in temperate zones.

Phthisis is common, and appears to be increasing in the East, but it must be remembered that the pulmonary lesions of paragonimiasis, histoplasmosis, bronchospirochætosis, and certain bronchomycoses, closely simulate this disease, and the examination of the sputum is imperative. The occurrence of Porocephalus in the lungs must also be remembered, and the intense congestion in heat-stroke. There are several conditions which deserve special mention with regard to tropical disease.

RHINITIS SPASTICA VASOMOTORIA.

Synonyms.—Rhinitis nervosa, Coryza spasmodica, Dispnée tropicale, Tropical hay fever.

Definition.—A rhinitis characterized by fits of sneezing, with the production of much nasal mucus, and obstruction of the nose from swelling of the mucous membrane over the turbinated bones. The affection has the greatest resemblance to hay fever.

History.—This disease appears to have been first described by Zegers in 1901, in Batavia, while Brero gives a full description in Mense's 'Tropenkrankheiten,' and we have seen several cases in Ceylon. O'Zoux has recorded numerous cases in the island of Réunion.

Symptomatology.—The affection is characterized by attacking adults, in whom it causes violent fits of sneezing, lasting from a few minutes to two hours, during which time the victim sneezes ten to seventy times, while fluid pours from the nose, tears roll down from the eyes, the conjunctivæ are injected, the eyelids swollen, the head aches, and the patient is unable to do his work. The attacks are repeated constantly, and may take place several times during the day, or may not recur for weeks. They may be associated with or followed by dyspnœic conditions resembling to some extent asthma. At the beginning the mucosa of the inferior turbinated bone may appear hyperæmic, but later it becomes swollen, and has a macerated appearance. The disease therefore closely resembles hay fever, but is supposed to be caused by dust acting upon the nasal mucosa of persons, the resistance of whose nervous system has been lowered by long residence in the tropics. We have frequently met with the disease in people exposed to the dust of tea and copra.

Treatment.—The only successful treatment in many cases is a change of climate, when the symptoms stop at once. When the patient cannot have a change of climate, atropine and strychnine pills, or small doses of quinine, may be recommended, and locally a spray of a solution of cocaine (½ or 1 per cent.) and adrenalin (1–2 per cent.).

GANGOSA.

Synonyms.—Rhinopharyngitis mutilans (Leys); Granuloma gangrenosum; Kaninloma (Fiji).

Definition.—Gangosa is an ulcerative condition of the palate, nose, pharynx, and skin surfaces of the body, of unknown cause, though possibly a late sequela of yaws, which slowly spreads to the nose and larynx, destroying cartilage and bone, and causing much deformity.

History.—The disease appears to have been first described in 1828 by a Spanish Royal Commission to the Marianne or Ladrone Islands under the name 'gangosa,' which means 'nasal voice,' and is derived from *gangoser*, 'to snuffle.' It was carefully studied by Seligmann in British New Guinea in 1898 and 1904, who describes the implication of the skin of the face, and draws attention to the fact that it is the disease described by Sir William MacGregor as lupus and by the white residents as cancer. In 1906 the disease in the endemic area was studied by Fordyce and Arnold, by Leys in Guam, an island to the south of the Ladrone Islands, and by Mink and McLean in the Ladrone and Caroline Islands. In 1907 a paper appeared by Musgrave and Marshall on a case from the Batanes Islands, 120 miles north of Luzon, and by Stitt on a case in a European in Guam. It has been studied by Angeny and Kerr. Breinl has found it on Murray Island, and thinks that it closely resembles the condition known in Fiji as Kaninloma.

Climatology.—There appears to be an endemic area for the disease, it being common in the Batanes Islands (where the cases are mistaken for leprosy), in the Ladrone Islands, Guam, and the Caroline Islands. Cases occur also in Fiji, Murray Island, Panama, British Guiana, Ceylon, Nevis, Dominica, and Equatorial Africa. In the Anglo-Egyptian Sudan there is a disease closely resembling gangosa, though probably syphilitic.

Ætiology.—Daniels and several other authors believe it to be a sequel to yaws, but Rat is opposed to this, as are Mink, McLean, Musgrave, and Marshall and Angeny, who point out that the disease is absent or very rare in many countries where yaws is common. Kerr, however, has noted that yaws is an almost constant antecedent of gangosa. Alverez suggested that it was syphilis, but Musgrave, Marshall, and Leys are opposed to this, because no syphilis exists in Guam, where gangosa is common. There are no signs or symptoms of syphilis in this disease. Treponemata cannot be found, and mercury is without effect. It is not leprosy, because of the absence of nodules, infiltration, anaesthesia, and Hansen's bacillus. It is distinguished from epithelioma by the absence of the histological characters and metastases, as well as by the rapid onset and protracted course. It is excluded from tuberculosis by the absence of Koch's bacillus and other symptoms of the disease, and the failure to inoculate guinea-pigs successfully. It may therefore be a separate disease of unknown causation, though we believe that it is probably a late manifestation of yaws. Schnitter regards it as a sequela of a special variety of yaws. It appears to be equally common in males and females.

Pathology.—It appears to begin sometimes as a sore throat or coryza, or as a tubercle on the palate. In any case, an ulcer soon forms, which, though superficial at first, eats through cartilage and bone, with periods of quiescence and of activity. This ulceration is due to a necrosis of the tissue elements, with very little reaction on the part of the body. This reaction is apparently limited to a small-celled infiltration, some giant-celled formation, and proliferation of bloodvessels with formation of granulation tissue.

Morbid Anatomy.—The post-mortem may reveal signs of some concomitant affection—for example, tuberculosis, pleurisy, or cardiac hypertrophy—which have nothing to do with the disease, the important features of which are ulceration and destruction, together with scar formation in the larynx, pharynx, palate, nose, and perhaps the antrum of Highmore.

Histopathology.—Microscopically, the following changes are observed as the diseased area is approached from healthy tissue: First there is an œdematous infiltration, then an infiltration with round cells, which are principally lymphocytes, associated with another variety possessing more protoplasm, and a small dark nucleus. Sometimes there are giant cells and proliferating vessels, and there are always hæmorrhages. Then comes a layer of necrosis, forming the surface of the ulcer, at the edges of which the epithelium can be seen sending processes into the subcutaneous tissue, which consist of large vacuolated cells with pale vesicular nuclei. Some diplococci, micrococci, and bacilli have been noted, but no acid-fast bacilli or Treponemata have been seen.

Symptomatology.—The disease begins sometimes as a sore throat, and on examination a nodule may be seen on the back of the pharynx, the posterior pillars of the fauces, or the edge of the soft palate. This becomes a superficial ulcer covered with a brownish-grey slough. This ulcer spreads rapidly at first, but more slowly later, and eats away first the soft parts, and then the bone of the palate, the nasal septum, and the cartilages of the nose, so that the skin falls in, and the nose and mouth are converted into one cavity. It may then extend on to the face or lip, or affect the larynx. When it spreads over the face it may involve the eyelids, erode the cornea, and even destroy the vision. In some advanced cases the entire front of the face is replaced by a large opening ringed about by foul ulcers. Sensation is diminished over the ulcer, and a most objectionable odour is exhaled, while a slight discharge of granular and necrotic débris is generally present. The ulcers may also appear on the skin of the extremities or on parts of the body not usually covered

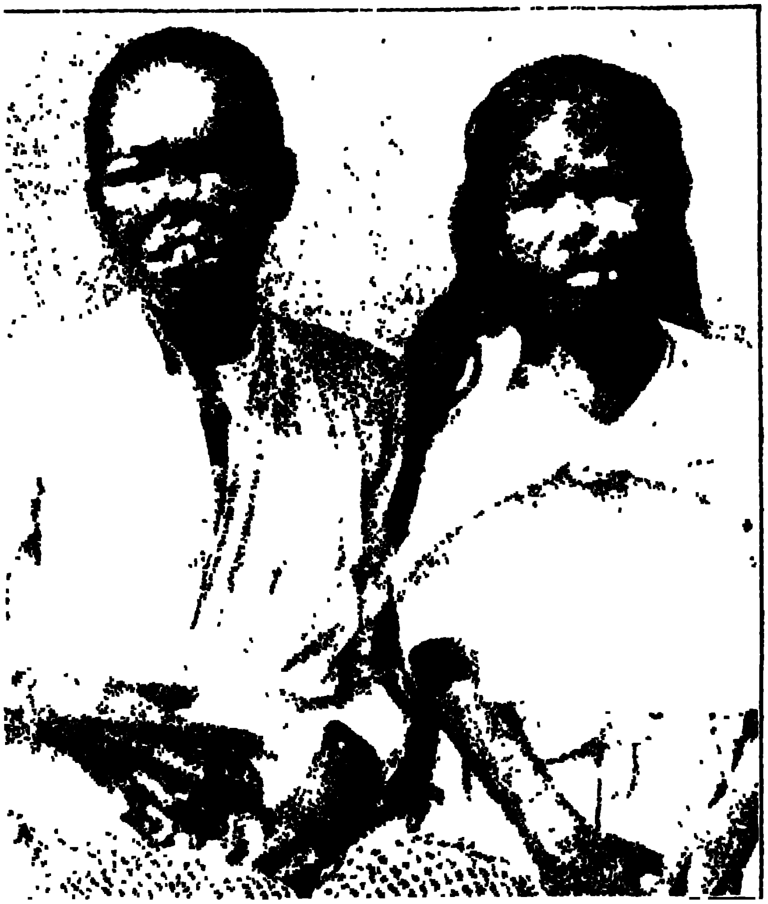

FIG. 772.—GANGOSA.
(From a photograph by Arnold.)

with the clothing. At times the ulcers may remain quite superficial, spreading at one edge while healing at another. Scarring similar to that seen after burns may result, which by contraction may lead to obliteration of the palpebral fissures, the nasal orifices, and to reduce the size of the mouth, as well as to produce great deformities in the hands and feet. It may cause a chronic osteitis resembling that seen in syphilis. It appears to be in some way self-limited, as it does not attack the trachea or genital organs. The ulceration may progress continuously for a period of ten to thirty-five years, or it may advance at certain times and be quiescent at others, or it may cease at any time, leaving a chronic ulcer. Its duration varies, therefore, from a few months to many years.

With regard to the blood, Musgrave and Marshall report that their case showed no marked leucocytosis and no abnormal elements. The hæmoglobin was 80 per cent., the leucocytes 11,600 per cubic millimetre, the small lymphocytes 10 per cent., large lymphocytes 4·6 per cent., polymorphonuclears 82 per cent., eosinophiles 2·6 per cent., basophiles 0·4 per cent. Wassermann's reaction is often positive. Kerr believes this to be due to pregressed yaws. Noguchi's cuti-reaction may be positive.

The disease is not limited to the throat and nose, but, as already stated, may spread to the face or appear on the extremities, but as a rule the general health is but little affected.

Variety.—A fulminating variety has been described by Mink and McLean in children, which is fatal in forty-eight hours, and closely resembles diphtheria, without, however, the presence of the specific bacilli.

Diagnosis.—The diagnosis has been practically discussed in the Ætiology, and need not be repeated, except to say that it must be made by a process of exclusion.

Prognosis.—The disease is rarely fatal, and all cases tend to ultimate recovery, but the course is very long and the disfigurement great. The general health is also good as a rule, although death may take place from intercurrent disorders, such as tuberculosis, dysentery, and other internal causes.

Treatment.—Mercury is useless and potassium iodide has little action on the condition. Salvarsan and neosalvarsan, or their substitutes, seem to give much better results. An application of a strong solution (1 per cent.) of permanganate of potash is recommended as a deodorant, and local application of tincture of iodine or the actual cautery.

Prophylaxis.—Nothing definite can be said under this heading, as the ætiology is not known with certainty, but segregation of the patients in a colony or special hospital until they are cured is advisable. In Guam, according to Angeny, the disease is steadily decreasing, thanks to the measures taken of segregating the patients, and possibly to the thorough treatment of yaws patients, and also probably to the improvement in general sanitation since the American occupation.

HIRUDINIASIS.

Definition.—Hirudiniasis is the invasion of the nose, mouth, pharynx, or larynx by leeches.

Remarks.—Leeches have already been described in Chapter XXVII. (p. 683), when it was mentioned that they were apt to invade the nose, mouth, pharynx, or larynx. Masterman has given a very excellent account of hirudiniasis as seen in Palestine.

Climatology.—Leeches are most troublesome in Algeria, Palestine, and Ceylon, less so in the Philippine Islands, Java, Sumatra, Australia, and Japan.

Ætiology.—It is the water-leech, which lives in springs, which is the cause of the trouble to man, as it is apt to be swallowed with drinking-water. This is particularly liable to take place when the traveller drinks the water hastily at dusk.

Pathology.—The leech, when in the mouth, nose, pharynx, or larynx, does not suck blood until gorged, and then detaches itself from the affected part, as is the rule when it attacks the skin, but apparently bites and sucks a little in one place, and then passes to another, and bites and sucks again, and so on. Of course the sites of the bites bleed, and hence the patient may in course of time become very anæmic, and even die. It is hardly likely that a leech could live in the stomach if swallowed, though such an occurrence has been described.

Symptomatology.—The patient usually knows that he has swallowed a leech, and has felt the animal catch hold of the mucosa of the pharynx during the swallowing of the water. But children, and even adults, may be quite unaware of the accident having happened. The most important sign is the bleeding from the nose or mouth, or the hawking up of blood from the pharynx, or hæmoptysis from the larynx, accompanied by a short irritating cough, dyspnœa, and sometimes cyanosis from the impediment to the respiration. Rhinoscopic or laryngoscopic examination may be necessary in order to see the parasite, and will require to be done with cocaine. In the larynx the head of the leech is usually fixed just inside or outside of the vocal cords, and the body may flop backwards and forwards with respiration.

Diagnosis.—The bleeding and the examination with a nasal speculum or a laryngoscope make the diagnosis easy.

Prognosis.—This is usually good if the parasite is removed in time, but if left for long, removal may be too late, and the patient succumb.

Treatment.—Apply a pledget of cotton-wool soaked in 30 per cent. solution of cocaine to the parasite. This produces a paralyzing effect on the animal, and it can then be removed. As, however, the drug requires some time to act, and the leech might fall from the larynx into the trachea, it is advisable to make the patient lie prone on a couch, with the head hanging over, when the paralyzed parasite will be coughed up.

Prophylaxis.—Filtration of the water will prevent the parasite entering the body. Masterman says that a kind of carp, *Capoëta fraterculu*, will keep the water free from leeches.

RHINAL CHILOPODIASIS.

Definition.—Rhinal chilopodiasis is the invasion of the nose by a species of the *Chilopoda* (see p. 739).

Ætiology and Symptomatology.—The *Chilopoda* have already been described in Chapter XXVIII., and it has been pointed out that *Geophilus carpophagus* Leach, *G. similis* Leach, *G. electricus* Leach, *G. cephalicus* Wood, *Lithobius forficatus* Leach, and *L. melanops* have been found in the nasal cavities, causing inflammation, with at times a great flow of mucus, while at others there is a stoppage of the discharge. Associated with this flow there is headache, with more or less marked remissions at times, and also general symptoms, such as convulsions, angina, dyspnœa, etc., which are thought to be produced reflexly by stimulation of the fifth nerve. The symptoms are thought to be produced mechanically, and not to be due to any action of venom secreted by the parasite.

Diagnosis is to be made by examination of the nose by a speculum.

Treatment.—The affection is not serious, and often the parasite is expelled by merely sneezing. More rarely chloroform-water injections, snuff, eau-de-Cologne, or turpentine injections are needed. Still more rarely will a sinus, such as the frontal sinus, require to be opened.

LINGUATULIASIS.

Linguatula serrata Frölich, 1789, has been found occasionally in the nose of man in Europe and in the tropics (*vide* p. 732).

RHINO-PHARYNGITIS SPIROCHÆTICA.

Definition.—A rhino-pharyngitis characterized by the presence of numerous spirochætes in the nasal and pharyngeal secretion.

Historical and Geographical.—This affection has been described by Castellani, who has found cases of it in the tropics, in the Balcanic-Adriatic zone, and one in England.

Ætiology.—In the nasal and pharyngeal secretion large numbers of spirochætes are present at the beginning of the attack, while other organisms are practically absent; in a later stage, however, bacteria are present in great abundance. The spirochæte found—*Spiroschaudinnia minuta* Castellani—is very delicate, more delicate than *S. bronchialis*. It can be put in evidence by the ultra-microscope, or by staining with various modifications of Romanowsky, the best for this particular spirochæte being apparently Jenner's modification. Silver methods of staining (especially using Fontana-Tribondeau's technique) give good results. In preparations stained with Romanowsky, or other modifications of this method, the organism takes often a pinkish-red or purplish tinge. The length of the organism varies from 3 to 10 or 12 or more microns. The beginner should be careful not to mistake for spirochætes undulating fibrin threads, particles of detached ciliated epithelium, and detached cilia.

Symptomatology.—The affection does not clinically differ from an ordinary attack of coryza. There is sneezing, sero-mucous nasal discharge, occasionally a slight cough. The patient may complain of headache, and there may be some slight fever.

In a few days, as a rule, all the symptoms disappear, but occasionally the affection may run a much longer course, and may spread to the larynx, trachea, and bronchi. In two cases of bronchitis following an attack of spirochætic coryza above described Castellani observed in the expectoration the same type of spirochæte, and it would appear, therefore, that there may be several types of bronchial spirochætosis.

Diagnosis.—This is based on the microscopical examination of the nasal and pharyngeal secretion. The beginner should be careful not to recognize as spirochætes detached cilia and segments of undulating fibrin threads.

Prognosis.—This appears to be favourable.

Treatment.—A carbolic cocaine spray (carbolic acid 3 minims, cocaine hydrochloride 1 grain, water 1 ounce) will be found useful. Aspirin, pyramidon, and quinine may be administered internally in 5 grain doses three or four times daily. In cases running a protracted course arsenic may be tried.

In a few cases of naso-pharyngitis preceding, at times, typical cases of bronchospirochætosis the nasal and pharyngeal secretion may contain *S. bronchialis*, though this is rare. Several ætiological types of nasal spirochætosis might therefore be, perhaps, distinguished. In the tropics one comes across occasionally ulcerative affections of the nose, with presence of numerous coarse spirochætes and *Bacillus fusiformis*, but these conditions have nothing to do with true rhino-pharyngitis spirochætica.

BRONCHIAL SPIROCHÆTOSIS.

Synonyms.—Castellani's bronchitis (Galli Valerio). Spirochétose bronchopulmonaire de Castellani (Violle). Bronchite sanglante (Violle).

Definition.—A type of bronchitis and broncho-alveolitis characterized by the presence of enormous numbers of spirochætes in the expectoration.

History.—The affection was described by Castellani in 1905 and 1906. He named the causative spirochæte *S. bronchialis* in 1907. Castellani's findings were speedily confirmed by Branch, in 1906 and 1907, in Kingstown, St. Vincent, and by Jackson, in 1908, in the Philippine Islands. In 1909 Waters described numerous cases of the disease occurring in India, and Phalen and Kilbourne a case in the Philippine Islands, where, in 1911, Chamberlain recorded two further cases.

In 1913 Chalmers and O'Farrell carried out an investigation on the malady in the Sudan, and succeeded in reproducing it in a monkey. In 1914 Taylor investigated the condition in Uganda. In 1915 Fantham published a classical paper on *Spirochæta bronchialis*, studying it completely from a morphological point of view, and described its granular stage and the intracellular forms of the parasite.

In the same year Macfie reported cases from West Africa, and

Galli Valerio recorded several interesting cases of the malady in Switzerland, and Lurie one in Serbia. In 1917 Galli Valerio recorded further cases in Switzerland. In 1917 Violle first discovered the affection in France, making a very complete investigation and publishing numerous papers on it. Violle's observations stimulated further research in France, and a number of cases of the malady were reported by Bine, Dide, and Ribereau, by Netter, by Dalimier, by Barbary, and others. Alcock has described a case in an English soldier in the North of Italy. Villa and, later, Corvetto have recorded cases in South America.

Geographical.—The disease has probably a cosmopolitan distribution. It has been found in Ceylon, India, Philippine Islands, China and Indo China, North and Equatorial Africa, being especially common in the Sudan, West Indies, America, and recently in Europe in the Balkans, Italy, Switzerland, France, and England.

Ætiology.—The disease is due to *S. bronchialis* Castellani, 1907. The parasite has been further investigated by several observers, and in a masterly manner, in 1914, by Fantham, who described its coccoid and intracellular stages. The organism is extremely polymorphic, being very variable in length, thickness, and the number of waves. One may distinguish thick and thin forms, long, short, and intermediate types. The length may vary between 5 and 30 microns, its breadth between 0·2 and 0·6 micron. A number of the parasites are between 14 and 16 microns, or 7 and 10 microns, the latter resulting, as shown by Fantham, from transverse division of the former.

The ends are of variable shape, but mostly somewhat acuminate. The number of spirals varies between two and eight. Flagella seem to be absent, but Fantham has noticed the presence of a delicate membrane or 'crista' in certain specimens.

In fresh preparations *S. bronchialis* is actively motile for only a short time; the motile phase, as demonstrated by Fantham, is succeeded by one of granule formation the granules or coccoid bodies representing a resting stage from which new spirochætes develop. Fantham has carefully compared *S. bronchialis* with the common mouth spirochætes, and has come to the conclusion that they differ in several features. *S. bronchialis* is more actively motile than the oral spirochætes; it dies, as observed first by Chalmers and O'Farrell, and later by Taylor, very quickly in fresh preparations, while the oral spirochætes may live for hours outside the human mouth. Coccoid bodies are much more frequently produced by *S. bronchialis* than by the spirochætes of the mouth. Intracellular stages are occasionally seen in the case of *S. bronchialis*, but not in the case of spirochætes from the mouth. *S. bronchialis* stains with more difficulty than the oral spirochætes, is slenderer than one of them, *S. buccalis*, and does not appear to produce pseudo-membranes.

Predisposing Causes.—A chill acts, in our experience, as a very important predisposing or secondary cause.

Experimental Reproduction.—Chalmers and O'Farrell have succeeded in reproducing the disease in monkeys. Cases of human laboratory infections have been recorded by some authorities. Attempts to infect guinea-pigs and rabbits have failed.

Method of Infection.—Infection takes place from infected to healthy persons, the spray exhaled in coughing, etc., being contaminated with the spirochætes or, more probably, according to Fantham, with the resistant coccoid bodies produced by *S. bronchialis*. It is also probable that a certain number of persons may harbour *S. bronchialis*, and that a chill or any cause decreasing their organic resistance may induce an increase in its virulence in the same way that a chill may act on the pneumococcus. To this latter possibility Violle and others have called attention.

Symptomatology.—Three types of the disease may be distinguished —the acute type, the subacute type, the chronic type.

Acute Bronchospirochætosis.—In the acute type the patient feels chilly and develops fever, which generally is not very high, rarely exceeding 103° F. The fever may last between two and eight days. The patient coughs a great deal, and may have rheumatoid pains all over the body. The expectoration is scanty, muco-purulent, very seldom containing traces of blood. In most cases the general condition of the patient is not much affected; in others the patient feels very tired and ill.

Subacute Bronchospirochætosis.—The attack begins suddenly or gradually, and lasts between two and several weeks; in many cases there is very little or no fever, and the general condition of the patient may be fairly satisfactory. The cough is frequent and there is often expectoration of pink jelly-like mucus, and true hæmoptysis may take place. The physical examination of the chest may reveal nothing at all, or only signs of simple bronchitis; but at times patches of slight dulness with crepitations may be observed. The blood may show a slight degree of anæmia, but the number of leucocytes is normal, and so is the differential leucocytic count.

Chronic Bronchospirochætosis.—Chronic bronchial spirochætosis may follow on an acute or subacute attack or several such attacks, but frequently the onset is quite insidious and slow. The patient has a chronic cough, which is in certain cases more severe in the morning. The expectoration is not very abundant, and may be muco-purulent in character, but in many cases for periods of two or three days, and even much longer, the expectoration contains blood. Sometimes attacks of genuine hæmoptysis occur, one or two teaspoonfuls or much more of blood being expectorated. In some cases there is no fever; in others a true hectic-like fever may be present. In some cases, however, the rise of temperature takes place in the morning, and not in the afternoon; in others the fever is present only occasionally, and is very irregular. The physical examination of the chest reveals in many cases very little except a few dry or coarse moist râles. In others there may be signs of consolidation. The general condition may remain fairly good for a long time, though a certain degree of anæmia is often present. A few cases waste rapidly.

The course of the disease may be prolonged, with periods of great improvement and even apparent cure.

Bronchospirochætosis in the Lower Animals.—Mendelson in Siam has recently made the interesting observation of the occurrence of a form of bronchopulmonary spirochætosis in cats.

Complications.—Pneumonia and bronchopneumonia have been observed. Rhinitis has been noted. The disease may be complicated with tuberculosis and bronchomycosis.

Diagnosis.—This is based on the microscopic examination of the expectoration collected after rinsing the mouth and gargling with sterile water. The sputum may be examined fresh, using the dark ground illumination, or may be stained, using one of the many modifications of the Romanowsky stain, or nitrate of silver staining methods, such as the Fontana-Tribondeau, may be employed. The *Spirochæta bronchialis* is generally present in large numbers, while bacteria are very few.

Differential Diagnosis.—The acute type is often mistaken for influenza or malaria. The examination of the sputum, in which no Pfeiffer's bacilli are found, will distinguish the affection from influenza, and the examination of the blood will exclude malaria.

Cases of the subacute and chronic type presenting blood in the expectoration are generally diagnosed as phthisis. The examination of the sputum for tubercular bacilli will be always negative, and the animal inoculations will remain without effect. The ophthalmo- and cuti-reactions are negative in the great majority of cases. Occasionally, however, cases of mixed infections of tuberculosis and spirochætosis occur. From bronchomycosis the affection is distinguished by the absence of fungi; cases of double infection, however, bronchospirochætosis, and bronchomycosis, may at times be observed, though very rarely.

Spirochætosis is easily distinguished from endemic hæmoptysis by the examination of the sputum, which will show absence of the ova of *Paragonimus ringeri* Cobbold, and from bronchomycosis by the absence of fungi.

Prognosis.—The prognosis is favourable *quoad vitam*, but the disease may take a chronic course with anæmia and wasting.

Treatment.—In the acute cases all the symptoms as a rule disappear after a few days' rest in bed. Codeine ($\frac{1}{3}$ grain) and aspirin (5 grains) may be administered when the cough is painful and the patient complains of rheumatoid pains. In the subacute and chronic types of the disease, arsenic, introduced by Castellani in the treatment of the malady since 1906, gives good results. It may be administered by the mouth in the form of liquor arsenicalis or arsenious acid pills, or may be given subcutaneously in the form of cacodylates. Plaut and Galli Valerio recommend salvarsan. When the expectoration is profuse, glycerophosphates and balsamics are useful.

In certain cases tartar emetic, especially if combined with arsenic, is efficacious. The following formula may be used:—Tartar emetic, $\frac{1}{8}$-$\frac{1}{4}$ grain; liquor arsenicalis, 2-3 minims; codein, $\frac{1}{8}$ grain; glycerine, 1 drachm; syrup of tolu, 1 drachm; aquæ chloroformi, 1 drachm. One ounce to be taken three times a day well diluted.

Occasionally in cases with very dry cough, potassium iodide may be found useful; for instance:—Tartar emetic, $\frac{1}{8}$-$\frac{1}{4}$ grain; potassium iodide, 5 grains; bicarbonate of soda, 10 grains; glycerine, 1 drachm; syrup of tolu, 1 drachm; chloroform water, 1 ounce. One ounce to be taken three times a day well diluted with water.

Dalimier recommends injections of camphorated oil with gomenol in acute cases, and Liquor Fowleri in cinchona wine in chronic cases.

TROPICAL BRONCHOMYCOSES.

General Remarks.- Affections of the bronchi and lungs due to fungi are common in the tropics, though very little attention has been paid to them till recently. These conditions may be due to a variety of fungi, and may be classified in several groups:-

1. Due to fungi of the genus *Monilia* Persoon, 1797; *Oidium* Link, 1809; *Saccharomyces* Meyen, 1833; *Willia* Hansen, 1904; *Cryptococcus* Gilchrist and Stoker, 1896; *Coccidioides* Rixford and Gilchrist, 1898.
2. Due to fungi of the genus *Hemispora* Vuillemin, 1906.
3. Due to fungi of the genus *Nocardia* Toni and Trevisan, 1899; *Cohnistreptothrix* Pinoy, 1911.
4. Due to fungi of the genus *Aspergillus*, 1729; *Sterigmatocystis* Cramer, 1859; *Penicillium* Link, 1908; *Mucor* Micheli, 1729; *Rhizomucor* Lucet et Costantin, 1900; *Lichtheimia* Vuillemin, 1904.
5. Due to fungi of the genus *Sporotrichum* Link, 1809.

For description of above fungi the reader is referred to Chapters XXXVII., p. 967, XXXVIII., p. 978, and XXXIX., p. 1035.

The symptoms are somewhat similar, whichever fungus is the ætiological factor. In *mild cases* there are signs of slight bronchitis with muco-purulent expectoration in which the fungi are found. In *severe cases* the patient presents all the symptoms of phthisis, with hectic fever and hæmorrhagic expectoration.

Mild cases may get cured spontaneously: but they are often benefited by potassium iodide. We will describe in detail the forms of bronchomycosis which has been more completely investigated.

Bronchomoniliasis.

Synonyms.—Broncho-alveolar moniliasis (Castellani), Bronchoblastomycosis *pro parte*.

Definition.- An infection of the bronchial mucosa due to fungi of the genus *Monilia* Persoon, 1797.

Historical.—Since 1905 Castellani has published many cases, divisible into a mild type and a severe type of the disease, and has described several new species of *Monilia*. Castellani's work has recently been confirmed by Pijper, Pantin, and other observers. Magrou has recorded a case in France in 1916.

Geographical Distribution.—The disease is found all over the tropics, especially in places with a damp climate, such as Ceylon and the Malay Peninsula. The affection may be met with also in Europe and America, cases having been recently recorded by Pinoy, Iacono, and others.

Ætiology.—In Ceylon the malady is generally due to *Monilia tropicalis* Castellani, 1910. The same fungus may be found in cases coming from South India and the Malay States. It would appear that the fungus is the real cause of the disease, as no other ætiological agents, such as the tubercle bacillus, etc., are found. Moreover, when the patient gets better, the fungus becomes very scanty, or disappears completely. In some cases other species of the fungus may be observed, but it is doubtful whether all of these are really pathogenic. These species are *Monilia paratropicalis* Castellani, *M. pinoyi* Castellani, *M. guilliermondi* Castellani, *M. negrii* Castellani, *M. candida* Castellani, *M. nivea* Castellani, *M. insolita* Castellani, *M. pseudotropicalis* Castellani, *M. lacticolor* Castellani, *M. nitida* Castellani, *M. lactea* Castellani, *M. krusei* Castellani, and other monilias, among which *M. bethaliensis* Pijper. For the cultural characters of these species see p. 1079.

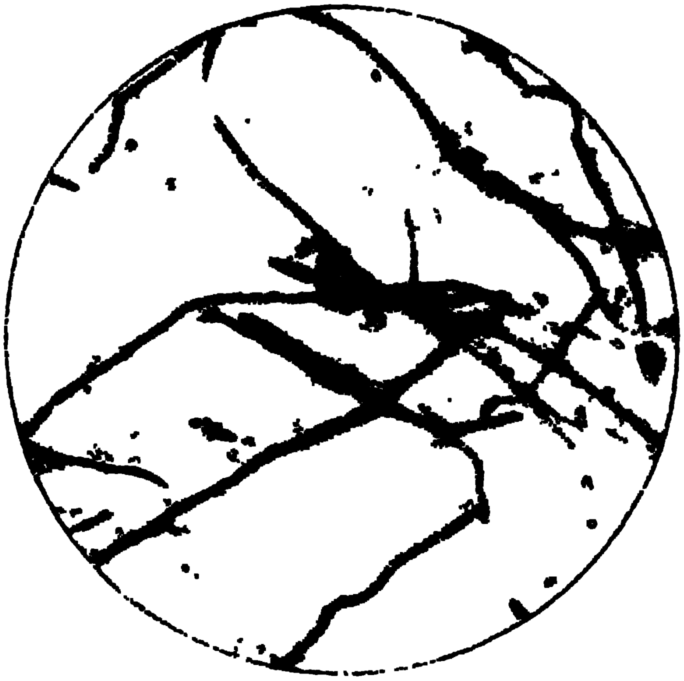

FIG. 773.—FUNGUS FROM A CASE OF BRONCHOMYCOSIS (UNDETERMINED)

The infection may take place from man to man, and also probably by the fungi living saprophytically in nature. Monilia-like fungi are extremely common in Ceylon in tea-dust, and it is very probable that the so-called 'tea-factory cough' is a type of moniliasis.

Symptomatology.—A mild and a severe type of the malady may be distinguished. In the *mild type* the general condition of the patient is fairly good, there is no fever, and he simply complains of cough. The expectoration is muco-purulent and very often scanty, and no blood can be seen. The physical examination of the chest will reveal only a few coarse râles or absolutely nothing. The condition may last several weeks or months, and may get cured spontaneously, or, continuing, may turn into the severe type. The *severe type* closely resembles phthisis; the patient becomes emaciated, there is hectic fever, muco-purulent and bloody expectoration. Occasionally true hæmoptysis occurs, a teaspoonful or more of bright blood being spat up at a time. The physical examination of the chest may show patches of dulness, fine crepitations, and pleural rubbing. This type is often fatal. Between these two extreme types there are of course cases of intermediate severity, apyretic or with subcontinuous and continuous fever, and more or less marked bronchial and broncho-alveolar symptoms.

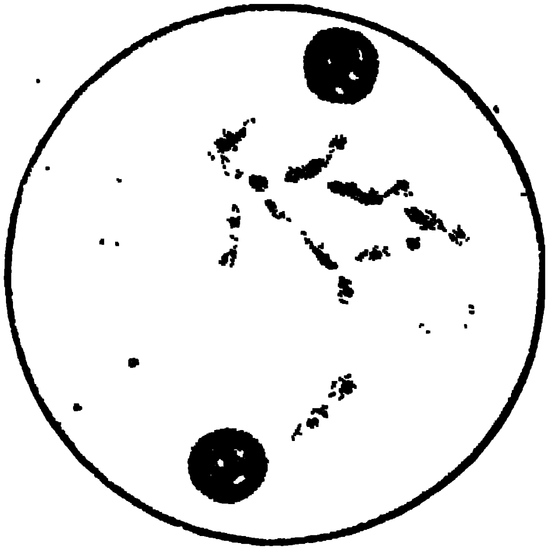

FIG. 774.—SPUTUM IN BRONCHOMONILIASIS (SEVERE CASE).
(From a preparation stained with methylene blue.)

Diagnosis.—The diagnosis of moniliasis is based on finding the fungus in the sputum. It is absolutely necessary that this should be collected in sterile petri dishes and examined as soon as possible, as sputum exposed to the air becomes contaminated with all sorts of fungi in the tropics. In fresh preparations of the expectoration spore-like, roundish, or oval cells 4 to 6 μ are seen, often presenting a double contour, alone or more rarely with some mycelial articles. The fungus is Gram-positive.

To identify the fungus cultural researches are necessary. A particle of the sputum is smeared on maltose or glucose agar plates; after two or three days white, rather large, roundish colonies appear, easily distinguishable, even macroscopically, with a little practice, from the colonies of cocci and other bacteria. The fungus colonies are further investigated by inoculating maltose agar, ordinary agar, gelatine, serum, and a set of sugar broths. All the species of *Monilia* found in our cases grow well on ordinary agar, but much more abundantly on maltose and glucose agar, especially if slightly acid.

On these media the growth, which is generally white with a smooth surface when young, slightly crinkled when old, is composed practically of globular, yeast-like cells, while in the water of condensation globular cells and mycelial elements are found together. A little mycelium may, however, be found also occasionally in the growth on the slope. On serum all the strains produce at first a white growth, but some, later on, induce a peculiar brownish-black discoloration of the medium round the growth. Most species do not liquefy the medium.

On *gelatine* all the species grow fairly well; a few, including *Monilia albicans*, produce liquefaction of this medium. In milk some do not produce either acid or clot, others produce a temporary or permanent acidity, others clot the milk or peptonize it. The reactions in the various sugar broths are important, and in association with the behaviour of the fungi on serum, gelatine, and milk, give the data on which to differentiate the various species (*vide* p. 1081).

Differential Diagnosis.—Primary bronchomoniliasis, as described in this chapter, should be distinguished from the secondary bronchomoniliasis occasionally met with in cachectic patients suffering from cancer, diabetes, tuberculosis, etc. In such cases there is generally thrush of the oral mucosa, and the thrush *Monilias* spread to the pharynx, larynx, and bronchial mucosa, while in primary bronchomoniliasis the oral mucosa is not, as a rule, affected.

From pulmonary tuberculosis the condition is distinguished by the absence of the tubercle bacillus in the sputum and the negative animal inoculations. Cases of mixed infection, however—tuberculosis and moniliasis—are occasionally met with, the sputum containing both the tubercle bacillus and the *Monilia* fungi.

From bronchospirochætosis it is recognized by the absence of spirochætes, though occasionally cases of mixed infection occur; from endemic hæmoptysis by the absence of the ova of *Paragonimus ringeri* Cobbold.

Prognosis.—The cases of a mild type may recover spontaneously or under appropriate treatment. Those of the severe type usually end fatally.

Treatment.—Mild cases and those of medium gravity respond often to potassium iodide (gr. x. to xx.) given well diluted in water or milk three times daily. When potassium iodide causes severe symptoms of iodism, saiodin in the same doses (in cachets) may be administered. In the cases of the severe type we have seen no improvement from the many different treatments administered. Potassium iodide, however, should always be tried also in these cases, as well as balsamics. The diet should be nourishing; hypophosphites and glycerophosphates may be tried to keep up the strength of the patient, as in phthisis.

Broncho-Oidiosis.

Synonyms.—Bronchial oidiomycosis, Broncho-endomycosis.

Historical.—Cases have been described by Blanchard, Chantemesse and Vidal, Linossier, Pinoy, Castellani, and others.

Geographical Distribution.—The same as bronchomoniliasis.

Ætiology.—The following species of the genus *Oidium* Link have been found in cases of bronchitis, although it is doubtful whether they are all pathogenic:—

Oidium lactis Link, including *O. lactis A*, a variety described by Linossier.
Oidium matalense Castellani.
Oidium rotundatum Castellani.
Oidium asteroides Castellani.

For description of these fungi the reader is referred to Chapter XXXIX., p. 1093.

Symptomatology.—This is identical with that of bronchomoniliasis, and two types may be distinguished: the mild type and the severe one.

Prognosis.—Favourable in a certain number of cases but cases are met with which do not respond to any treatment and terminate fatally.

Diagnosis.—This can be made only by cultural methods.

Treatment.—Potassium iodide should be tried in all cases, but its action in a large number of them is very uncertain or completely negative. It may be given in combination with glycerophosphates. A change of climate is often useful.

Bronchohemisporosis.

General Remarks.—This bronchomycosis has been described by Castellani. The fungus found so far is *Hemispora rugosa* Castellani, a description of which will be found in Chapter XXXIX., p. 1108.

Symptomatology.—The symptoms are very similar to those seen in bronchomoniliasis, and a mild and a severe type of the affection may be distinguished. In the mild type the general condition of the patient is good, there is no fever, and he simply complains of cough. The expectoration is muco-purulent and does not contain blood. The physical examination of the chest is negative or reveals only a few râles. The *severe type* closely resembles phthisis. The patient becomes emaciated, there is hectic fever, and the expectoration may be bloody. The physical examination may reveal patches of dulness, fine crepitations, pleural rubbing.

Complications.—The affection may be complicated with a tonsillitis, caused by the same fungus and characterized by the presence of yellowish or greyish patches: at other times the tonsillitis is the primary lesion.

Treatment.—Potassium iodide seems to be more efficacious in this condition than in bronchomoniliasis. It should be given in 10-grain doses, well diluted in water or milk, twice or four times daily. Glycerophosphates and balsamics are useful.

Tea-Factory Cough.

This affection described by Castellani in 1910, is common in Ceylon. It is probably a form of broncho-mycosis. Coolies working in tea-factories are occasionally observed to deteriorate in their general health, losing flesh and becoming easily tired; at the same time they develop a cough with muco-purulent expectoration. The physical examination of the chest reveals nothing except occasionally a few coarse râles. If these coolies are taken away from the factory and sent to work in the fields, all the symptoms slowly disappear.

A similar affection may be observed in tea-tasters. Tea-tasters, in order to judge of the quality of teas, not only taste infusions, but frequently fill their hands with the leaves and bury their noses in them, snuffing them up; in this way a certain amount of tea-dust enters their nasal cavities, and with the tea-dust the micro-organisms which are found in it. According to the researches of one of us, tea and tea-dust in Ceylon contain:—

1. Fungi of the genus *Monilia* constantly.
2. Fungi of the genus *Oidium* occasionally.
3. Fungi of the genus *Aspergillus*, *Sterigmatocystis*, and *Penicillium* frequently.
4. A peculiar *streptococcus*, somewhat different from *S. pyogenes*, frequently.

It is interesting to note that such germs are very rare or absent in samples of tea examined in England. The same organisms may be found, in Ceylon, in nasal cavities of tea-tasters: in their expectoration the *Monilia*-like fungi are practically constant, the *streptococci* very frequent, while *Aspergillus* and *Penicillium* fungi are rare. Guinea-pigs in whose nostrils tea-dust is daily insufflated for months develop a broncho alveolar moniliasis.

Bronchial Aspergillosis.

Synonyms.—Broncho-alveolar aspergillosis, Aspergillar pseudo-tuberculosis, Pneumomycosis of aspergillar origin.

Definition.—A form of bronchitis and broncho-alveolitis due to fungi of the genus *Aspergillus* Micheli, 1729, and *Sterigmatocystis* Cramer, 1869 (p. 1026).

Historical.—The condition has been studied by Virchow, Lichtheim, Dieulafoy, Chantemesse, Widal, one of us, Wise, and others.

Climatology.—The geographical distribution of the disease seems to be cosmopolitan. It is very common in certain parts of France, and one of us has seen two cases in the Balkans. In the tropics we have seen some cases in Ceylon and Tropical Africa, and Wise has reported a case from British Guiana.

Ætiology.—The condition is due to fungi of the genus *Aspergillus* Micheli and *Sterigmatocystis* Cramer. It is common especially in people who have to handle various grains on which spores of those fungi are often found. In France it is extremely frequent among pigeon-breeders (*gaveurs de pigeons*), who fill their mouths with grain and blow it into the mouths of the pigeons. Of the two cases observed by us in the Balkans, one was apparently due to *Aspergillus fumigatus* Fresenius, the other to *Sterigmatocystis nigra* Cramer.

It is probable that the deleterious effects caused by the fungi are due not only to a mechanical irritative action, but also to toxins secreted by the fungi.

Morbid Anatomy.—The lungs, and occasionally the liver, kidneys, and other organs, may show a type of pseudo-tuberculosis characterized by the presence of numerous mycotic tubercular-like nodules.

Symptomatology.—The presence of the fungi in the bronchi, when in smal amount, may not give rise to any symptom. When the infection is heavy, symptoms of bronchitis with muco-purulent, and occasionally bloody, expectoration are present, and in severe cases the patient may have hectic temperature, with sweatings and great wasting.

Diagnosis.—This is based on finding the fungus. It is to be noted that in the sputum as a rule only mycelial threads are found, and cultivations are therefore necessary.

Prognosis.—Mild cases often recover, but in severe cases with bloody expectoration the prognosis is bad.

Treatment.—A change of climate and, when the condition is brought about by certain occupations, a change of occupation is very beneficial. Potassium iodide (gr. xv. to xx.) may be administered.

Bronchial Penicilliosis.

One of us has observed cases of bronchitis and broncho-alveolitis due to fungi of the genus *Penicillium* in the tropics and one in the Balcanic zone. The fungus isolated from the last case was *P. crustaceum* Linnæus.

The symptomatology, diagnosis, and treatment are the same as in Bronchial Aspergillosis.

Bronchial Mucormycosis.

Cases of bronchitis caused by fungi of the genus *Mucor* Micheli, 1729, *Lichtheimia* Vuillemin, 1904, *Rhizomucor* Lucet and Costantin, 1900, *Rhizopus* Ehrenberg, 1820, may be met with, but are of rare occurrence. The symptomatology is the same as that of Bronchial Aspergillosis. We have seen a case in the Balcanic zone due to *Mucor mucedo* Linnæus. For description of the fungi see p. 972.

Bronchial Sporotrichosis.

A few cases have been described of a bronchitis due to fungi of the genus *Sporotrichum* Link, 1809

Undetermined Bronchomycosis.

One of us has described cases of bronchomycosis due to fungi which have not yet been classed.

PULMONARY NOCARDIASIS.

Synonyms.—Pulmonary streptothromycosis, Pseudo-tuberculosis.

Definition.—Pulmonary nocardiasis is an infection of the lung, and usually other organs, with a species of the fungal genus *Nocardia* Toni and Trevisan, in which the signs and symptoms more or less resemble those of phthisis.

Historical.—In 1897 Flexner described this disease, isolating the causal organism, which he named *Streptothrix pseudotuberculosa* Flexner, 1897. In the same year Buchholz found a similar case in Berlin, and Scheele and Petruschky described a third at the Wiesbaden Congress. In 1902 Birt and Leishman met with a case in a soldier, and since then similar cases have been recorded by Foulerton, by Roger, Bory, and Sartory in 1909, and have been seen by ourselves in Ceylon, the Balcanic zone, and the Anglo-Egyptian Sudan, and by Pijper in South Africa

Climatology.—The disease occurs in the Temperate and Tropical Zones, in the New and the Old World, and may therefore be widespread.

Ætiology.—The causal agents appear to be varying species of nocardia—thus, for example, Flexner's case was caused by *Nocardia pseudotuberculosa* (Flexner, 1897); Birt and Leishman's case by *Nocardia leishmani* Chalmers and Christopherson, 1916; Scheele and Petruschky's case by *N. gedanensis* (Scheele and Petruschky, 1897); and Foulerton's organism by *N. foulertoni* Chalmers and Christopherson, 1916; while Roger, Bory, and Sartory's organism is called *N. pulmonalis* (Roger, Bory, and Sartory, 1909). Very commonly these fungi are present in the sputum as acid-fast rods which may or may not appear in branched form. When present in rod-like forms they give rise to an appearance somewhat resembling the tubercle bacillus. Other species of nocardia, also found in sputum, may not be acid-fast, and these are more easily recognized.

Morbid Anatomy.—As a rule the appearances found post-mortem are not unlike that of tuberculosis. There is consolidation, necrosis, and cavity formation in the lung, with or without the signs of caseous pneumonia or of calcareous deposition, or there may be small cirrhotic nodules scattered through the lung. There may also be nodules in the liver, spleen, peritoneum, and lymph glands, and there may be chocolate-coloured exudate into the pleural or peritoneal cavities. This exudate may be odourless or fœtid in odour. The fungus can be easily found in these pseudo-tubercles.

Symptomatology.—In general it may be stated that the symptoms resemble those of phthisis, and as such the disease is usually recognized. Usually there is fever, cough, a muco-purulent sputum containing blood at times and showing acid-fast rods resembling the *Bacillus tuberculosis*, but careful search may reveal a few elongate or branching forms. The physical signs are those of chronic broncho-pneumonia, with or without cavity formation, and with or without those of pleural effusion. The liver and spleen are often enlarged. The cases usually go from bad to worse, and end in death.

Diagnosis.—Many of these cases are diagnosed as *pulmonary tuberculosis* at the present time. The correct diagnosis can only be established by a careful examination of the sputum, by microscopical and bacteriological methods, including the culture of the organism.

The differential diagnosis has to be made from *phthisis* and *liver abscess*.

It may be distinguished from phthisis by the recognition of the beaded branched organism in the sputum and the culture of it therefrom.

In cases giving a history of dysentery and exhibiting enlargement of the liver, fever, and a purulent chocolate coloured effusion into the pleural cavity, the diagnosis can only be effected by finding the fungus and by the absence of any pus in the liver. In such cases the dysenteric amœba may be present in the fæces.

For the morphological and cultural characters of the species of nocardia see Chapter XXXIX., p. 1040.

Prognosis.—So far the prognosis is very bad, as all known cases have died.

Treatment.—Iodide of potash in large doses may be tried or a vaccine made from the patient's causal organism.

Prophylaxis.—Nothing whatever can be said on this part of the subject.

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CHAPTER LXXXII

DISEASES OF THE CIRCULATORY SYSTEM

General remarks—The blood—Blood puzzles—Anæmia and allied conditions—Leukæmia—General dropsy—The heart—The vessels—The spleen—The bone-marrow—References.

GENERAL REMARKS.

In this chapter we merely make a *few allusions* to some points of tropical importance with regard to the blood and the organs which produce and circulate it. The subject is not merely a large one, but is of great importance in the tropics, and our few remarks are merely of an introductory nature.

THE BLOOD.

We in no way intend to enter at all fully into an important study of the blood, which is to be found in detail in the special books devoted to its elucidation; but we desire, in the briefest manner possible, to present to the reader a few remarks which have a direct bearing upon the various references which we have made from time to time in the preceding chapters with regard to it.

The Erythrocyte.

In embryonic life the first sign of the blood cell is to be found in those mesoblast cells of the vascular area which contain hæmoglobin and are called megaloblasts, and to these are added later similar cells without hæmoglobin and found in the liver. In post-embryonic life these cells are found in the red marrow lying at the ends of long bones and in flat bones, and normally do not appear in the circulating blood, but are the parents of the normoblasts, which are commonly found in the blood after mid-term of fœtal life and in the red bone-marrow of post-embryonic existence.

These normoblasts, multiplying by mitosis, are the source of the erythrocyte, which alone is the proper denizen of the circulating blood.

An erythrocyte, according to von Schilling-Torgau, is saucer-shaped, with a thickened edge, and consists of:—

1. An ectoplasmic cell *membrane*, inside which lies the endoplasm, of which the peripheral portion is condensed to form the *endoplasmic capsule*, which is Weidenreich's cholesterin-lecithin membrane, inside

which lies the *stroma*, in the form of a network of protoplasmic threads and nodes, which contains the hæmoglobin, and in the saucer-shaped corpuscle forms a cap over the archoplasm, which lies just over the concavity of the saucer.

2. The *archoplasm* is composed of a central clear hæmoglobin-free area, and is composed of a *glassy body*, which is rest material, and which in ordinary cells forms the achromatic spindle in mitosis. Excentrically placed and surrounded by the glassy body lies the *capsule corpuscle*, near which lie two sharply defined bodies embedded in a substance which may contain a vacuole. These are the *centrioles*.

3. The *blood plate* is the metamorphosed nucleus of the normoblast, which lies excentrically on one side of the archoplasm. It is easily extruded in making the blood film, and gives rise to the blood platelets which are so well known. Its peculiar appearance is possibly due to physiological modification during mitosis of the normoblast.

4. *Meve's plastokonten* are granular bodies of unknown nature scattered through the erythrocyte, but mostly seen near the archoplasm.

As we shall see later, these various parts of the erythrocyte are the explanation of the intracorpuscular blood puzzles and the origin of the numerous intracorpuscular pseudo-parasites of many observers.

The red corpuscles number some five millions in a healthy male, and some four and a half millions in a healthy adult female under the climacteric age, but there are physiological increases of these numbers in infancy, by cold and at high altitudes, while race has but little influence.

Pathologically they can be increased by mechanical means—*e.g.*, the concentration of the blood caused by diarrhœa, sweating, vomiting, and polyuria, or by heart disease. They can also be increased in toxic conditions and in polycythemic splenomegaly. They may be decreased by any mechanical, toxic, or parasitic cause which induces blood destruction.

The normoblasts of the bone-marrow may accidentally occur in the normal circulating blood as an isolated form, but in numbers they indicate that there is an abnormal demand for erythrocytes—as, for example, after a hæmorrhage. A normoblast is about the same size as an erythrocyte (7·5 microns), but contains a rounded nucleus composed of a nuclear membrane containing dense chromatin and measuring about 4 microns.

The megaloblasts may be found in the circulating blood if some toxin is attacking the bone-marrow. They are usually of large size (20 microns), but this is not their characteristic, which is the large nucleus measuring some 10 microns and containing loosely arranged hromatin. The nucleus may undergo the usual changes, and the egaloblast become a megalocyte.

Microblasts are small cells or abnormal normoblasts or megaloasts.

The Leucocyte.

In post-embryonic life the home of the leucocyte or colourless blood cell is the bone-marrow. They may be divided into the hyaline cells or lymphocytes, which are the least differentiated cells, both ontogenetically and phylogenetically, being the first to appear in the embryo and in the lower animals, and the granular cells or leucocyte *sensú stricto*, which are more highly evolved cells.

It is usual to consider the large lymphocytes, the small lymphocytes, the large mononuclears, and the transitional cells, as all belonging to the same denomination. According to Heidenhain, there is a tendency on the part of the centrosome to reach the centre of the lymphocyte, being pulled thereto by cytoplasmic radii. It is, however, prevented from assuming this position by the nucleus, which succeeds in this obstruction in the case of the small and large lymphocyte, because there is insufficient cytoplasm; but in the case of the large mononuclear it pushes the nucleus to one side, and in the case of the transitional it so indents the nucleus that it attains in both cases the central position. Thus the small lymphocyte by growth can become the large lymphocyte, from which are descended the large mononuclear and the transitional, which may, therefore, be reckoned as a single type in making a differential count.

The small lymphocyte is about the size of an erythrocyte, but somewhat smaller; it possesses a rounded or slightly indented nucleus, colouring deeply with basic stains, and surrounded by a very slight amount of cytoplasm, which shows a reticulum with basophile granules as the nodal points. There are also some azurophile granules.

The large lymphocyte is larger, reaching to 20 microns, and is characterized by a central roundish or slightly indented nucleus, which contains less chromatin than in the small variety. There is more abundant cytoplasm, which does not stain so deeply, but contains the same reticulum and Wolff's azurophile granules.

The large mononuclear leucocyte possesses an excentric nucleus relatively poor in chromatin, surrounded by a larger amount of cytoplasm, with the usual reticulum and azurophile granules.

The transitional cell has its nucleus indented into a horseshoe or sometimes twisted. Lymphocytes and myeloblasts may contain fuchsinophile granules called Schridde's granules. The true leucocytes or granular white cells are classified according to their granules into neutrophile, eosinophile, and basophile. Their parents are the myelocytes of the bone-marrow, which are cells of large size possessing rounded pale-staining nuclei and the granules typical of the particular leucocyte to which they are to give rise.

The most primitive form is the eosinophile leucocyte which is so common in lower animals. It probably has a secondary home in connective and lymphoid tissue. They are characterized by their large refractile granules, which have an affinity for acid stains and a twisted, trilobed, or dumb-bell-shaped nucleus.

The polymorphonuclear neutrophile leucocyte is generally called by the first portion of its name. It varies considerably in size, and is characterized by a lobulated nucleus in which the lobules vary in number, but however separate they may appear, are always connected by fine threads. It is upon this lobulation that the *Arneth count* is based, and the form of the nucleus can be explained in the same way as in the transitional (*vide supra*).

The basophile leucocyte or mast cell has a trilobed nucleus poor in chromatin and a cytoplasm containing basophile granules. The corresponding myelocytes may under abnormal circumstances be found in the circulating blood, and even at times the pro-myelocytes, which resemble myelocytes, but possess a basophile cytoplasm with a few neutrophile granules. More rarely cells with a large rounded nucleus containing a fine chromatinic network and three to four nucleoli, and surrounded by an intensely basophile cytoplasm, may be seen. These are Naegeli's myeloblasts.

Under pathological conditions such as anaemia, with jaundice and leucocythemia, a few plasma cells may be seen in the blood. They are triangular, with an excentric nucleus and a markedly basophile granular cytoplasm.

The number of white cells varies from time to time from about 5,000 to 9,000 per cubic millimetre, but the average is about 7,000, or one to every 700 erythrocytes.

lowing Gulland and Goodal the average differential count is as follows:-

	Per Cent	
Polymorphonuclear neutrophile leucocytes ..	70	Average.
Small lymphocytes	20	
Large lymphocytes	5	
Eosinophile leucocyte . ..	4	Maximum.
Basophile leucocytes	1	

The *Arneth count* formulated in 1904 is based upon the number of lobules in the nucleus of 100 polymorphonuclear or 100 eosinophile leucocytes. Class I. contains those with a single rounded or indented nucleus, and would include any neutrophile myelocyte which happened to be present. Class II. has two, Class III. three, Class IV. four, and Class V. five lobules. The numbers in Classes I. and II. added together give the Arneth index, and in Classes I., II., and half III., give the Bushnell-Trenholtz index. Arneth subdivided each class into smaller groups by the indentations and the character of the loops and lobes, but these are not now considered. He restricted his counts to polymorphonuclears, but to-day eosinophile leucocytes are also considered. In counting it is wise to follow Chamberlain and Vedder, and to consider as one, lobules with a distinct isthmus, and in cases of doubt to place the number in the higher class. Arneth considered that the youngest cells were those in Classes I. and II., and that those in Class V. were the oldest, while Classes III. and IV. are believed to be adult. These views have been contested, as has Pottenger's opinion that the phagocytic power increases from Class I. to Class IV., and falls in Class V. When the numbers in Classes I. and II. are increased above normal it is called 'a shift to the left,' and the reverse 'a shift to the right,' terms which have been used in Chapter IV. According to Arneth, a shift to the left is evidence of lower resistance on the part of the patient to a disease. This count has been tested in the tropics by Chamberlain and Vedder, Macfie, Breinl, and others, as has been set forth on p. 75.

A few examples may be given as follows:—

ARNETH COUNT.

Kind of Leucocyte.	*Nature of Observation.*	*Observer.*	*Class I.*	*Class II.*	*Class III.*	*Class IV.*	*Class V.*	*Arneth Index.*
Polymorphs	Normal in Europe	Arneth	5	35	41	17	2·0	40·0
Polymorphs	Normal in America	Kagan	5	19	46	25	5·0	24·0
Polymorphs	Normal Americans in Philippines	Chamberlain and Vedder	13·3	32·9	37·2	14·6	2·0	46·2
Polymorphs	Normal Philippinos	Chamberlain and Vedder	27·5	38·3	25·8	7·5	0·9	65·8
Polymorphs	Normal limits	Simon	4-9	21-47	33-48	9-23	2-4	25-56
Eosinophiles	Normal in Europe	Arneth	11	69	19	1	--	80

Von Schilling-Torgau suggests a modification, which is to classify the neutrophiles as myelocytes, myelocytes with indented nucleus, polymorphs with rod-shaped nuclei, polymorphs with segmented nuclei. It is said that this simple method gives the same results as the Arneth count.

The Arneth count is being used at present in tropical work, but its value is still *sub judice*.

The leucocytes vary in number under physiological and pathological conditions:—

Leucopenia, or diminution in their numbers, may occur in physiological conditions such as hot or cold baths, or in pathological conditions such as certain protozoal infections, malaria, trypanosomiases, and kala-azar; in bacterial infections such as enteroidea, undulant fever, tuberculosis, and influenza, or in severe toxæmias of any kind. The leucopenia is usually polymorphonuclear, but in fevers there is a diminution of eosinophiles.

Leucocytosis, or increase in their numbers, may occur in physiological conditions such as infancy, pregnancy, digestion, and exercise, and there is a terminal or agonal leucocytosis before death. In pathological conditions a leucocytosis due to polymorphonuclear leucocytes may occur in septic or inflammatory conditions, many fevers and toxæmias, after hæmorrhage, and with malignant disease.

Lymphocytosis may be relative when there is a relatively high percentage of lymphocytes and low of polymorphs, with no increase in the total number of white cells, or absolute when the total number of white cells as well as of lymphocytes is increased. The former occurs in protozoal infections such as malaria, amœbic dysentery, etc., and the latter in leukæmia, etc.

Eosinophilia, or increase in the eosinophile leucocytes, occurs in helminth infections, in skin diseases, in asthma, in toxic states, and in myelocythæmia.

Basophilia occurs in myelocythæmia and staphylococcal infections, but in the latter only slightly.

Blood Platelets.

These are probably derived from the erythrocytes, and may possibly not be present in normal circulating blood, but formed in preparing the films. Their clinical value is not absolutely certain. They are said to number about 300,000 per cubic millimetre in health. They are colourless, refractile, discoidal bodies, some 1-3 microns in diameter, having a great tendency to adhere together and having an affinity for basic dyes.

Hæmoconia.

These are colourless refractile bodies, 0·5-4 microns in diameter, which do not colour with ordinary stains and are of unknown origin and function, though they may be fat particles, as shown by Neumann.

BLOOD PUZZLES.

Blood puzzles consist of bodies which from the first have been recognized as such or in other instances have been thought to be parasites.

It is difficult to give a systematic account of these bodies, but, following Balfour, we may classify them as follows:—

A. Heterogenetic:—Not in the blood.
B. Autogenetic:—Actually in the blood.
    I. Found in fresh blood:—
        (*a*) Erythrocytic.
        (*b*) Leucocytic.
    II. Found in stained blood:—
        (*a*) Erythrocytic.
        (*b*) Leucocytic or lymphocytic.

Heterogenetic.

These are external or adventitious, and may be divided into:—

I. Those belonging to the glass slide.
II. Those belonging to cleaning or drying materials.
III. Those coming via the air.
IV. Those coming from the skin.
V. Those coming from the intestines.

The Glass Slide.—Everyone is well aware of the peculiar marks which may appear on old glass slides, and which retain the stain, thus giving rise to pseudo-trypanosomes, yeasts, and many other forms.

Perhaps the most interesting of these are the 'X bodies' (Horrocks and Howell) which appear in Romanowsky films as roundish bodies, with a small blue circular centre surrounded by four or more faint concentrically arranged capsules, and which Chamberlain and Vedder have shown to be artefacts present in the glass slide.

Cleaning and Drying Materials.—Cotton fibres may be introduced from a cloth in cleaning slides. Blotting-paper, if used twice for drying blood slides, may introduce one kind of blood into another or bacteria into a blood film.

The Air.—Insect scales, plant hairs, animal hairs, yeasts, and pollen grains, may all be introduced into blood films from the air, and especially multiseptate fungal spores.

The Skin.—Pieces of dirt, epithelial scales, and bacteria, may come from the skin.

The Intestine.—In obtaining films during a post-mortem or from an animal which has been shot there is danger of contamination of the blood with spirochætes and other organisms from the intestine.

Autogenetic.

These are bodies which are really in the blood, whether natural products or artificial productions.

Fresh Blood—ERYTHROCYTE.—In anæmic blood the erythrocytes become deformed, forming oval, pear-shaped, tailed, or irregular bodies called poikilocytes, allied to which are the peculiar chain-like, droplet-like, and filament-like bodies figured by Nuttall and Balfour as produced when taking films in high air temperatures. Some of them may be mistaken for parasites, but only by beginners.

A crenation seen in a deformed or in an ordinary corpuscle may in certain focal planes look like a malarial parasite.

Vacuoles have clear-cut margins, do not move, do not possess pigment, and are quite clear, yet they give rise to trouble, and may be mistaken for piroplasma or for malarial parasites.

The glassy body mentioned above, when easily visible, is often mistaken for a parasite, and is probably the explanation of the 'maraglianos' or dehæmoglobinized spots which have been described, as well as of such pseudo-parasites as those mentioned by Balfour as being described by Foran and Breeze. The dark spot mentioned as being visible in the maraglianos may be the centrosome.

A granule from a leucocyte or a blood platelet lying on an erythrocyte may simulate a parasite.

LEUCOCYTE.—The leucocyte, especially the eosinophile, is responsible for the free granules, and worse for the free or attached wavy process, which is apt to be mistaken for a spirochæte, especially when a beginner is using the dark-ground illumination.

Stained Blood.—ERYTHROCYTE.— When the glassy body swells it gives rise to pale large red blood cells 15-50 microns in diameter, which are the half-moon-shaped or sickle-shaped corpuscles of Stephens and Christophers.

The hæmolyzed stroma is the cause of the shadow corpuscles, and polychromatophilia is due to diffuse colouring of the reticulum, while the punctate form is due to the nodes being especially tinted.

Schüffner's dots are caused by the coloration of nodes of the reticulum in older cells, while pathological karyolysis of the nuclear plate may be the cause of the Howell-Jolly bodies and the ring-shaped bodies of Cabot, and perhaps the so-called *Paraplasma flavigenum* is due to the same cause.

The capsule corpuscle may be the origin of Arnold's nucleoids, Schmauch's bodies, Heinz's corpuscles, and many pseudo-parasites.

A blood platelet lying on an erythrocyte may resemble a malarial parasite.

LEUCOCYTE.—The puzzles in connection with the leucocyte or lymphocyte may be divided into.—

1. Extranuclear.
2. Intranuclear.

Extranuclear.—Kurloff's bodies seen in the large lymphocytes, especially in guinea-pigs, are large vacuoles with a homogeneous structure, and may be a secretion, but have been considered to be parasites. They take a purplish or reddish colour with Giemsa's stain.

Oval or round rings may possibly be connected in some way with the area around the centrosome. Ferrata's plasmosomes are small metachromatic bodies which are thought to indicate retrogressive changes: they may be derived from the chromatin of the nucleus.

In 1912 Castellani described extranuclear non-parasitic bodies in leucocytes. They take, with Giemsa's stain, a blue colour, almost constantly show dots of chromatin, and measure 2-6 microns in diameter. They also occur free in the liquor sanguinis, and are by him considered to be degenerate red blood cells engulfed by the leucocyte.

Intranuclear.—The nucleus of the mononuclear leucocyte is apt to undergo changes and to show bodies with a blue cytoplasm, with or without chromatinic spots, which look very like parasites, as also described by Castellani in 1913.

BLOOD PARASITES.

The blood may contain a number of parasites—*e.g.*, the malarial parasites, the spirochætes, the trypanosomes, the kala-azar parasites—as well as certain worms—*e.g.*, the Microfilariæ, *Schistosoma hæmatobium*, *S. japonicum*, and *S. mansoni*.

ANÆMIA AND ALLIED CONDITIONS.

Anæmia is common, being generally associated with ankylostomiasis, malaria, kala-azar, chronic dysentery, or in women repeated pregnancies and prolonged lactation. It is especially common among coolies working on estates. The treatment is to remove the causal agent, and then to administer the old mixture of sulphate of iron, sulphate of magnesium, and nux vomica to the poorer classes, while intramuscular injections of iron alone or combined with arsenic or sodium glycerophosphate are more scientific and more suitable for the better classes.

Chlorosis is rare, but we have seen cases in Europeans and in better-class native girls.

Paranæmia Tropicalis.

Everyone residing in the tropics is acquainted with the pallor which is visible in the faces of many European residents who, apparently, are in good health. An examination of the blood fails to reveal any marked diminution in the red cells or hæmoglobin, or, at all events no such reduction as would be compatible with the pallor. We have used the term paranæmia to indicate the condition.

In Chapter III., section Effects on the Blood (p. 75), we have shown that this apparent anæmia has been carefully studied by W. M. Strong, who considers that this pallor is really caused by the deposition of pigment in the epidermis. This pigment renders the skin opaque to the red rays contained in sunlight, and hence the colour reflected therefrom appears to the eye white.

In diagnosing this condition care must be taken to exclude true anæmia by a count of the red cells in the blood and an estimation of the hæmoglobin.

De Langen believes there are real differences between the blood of Europeans in the Tropics and at home: a shift to the left of Arneth's count, diminution of cholesterin, increase in blood sugar. He attributes to the hyperglycæmia the low fever so often found in the Tropics.

LEUKÆMIA.

Leucocythemia cannot be said to be very rare, at all events in our experience, and may be either spleno-medullary or lymphatic in type. It is most necessary to remember the possibility of the occurrence of this disease, and to make it a rule to examine the blood microscopically before performing splenic or hepatic puncture in cases of splenomegaly.

Pseudo-leukæmia and **Banti's disease** are also known.

GENERAL DROPSY.

Cases of general dropsy not due to heart or renal disease may be caused by beri-beri or ankylostomiasis.

THE HEART.

Heart disease has not been carefully studied by modern methods in the tropics, but cases of heart-block due to malaria and syphilis have been recorded by us.

Pericarditis and *endocarditis* are not as common as in other regions, probably because rheumatism is rare, and therefore they are due to such other causes as gonococcal infection, etc. Atrophies of the heart, especially brown atrophy, are quite common as the result of some general disease. Heart-block is rare, but has been met with. Rupture of a perfectly normal myocardium, the pericardium being intact, is recorded by Herzog as due to fracture of the second, fourth, and fifth ribs.

Tropical Heart.

Under this heading MacLeod has described the conditions of palpitation and dyspnoea on going up hills met with in persons who have resided long in the tropics. He assigns this to degeneration of the heart, brought on by the heat and by the exceptional work which it has to do owing to the changes in the circulation which result from the high temperature of the tropics. He considers this to be the basis of the syncopal form of heat exhaustion. Ernest Black believes that the condition is associated with subnormal blood coagulability, and recommends the administration of calcium salts. The salt he prefers is calcium lactate, which he gives in 10-grain doses. He points out that calcium salts are essential for the systole of the heart as well as for the normal cogulability of the blood, and refers their beneficial action to this property. He considers that citric acid or its salts should be avoided when calcium salts are administered, as they increase the calcium excretion.

THE VESSELS.

Atheromatous degeneration of the arteries is quite common, and aneurysm is found, generally affecting the thoracic aorta, while varicose veins and varicocele are usual, and, associated with hypertrophy of the heart, are very common among rickshaw coolies.

Thrombosis is often met with as the result of typhoid fever and other diseases, and we have seen thrombosis of a coronary artery with myomalacia cordis or aneurysm of the heart.

THE SPLEEN.

The spleen is affected in malaria, kala-azar, relapsing fever, etc., s already described. Capsulitis is very commonly met with in post-mortems, but splenic abscess is, in our experience, rare, and may be of entamœbic origin. Infarcts and tuberculosis are, however, not so rare, and spleno-medullary leukæmia, as has been mentioned above, is not very rare. Rupture of the enlarged malarial spleen has already been mentioned, and may cause death within a few minutes, or the patient may live for several hours.

BONE-MARROW.

The importance of the bone-marrow is often overlooked in the tropics. It requires especial study in anæmias, kala-azar, and malaria.

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CHAPTER LXXXIII

DISEASES OF THE LIVER AND PANCREAS

General remarks—Tropical liver—Amœbic abscess of the liver—Opisthorchiosis—Clonorchiosis—References.

GENERAL REMARKS.

DISEASES of the liver and pancreas are of common occurrence in the tropics. *The liver* may be affected in the course of tropical fevers, especially in malaria and kala-azar, in the latter of which Rogers has described a special form of cirrhosis. The disease called '*infantile biliary cirrhosis of the liver*,' described by Ghose and Mackenzie as occurring in Calcutta and other parts of India in Hindu and Mohammedan children, appears to us to require reinvestigation, with a view to deciding whether it also is a variety of kala-azar. It is said to attack children under one year of age, and to be characterized by a low type of fever, associated with enlargement of the liver and spleen, jaundice, pale motions, dark urine, and sometimes vomiting of blood, œdema, and ascites, and ends fatally in three to eight months.

Acute yellow atrophy of the liver is not [illegible] ommon in Ceylon as in Europe, for, on an average, we have met with one or two cases per annum. It occurs in Ceylon more commonly in men than in women, but the cause appears to be quite obscure.

An extraordinary case of acute severe hepatitis and gastritis, which caused a considerable hæmorrhage to take place, filling all the small biliary ducts, the gall-bladder, the common bile-duct, the duodenum, jejunum, and ileum with blood, has been recorded by one of us in Ceylon. The inflammation occurred in a stomach which was altered by chronic atrophic gastritis. The hæmorrhage was caused by the blood passing from the damaged hepatic capillaries into the minute bile channels, and was due to the destruction of the walls of these capillaries and the liver cells. No definite cause could be found for this condition, which is decidedly rare.

Congestion and inflammation of the liver, together with abscess, are common in the tropics, and require special consideration (p. 1910).

Atrophic cirrhosis of the liver is very common in the tropics, and though generally there is a history of alcohol, still, this is by no means always so, and sometimes the cause is not evident. We believe that cirrhosis of the liver of malarial origin is much less frequent than is admitted by many authors. It will be shown presently that various parasites cause cirrhosis.

Primary cancer of the liver has been met with, but is very rare. On the other hand, secondary cancer is by no means rare. The only ***non-malignant growth*** which we have met with was an angioma.

The protozoal parasites which occur in the liver are ***Loeschia histolytica***, the cause of liver abscess; ***Leishmania donovani*** and ***L. infantum***, the causes of kala-azar and the infantile kala-azar; and the malarial parasites, as has already been noted. Coccidiosis has been found in the tropics in man several times.

With regard to the *trematode parasites* of the liver, *Fasciola hepatica* is only an occasional parasite of man. *Fasciolopsis buski* (*rathouisi*) has been seen in a Chinese who showed obscure liver symptoms, and no doubt microscopical examination of the faeces would make diagnosis possible but there is only one certain case, and the information regarding the symptoms is meagre. *Opisthorchis felineus* and *Amphimerus noverca* are the cause of opisthorchiosis, which will be considered late[illegible]s will clonorchiosis, caused by *Clonorchis sinensis*. *Dicrocoelium lanceatum* is considered to be too small to cause any serious symptoms while living in the bile-ducts. *Schistosoma mansoni* and *S. japonicum* may both affect the liver (pp. 1589 180[illegible]

With regard to *tape-worms*, *Tænia [illegible]inococcus* is not common, but we have met with one case of echinococcus in Ceylon, which was brought by a Boer prisoner [illegible] and Begbie has recorded another, not in the liver, but associated with the lung, in an old resident in Ceylon. One of us has recorded an invasion of the liver by Ascarides, and the formation of abscesses by the agency of these worms. We have [illegible] *Poro[illegible]halus armillatus* in the liver.

Disease of the [illegible]bladder is common in [illegible] tropics, and we have met with acute [illegible] chronic inflammation. Gall-stones are often met with [illegible]ably as sequelæ to typhoid [illegible] fever, but also arising from other causes. Suppuration of the [illegible]ile-ducts w[illegible] have only seen once, and œdema of the wall of the [illegible] bladder we have also only found once. *Obstructive* and *catarrhal jaundice* are met with fairly frequently in the tropics.

Rupture of the liver may take place as the result of traumatisms, and recently Herzog has recorded this accident in a Filipino woman as the result of a native obstetrical practice, which consists of traction on a cloth wound round the abdomen. In this case the rupture had been caused by the perforation of the tip of the eleventh rib into the fatty liver.

The pancreas, in our experience, is not infrequently found diseased. We have met with the following types of inflammation in Ceylon:—

1. Acute hæmorrhagic pancreatitis.
2. Acute suppurative catarrh of the ducts.

3. Subacute pancreatitis.
4. Chronic pancreatitis.
    (1) Syphilitic in the fœtus.
    (2) In the adult.
        (*a*) Chronic interlobular pancreatitis.
        (*b*) Chronic interacinar pancreatitis.
        (*c*) Chronic interlobular and interacinar pancreatitis combined.

It should be remembered that the subtertian parasite is one of the causes of *hæmorrhagic* pancreatitis. In addition we have seen cancer of the pancreas producing a blocking of the duct of Wirsung, and leading to a ranula which contained many pancreatic calculi. We have once seen an ascaris in the duct of Wirsung associated with a hyperæmic condition of the gland.

After this brief general statement, we must consider congestion of the liver, abscess of the liver, opisthorchiosis, and clonorchiosis.

TROPICAL LIVER.

Synonyms.- Congestion of the liver, Hyperæmia of the liver, Indian liver.

Definition.- Congestion of the liver is a hyperæmia brought about by many conditions, especially gastro-intestinal disorders.

Remarks. There can be no doubt that the European is apt to eat and drink more than is good for him on his first arrival in the tropics, and that this is bound to lead to an increase of blood in the liver, which physiological condition may easily become a congestion, with later blood stasis and diminution of the functional activity of the organ.

Climatology.- Congestion of the liver is a cosmopolitan complaint, but is much more commonly met with in the tropics than in the Temperate Zone.

Ætiology.- -Congestion of the liver is brought about by indiscretion in diet, such as too much, too rich, or too highly spiced foods, by alcoholic excess, and by chills.

Pathology.- Post mortem the liver is found to be swollen, dark red in colour, and drips with blood when cut into. The cells are often laden with fat, and, in addition to the changes in the liver, there will be added the pathological changes which have caused the congestion, and which are generally to be found in the alimentary canal, as well as those which have caused the death of the patient.

Symptomatology.- The illness begins with frontal headache, malaise and loss of appetite, with nausea or sickness, and a bitter taste in the mouth on awakening in the morning. The tongue is coated, and there are the usual signs of dyspepsia, associated with constipation and the passage of pale-coloured motions. The liver is enlarged and tender, and usually there is a sense of weight in the right hypochondrium, and pain below the right scapula or in the right shoulder, and there may be slight signs of jaundice in the yellow conjunctiva and sallow skin. The urine may be diminished in quantity, high-coloured, and with high specific gravity, and loaded with uric acid and urates. The nervous system is also affected, and the patient is usually very cross and irritable. The temperature is generally normal, but sometimes it rises, and when above 100° F. it is usual to call the disease hepatitis; instead of congestion of the liver. The common non-febrile variety lasts from two to seven days, but is liable to recur.

Varieties.- Congestion of the liver may be acute when associated with some other disease, or chronic when due to gastro-intestinal disturbance.

Diagnosis.--The diagnosis is based on the painful enlargement of the liver, which, in the absence of other disease, is usually unaccompanied with marked rise of temperature.

Treatment.- In the acute attack it is as well to keep the patient in bed and begin the treatment with a dose of calomel (gr. ii. to gr. v.), followed a few hours later by a saline in the form of magnesium and sodium sulphates or Carlsbad salts An effervescing mixture of ammonium carbonate (gr. ix. to gr. x.) and sodium bicarbonate (gr. xx.), with citric acid (gr. xv.), may be given every three hours, or a mixture containing ammonium chloride in some combination. At the same time hot fomentations or a thick coat of antiphlogistin may be applied to the region of the liver. The diet should consist of soups and milk, diluted with Vichy or barley water, and no alcohol in any form allowed.

When the condition has become chronic, the patient must be carefully dieted and placed upon a course of treatment with the above effervescing mixture and Vichy (Grande Grille), and when leave in Europe is available, should be sent to Vichy, Carlsbad, Harrogate, or Montecatini. He should avoid alcoholic stimulants and rich food of every description, and especially tinned food, and should restrict his diet to fowls, clear soups, fish, and well-cooked vegetables and milk, avoiding meat and curries.

Whenever the acute attack is over, the patient should be advised to take exercise daily -walking, riding, golf, or tennis, combined with the usual so-called liver exercises.

Prophylaxis.- Plain, simple, not highly spiced food should be taken, and such pernicious drinks as the heavy forms of beer, sherry, champagne, etc., should be avoided. If any form of alcohol is to be taken in the tropics, this should be Scotch whisky, well diluted, or light clarets, and then only in moderation. Chills must be avoided as carefully as possible, especially when there is a land wind, in the rains, and when changing from a warm to a cooler climate.

With regard to the cold bath, there is no doubt that the majority of people are unable to stand this in the tropics, and therefore it is better to use water with the chill removed.

Some persons are, however, distinctly benefited by a cold bath, and therefore individual peculiarities must be considered.

The most dangerous time for chills is in the night; therefore it is as well to sleep with some light blanket placed over the abdomen, and in flannel night attire. In the daytime a woollen undervest or cholera-belt may be worn. The clothes must be carefully changed whenever they become damp.

AMŒBIC ABSCESS OF THE LIVER.

Synonyms.—Hepatic abscess. *French:* Abscès du Foie. *Italian:* Epatite Suppurativa. *German:* Tropischer Leberabszess.

Definition.—Amœbic abscess of the liver is a suppurative hepatitis, caused by *Loeschia histolytica*—usually preceded by an attack of amœbic dysentery.

History.—Liver abscess was known to the ancients, and was operated upon as far back as the days of Hippocrates, while Galen recognized its connection with dysentery, and Morgagni studied its morbid anatomy. During the nineteenth century the disease was carefully studied by French surgeons, beginning with those of the army of occupation in Egypt, and also by the French colonial doctors and the Indian army surgeons. The discovery of *Amœbæ* or *Loeschiæ* emphasized the connection between liver abscess and dysentery. Kruse and Pasquale were the first to regularly find amœbæ in the liver abscess, and to state that, apart from the amœbæ, the pus was sterile. Later researches have confirmed this discovery, and have demonstrated that the pus of a liver abscess does not contain bacteria in most cases—a fact which agrees with our experience—and that the true cause of the malady is *Loeschia histolytica*.

Climatology.—Liver abscess is essentially a disease of the tropics and subtropical regions. It is very common in India and Indo-China, rather less so in Ceylon, Malaya, Java, Sumatra, and rare in Southern China. In Africa it is common in Egypt and North and West Africa (Gold Coast). In America it appears to be less commonly met with, being rare in the United States, West Indies, and British Guiana. It is also found, though rarely, in the Temperate Zone, in Spain, Italy, France, and even in such a northern country as England. There is no seasonal variation.

Ætiology.—The cause of the suppuration is *Loeschia histolytica*, and perhaps other varieties of *Loeschiæ*. It is more common in Europeans than in natives, and more so in males than females, and is usually a disease of adults. The most important predisposing cause is perhaps alcohol.

In monkeys one of us has recorded the occurrence of liver abscess due to an amœba (*Loeschia nuttalli* Castellani, 1907).

Pathology.—The *Loeschiæ* pass from the bowel via the portal vein into the liver, where they produce coagulative necrosis of the liver cells, which become formless and break up into granular débris. This necrosis is thought to be brought about by means of toxins produced by the *Loeschiæ*. The necrosed area undergoes liquefaction and forms the abscess, the contents of which consist of débris, endothelial cells, mononuclear leucocytes (rarely polymorphonuclears), red corpuscles, hæmatoidin, cholesterin, and rarely Charcot-Leyden crystals. The pus is usually sterile, and as a rule does not contain amœbæ, which are in the marginal wall of the abscess, and may extend into the liver tissue for some distance from the focal lesion. After the abscess has been opened, amœbæ may be found in the pus. The process of repair has not been fully worked out, but it appears as though the granulation tissue formed new connective tissue, in which new bloodvessels and proliferating bile-ducts may be seen, indicating the processes which may lead to repair.

Usually there is only one abscess, but it is not uncommon to find two, and there may be more. The abscess is generally found in the posterior part of the upper portion of the right lobe. It is rounded in form, with walls composed of degenerated liver cells and granulation tissue. Its contents may be thick, creamy pus, but more usually it is yellowish or brown coloured. On microscopical examination it consists largely of detritus, with a few degenerated liver and pus cells. The bacteria found in the pus, when it is not sterile, are streptococci, staphylococci, *B. coli communis*, and *B. pyocyaneus*, and occasionally some anaerobic germs. The abscess varies much in size, from a small hollow containing only 1 or 2 ounces up to a huge cavity with a couple of pints or more of pus, while even larger have been described. The size of the liver, apart from the abscess, also varies, being sometimes increased and sometimes diminished. Apart from the liver abscess, there are usually signs of old or recent dysentery in the colon, though these may be absent. There may be abscesses in other parts of the body, the spleen, the brain, etc., but these are rare.

FIG. 775.—AMŒBIC ABSCESS OF THE LIVER.

Symptomatology.—There is usually a history of a previous attack of dysentery, but this may be wanting. The disease begins insidiously with signs of congestion of the liver and fever. This fever is important, being irregular, sometimes remittent, sometimes intermittent, sometimes with long apyrexial intervals.

The X rays may show that the movement of the diaphragm is diminished on the right side, and attention has also been called to the arched 'cupola-like' curve of the upper aspect of the liver, as seen by radioscopy. The early stage, called by Rogers the 'presuppurative stage,' is of the utmost importance; for if it can be recognized and appropriate treatment applied, the disease may be stopped in a certain number of cases. If, however, this is not done, rigors may take place, and the fever usually becomes more severe, and a typical hectic temperature with night-sweats may ensue; while the patient complains of a dragging sensation on the right side, pain under the right shoulder-blade and in the right shoulder. This latter is a referred pain, due to the fact that the phrenic nerve arises from the fourth cervical nerve-root, the fibres of which supply the skin of the shoulder.

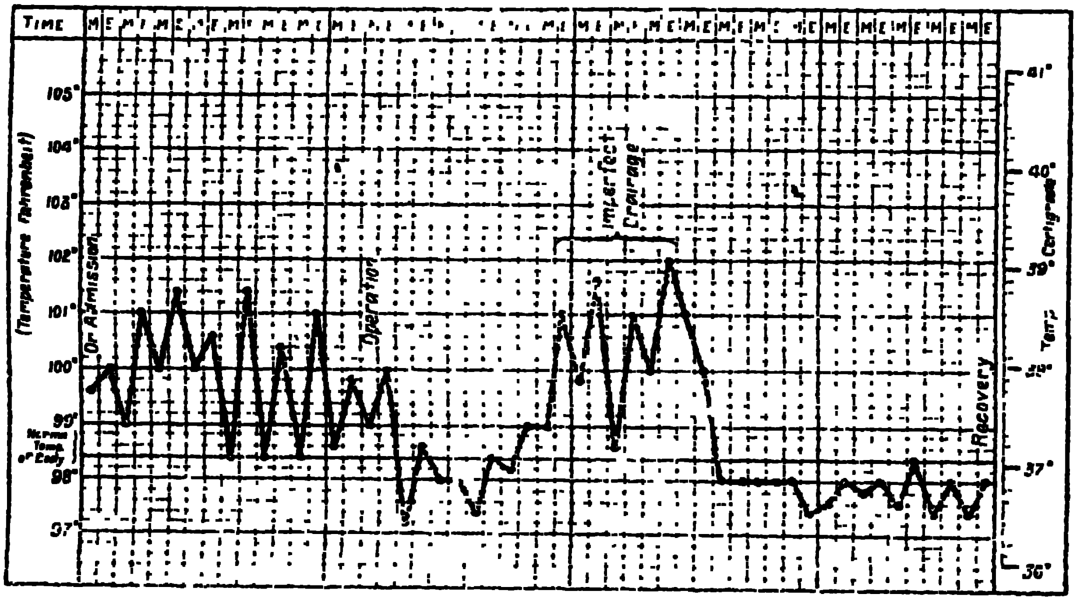

Fig. 776.—The Temperature Chart of a Case of Abscess of the Liver

A patient with an abscess of the liver often possesses a most typical facies. He lies on his back, with his legs drawn up; his face is drawn, and of a pale yellow colour, and the ocular conjunctiva possesses a peculiar bluey-whitish colour. It is said that sometimes the right pupil is dilated, but in our experience this is not a constant symptom. Generally he is emaciated, and deep inspiration is painful; hence the breathing is costal in character, and often there is a slight cough. The hands and feet are often cold and clammy to the touch.

On inspecting the abdomen and chest, the right hypochondrium will be noticed to be bulging, while the liver is enlarged and tender. On palpating the front of the abdomen, the right rectus muscle may be felt to become suddenly rigid—a most characteristic sign—while the left is not affected. On percussion the liver is found to be enlarged, and pain may be produced by pressure in the epigastrium or over an intercostal space. These painful spots are of importance in localizing the site of the abscess. On listening over the lower part of the chest, fine crepitations or friction sounds may be heard.

Usually liver abscess is accompanied by some anaemia and some increase in the number of the total leucocytes, but this appears to vary, being greater if the abscess is small and deeply seated, and less so if large and superficial. According to Rogers, the ratio of white to red corpuscles varies from 1 : 517 to 1 : 126. With regard to the differential count, the polymorphonuclear leucocytes are but slightly increased, but the lymphocytes are usually more than normal. Léger gives the differential count as being: Polymorphonuclears, 78·37 per cent.; lymphocytes, 17·44 per cent.; mononuclears, 3·15 per cent.; and eosinophiles, 0·70 per cent., which closely agrees with Rogers' figures, which are: Polymorphonuclears, 74 to 87 per cent.; lymphocytes, 7 to 22 per cent.; mononuclears, 3 to 7 per cent.; eosinophiles, 0 to 4 per cent. In some of our cases there was no polymorphonuclear leucocytosis, while on several occasions, even in non-malarial subjects, there was a relatively large mononuclear increase. The number of sudanophile leucocytes tested according to the Cesaris-Demel method is often increased.

The urine is usually diminished, and its excretion is said to be altered, so that the greatest quantity is passed between 12 midnight and 12 noon, being especially increased in the early morning.

If the abscess is allowed to continue its own course, it may burst into the lung, causing signs of pleurisy and pneumonia, associated with the expectoration of characteristic brown or reddish-brown gummy, viscid, purulent matter; or into the stomach, when a similar material will be vomited; or into the bowel, when it will be passed *per anum*. It may also burst into the pericardium or the peritoneum, or into the vena cava, all of which cases are bound to end fatally. If it does not burst, the patient may die of exhaustion.

The duration of a liver abscess is very variable, being from a few weeks to several months, and even years.

Diagnosis.—The diagnostic points in abscess of the liver are: A history of dysentery; fever, generally of a serotine type, with sweatings, not yielding to quinine; painful enlargement of the liver; the characteristic pain in the shoulder; the rigidity of the right rectus; the loss of movement in the right side of the diaphragm, and the frequent cupola-shape of the liver on radioscopy; and, above all, the discovery of the pus by exploratory puncture, as described below.

The differential diagnosis between the presuppurative and the suppurative stages is often impossible without a puncture, but sweating, high intermittent temperature, if present and not influenced by the emetine treatment, is suspicious that suppurative changes have begun.

Pleurisy with effusion on the right side can be distinguished from liver abscess by the presence of Grocco's paravertebral triangle on the left side. Moreover, in pleuritic effusions the upper limit of the dulness is horizontal, while in liver abscess it is convex.

Another diagnostic point to which Manson has drawn attention is that the enlarged liver gravitates with changes of position much more distinctly than pleural effusions. If the dulness in the mid-axillary line diminishes notably when the patient lies on his left side, the case is probably one of liver abscess. It is to be noted, however, that a right pleural effusion and a liver abscess may coexist. Pneumonia on the right side with congestion of the liver may also lead to difficulties, which must be met by careful physical examination and the microscopical and bacteriological examination of the sputum. Malarial fever can be diagnosed from the fever of hepatitis by examination of the blood and the presence of the enlarged spleen. In those cases of liver abscess in which fever is the only symptom the diagnosis may be extremely difficult, and may require all modern bacteriological methods to exclude Malta fever, malaria, septicæmia, and typhoid, etc. When in doubt, an exploratory puncture should always be made, for it can do no harm, and may relieve the congestion. When a long needle is introduced into a liver abscess, it moves regularly with respiration. Purulent cholecystitis in most cases gives no trouble on diagnosis, as the enlarged gall-bladder can be easily felt, and there is generally a history of hepatic colic.

Syphilitic gumma of the liver may show many symptoms in common with liver abscess, including the intermittent fever, as we have twice noted. The positive Wasserman reaction and the action of potassium iodide in full doses clears the diagnosis.

Cases of leukæmia, pseudo leukæmia, tropical splenomegaly, and kala-azar have been mistaken for liver abscess, but in all these conditions the spleen is also greatly enlarged.

In this connection we may emphasize the necessity for the examination of the blood in order to exclude leukæmia, otherwise a fatal hæmorrhage may follow such a simple operation as puncture of the liver. Liver abscess is usually easily diagnosed from hydatid disease, but when purulent changes have taken place in the latter the diagnosis may be impossible, except by the history and the eosinophilia.

Prognosis.—If the abscess is left unoperated for a long time, the prognosis is very bad, as the danger of exhaustion and septic infection is great. If the abscess has burst into the lung, the prognosis is also bad, but better than if it had burst into the bowel. Since operative measures have come into more common use the mortality has decreased, according to Dujardin Beaumetz, from 82 per cent. to 32 per cent. The operation wound may occasionally become phagedænic.

Treatment.—If a case is suspected by the symptoms and blood-counts to be in the 'presuppurative stage,' emetine or ipecacuanha should be administered, and should be given with the precautions already mentioned under Amœbic Dysentery, and the latter must be continued for several weeks after every sign of hepatitis has disappeared.

It, however, an abscess is believed to have formed, there should be no delay in making an exploratory puncture.

For this purpose a needle 3½ inches in length, but preferably not longer, because of the danger of injuring the vena cava, should be rendered sterile by boiling in plain water, but must not be dipped into an antiseptic lotion nor into spirit. This needle should be capable of being fitted on to a glass syringe or an aspirator.

The patient should be placed under chloroform, and all arrangements should be made so that an operation can be performed at once if necessary.

The needle should be driven into the liver in the region of any definite swelling or pain, or, failing these, through the eighth intercostal space in the anterior axillary line, about 1 or 1½ inches from the costal margin.

The direction of the needle should be inward, slightly upward and backward, because the usual site of an abscess is in the upper and back part of the right lobe.

Aspiration by the syringe or the aspirator may reveal pus, or may fail to do so, in which latter event the needle must be carefully and slowly withdrawn, and its contents ejected on to a clean white dish, to see if it is composed of the grumous material of liver abscess. The needle should now be driven into the liver in different places and directions until some six to twelve punctures have been made. There is no danger in this procedure if performed with reasonable care, and it may even benefit the patient by performing what has been termed 'hepatic phlebotomy.' When the abscess has been located, the needle should be left *in situ* as a guide, and one of two procedures may be carried out: A. Aspiration; B. Operation.

The operation should, however, always be performed if the abscess has already burst into the lungs, the peritoneal or pleural cavities.

A. Aspiration.—This is preferable if the abscess is small, and consists of evacuating its contents, and the injection of a solution of 1 grain of emetine hydrobromide in 2 ounces of water, or the repeated irrigation of the cavity with a solution of bi-hydrochloride of quinine (3 to 5 grains to the ounce) by means of Rogers' flexible sheathed aspiration cannula.

B. Operation.—An operation is necessary if the abscess is large, if the pus is not sterile, if the abscess has burst into the lungs or a serous cavity.

The site of the operation depends upon where the pus has been obtained. Two principal places may be mentioned: (1) through the thoracic wall; (2) through the abdominal wall below the ribs.

Giordano and others have recommended a laparotomy and the localization of the abscess by the hand prior to the actual operation for evacuation of the pus. This may be useful in certain cases when there are no signs indicating the position of the abscess.

1. *Operation through the Thoracic Wall.*—An incision should be made through the parietes, including the site of the puncture,

through which pus was obtained. After the skin has been well retracted, a piece of a rib may require to be removed, thus exposing the diaphragm below the pleura, which must be incised and stitched to the margins of the wound, and the wound well packed with gauze.

The liver is now exposed, and two methods of procedure are open to the operator either to push a pair of dilating forceps along the needle, which has been left *in situ*, and thus to open up the cavity and evacuate the pus, and then, after inserting a double drainage-tube, to wash out the cavity with the quinine solution mentioned above, close up the wound, fix the drainage-tube in position, and dress the wound aseptically, or to adopt Manson's special apparatus.

Manson, after the preliminary incision, thrusts a trocar and cannula into the abscess, and, after withdrawing the trocar, passes a drainage-tube stretched on a probe into the abscess cavity, and then, withdrawing first the trocar and then the probe, the drainage-tube is left in position in the liver abscess, and, being firmly gripped by liver tissue, prevents leakage of pus into the abdominal cavity.

2. *Operation through the Abdominal Wall.* The usual method is to cut down upon the swelling or on to the liver, and if adhesions are found, to evacuate and drain the abscess. If there are no adhesions, the liver is fixed to the peritoneum by a few stitches of thick catgut or kangaroo tendon, but preferably not silk, and the wound is lined by iodoform gauze and left for two days, when, adhesions having formed, the abscess can safely be evacuated as described above. Manson's apparatus can, of course, be used in this position as well as through the thoracic wall.

Post-Operative Treatment. The dangers of the operation itself are but slight. The pleura may be opened, and if this happens, it should be carefully closed by stitches.

The post-operative complications are many, and include hæmorrhage, pneumothorax, pyothorax, pyopneumothorax, gangrene of the lung, and delayed chloroform poisoning, while a second abscess is not uncommonly met with, and must be relieved.

After the operation the temperature should fall to normal, and if this does not happen, a second abscess or one of the above complications may be suspected, unless, indeed, it is due to imperfect drainage, which must at once be rectified.

The dressings should at first be frequently changed, usually twice a day, and the cavity irrigated with quinine lotion. Good drainage is the essential of the post-operative treatment, and care must be taken that the drainage-tube is not too rapidly shortened, otherwise the temperature is apt to rise.

On recovery, the patient should, if possible, be given a holiday in the Temperate Zone. A short course of emetine or ipecacuanha after the operation wound has quite healed is distinctly indicated in order to prevent the formation of another abscess.

OPISTHORCHIOSIS.

Definition.—Opisthorchiosis is an invasion of the bile-ducts with *Amphimerus noverca* Braun, 1903 (p. 577), and *O. felineus* Rivolta, 1885 (p. 576).

Remarks.—*A. noverca* is said to be common in dogs in India, but has only once been found in the dilated bile-ducts of an Indian in Calcutta, who died with dysenteric symptoms.

O. felineus has been found in the dilated bile-ducts, and incidentally also in the intestine of human beings, cats and dogs in Tomsk. It caused a form of hepatic cirrhosis.

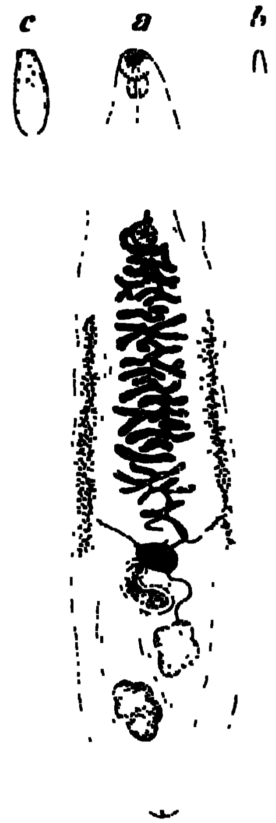

FIG. 777. *Opisthorchis felineus* RIVOLTA.

(After Looss.)

CLONORCHIOSIS.

Definition.—Clonorchiosis is the invasion of the bile-ducts with *Clonorchis sinensis* Cobbold.

Climatology. This parasite occurs in China, Indo-China, and Japan.

Pathology. These parasites occur in dogs and cats, but the method of infection is quite unknown. In man they live in the bile-ducts, in the recesses in the wall of the dilated gall-bladder or of the bile ducts, and in the duodenum. They may also be found in abscesses apparently unconnected with the liver. The ova are found in the alimentary canal and the fæces. The liver becomes enlarged, and may be darker in colour, while it is atrophied in the neighbourhood of the dilated ducts. The intestine may show catarrhal inflammation. Often the spleen is also enlarged, and there may be ascites or œdema. Ova have been met with in the abdominal lymphatics, while the flukes themselves have been found in a lumbar abscess. The blood shows an eosinophilia.

Symptomatology.—There is an abnormal appetite, but the general health remains good for some time, though the liver enlarges and becomes painful, while jaundice may be present. The spleen also enlarges. The disease is apparently very chronic, but towards the end emaciation, ascites, œdema about the feet and legs, and diarrhœa lead to death from exhaustion. Abscesses may form.

Diagnosis.—The presence of the worms can only be diagnosed by finding the eggs in the fæces (see p. 578).

Prognosis.—The prognosis is bad, as no cure is known.

Treatment.—An attempt may be made to kill the worms by thymol or *Filix mas*; otherwise the treatment must be symptomatic.

Prophylaxis.—Nothing can be said as to prophylactic measures until the method of infection is known.

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CHAPTER LXXXIV

DISEASES OF DUCTLESS GLANDS AND METABOLISM

General remarks—The thyroid system—The suprarenal system—The thymus system—Other ductless glands—Diabetes—Macies perniciosa—References.

GENERAL REMARKS.

Of late years much work has been performed with regard to the ductless glands, their functions, and their part in the production of disease. In the tropics McCarrison has been the pioneer with regard to the thyroid gland; and it is hoped that as years pass the other systems will be equally well studied. We are only able to give these important subjects a passing reference, but they deserve much fuller attention, and for this purpose we offer the reader references at the end of this chapter.

THE THYROID SYSTEM.

The thyroid system consists of the thyroid gland and the parathyroids, with probably the addition of the pars intermedia of the pituitary gland. The action of these organs has been the object of much study in Europe and America, as can be noted by a reference to Biedl's writings, while McCarrison in the tropics has opened up the way to the solution of many diseases in an excellent manner.

The various pathological phenomena associated with this system may be divided into two classes—viz., those associated with *hypothyroidism* or insufficiency of functional activity, and those connected with *hyperthyroidism*, or excess of functional activity, and each of these, again, may be applied to the thyroid gland or to the parathyroids.

Thus insufficient activity upon the part of the gland itself may produce benign chronic hypothyroidism of Hertoghe, myxœdema, and cretinism, while exalted activity is believed to be responsible for goitre, Graves' disease, and psychic exaltation. The parathyroid glands when working insufficiently may cause tetany, myoclonia, myotonia, myotonia periodica, and paralysis agitans, but when in a condition of hyper- or dysactivity may be responsible for myasthenia or myotonia periodica.

With regard to the factors which produce these changes in the thyroid system McCarrison points out that they are three in number —viz.:—

A. *Nutritional.*—Defective and improper foods.

B. *Infective.*—Insanitary surroundings, bacterial and other toxins, infectious disease, constipation, intestinal stasis, and their associated toxæmias.

C. *Psychical.*—Fright, grief, worry, consanguinity in marriage, and heredity.

He shows that these factors can produce more or less hyperplasia in the gland, followed by fibrosis and atrophy, and that during this there is an alteration in the quantity and quality of the secretion passed into the blood.

He divides the hyperplasias into two groups. In the first he places those of *endemic areas due to a specific infecting agency*, such as endemic goitre, slight hypothyroidism, and he shows that these conditions in the parent may become congenital goitre, hypothyroidism, endemic cretinism, cretinous idiocy, with deaf-mutism and tetany in the descendants.

In his second group he places such hyperplasias as are due to toxæmia or thyroiditis, and as such he mentions simple toxæmia, goitre, and slight hypothyroidism as one section, myxœdema as a second section, and Graves' disease as a third section; and these occurring in parents may produce much the same results in the descendants as in the first class, but in this condition it will be sporadic and not endemic cretinism.

Diseases of the thyroid gland are quite common in parts of the tropics with which we are acquainted. Myxœdema has been seen by us in Ceylon, but is rarer in the tropics than in the Temperate Zone; goitres, parenchymatous and adenomatous, have been met with by ourselves in Ceylon and in Africa, and by Singer in Abyssinia. Exophthalmic goitre has been especially noted as far from rare by Singer in Abyssinia and Émile in East and Central Africa, but is very rare in India and Ceylon.

ENDEMIC GOITRE.

Synonym.—Endemic thyromegaly.

Goitre is much more prevalent in the tropics than has been realized hitherto, and we have met with it frequently in Ceylon and Africa.

Climatology.—It is a cosmopolitan disease which though frequently met with in hilly districts, is also, in our experience, quite common in low-lying lands. It does not appear to be associated with any geographical or geological condition.

Ætiology.—The general tendency of the present time is to consider that goitre is a parasitic disease, and this view has been strengthened by the recent important experiments of McCarrison on men and Bircher on rats, which, together with the previous ones of Lustig, Grassi, and many others, tend to show that the causal agent lives in earth and passes via potable water to man, in whose alimentary canal it passes a parasitic existence. The nature of this *contagium vivum* is unknown, but McCarrison is inclined to suspect an amœba. Chagas has shown that goitre is a part of the syndrome in chronic American trypanosomiasis.

Symptomatology.—A new-comer to an endemic district may notice after a few weeks' residence that the neck has begun to swell, and on examination this is found to be due to an incipient goitre. On removal from the district, or after almost any method of treatment, the swelling will decrease. If, however, the person continues to reside in the endemic region, the swelling will either continue or return, and this will continue to occur until a more or less permanent hypertrophy results. Usually the swelling affects the whole gland uniformly, but often one lobe may be more hypertrophied than the other. As time goes on the gland becomes permanently enlarged, and may undergo cystic or adenomatous changes.

FIG. 778.—GOITRE IN A SINHALESE WOMAN.

Treatment.—The treatment consists in removal from the endemic area, and in a course of intestinal antiseptics e.g., salol and thymol, 10 grains night and morning. McCarrison recommends a polyvalent vaccine made from the bacilli found in the fæces of persons suffering from the disease. Iodine therapy is strongly recommended. The syrup of the iodide of iron in 5-minim doses combined with 5 grains of iodide of potash is advised as an initial dose, and this may be gradually increased to three or four times this quantity. The liquor thyroidei of the British Pharmacopœia is excellent, or fresh tabloids in doses of 2-5 grains combined with 10 grains of bicarbonate of soda and taken at night. The sour-milk treatment has also been recommended.

Prophylaxis.—The most important prophylactic measure is to filter and boil the drinking-water when compelled to visit or live in an endemic region. The patient must also lead a life free from emotion, if possible.

Congenital Goitre.

McCarrison has pointed out that this is extremely common in certain Himalayan villages. Nearly every man and woman in these situations is goitrous, and congenital goitre may be present in 60 per cent. of the infants at the breast. The mothers of these children are often myxœdematous. The condition rarely calls for treatment, as the victims usually die at or shortly after birth or recover spontaneously, but the mother and child may be given the British Pharmacopœia liquor thyroidei, of which 1 to 2 minims may be given to the child at night.

Endemic Cretinism.

According to McCarrison, the cretinism of the Himalayas, which does not show itself until about six months after birth, may be divided into:—

1. *The myxœdematous type.*
2. *The nervous type.*

Myxœdematous Type.—There is failure in growth, dwarfism, skeletal deformities, persistent infantile condition of the sexual organs, and a lack of intellect, and deafness or deaf-mutism, as well as impairment of the sensory and muscular systems.

Nervous Type.—This is a state of cretinous idiocy associated with cerebral diplegia and tetany.

The treatment of these conditions is the fresh liquor thyroidei (B.P.) in doses of 1-2 minims at bedtime, combined with grey powder and bicarbonate of soda during the first fortnight. The dose of the liquor is gradually increased until 5-10 minims are given in a day. If the liquor is not available, the dried gland in powder may be given in ¼-½ grain doses, working up to 5-7 grains per diem.

Endemic Tetany.

This is found in goitrous districts in the Himalayas, where it is called 'hatti fallategen,' or turning of the hands. It is characterized by bilateral, intermittent, and usually painful spasms of the hands and feet, and at times other parts of the body, and increased excitability of the nervous system.

During the attack calcium salts should be administered.

The curative treatment is to combat the intestinal toxæmia by calomel and intestinal antiseptics, followed by thyroid therapy as indicated above. Rickets must also be treated. The diet should consist of milk, *and meat should be avoided.*

THE SUPRARENAL SYSTEM.

In 1563 Bartholomeus Eustachius Sanctoseverinatus recognized the suprarenal capsules as distinct organs, but it was not until 1855 that Addison's researches aroused deep interest in these glands.

No case has been as yet recorded of the absence of these capsules *as well as* of the possible accessory suprarenals in man. *Acute suprarenal suppression* is caused at times in man by hæmorrhage, and we quote such a case below. The syndrome of these cases is fever, nervous symptoms, and signs of peritonitis followed by death. Malaria may cause these signs.

Chronic suprarenal suppression may be caused by malaria, and is characterized by the signs of Addison's disease viz., apathy, adynamia, gastro-intestinal and nervous disturbance, associated with bronzing of the skin and mucous membranes, and a chronic cachexia, with frequently attacks of diarrhœa or convulsions, and ending in coma and death.

In the tropics we have met with Addison's disease once in a European, and with hæmorrhage into both the suprarenal capsules twice—once in a still-birth after a breech presentation in a native child, and once in a case of acute suprarenal hæmorrhage in a European lady. This last showed symptoms so remarkable in character that a brief description may be given.

Acute Suprarenal Hæmorrhage.

After a year's residence in Ceylon, a young English lady, four months pregnant, was suddenly taken ill with fever associated with an abnormally quick pulse, great tenderness above the umbilicus, and pain in the small of the back on both sides. After a short intermission the fever returned, and rose to 104° F., with a pulse of 130, and quick respirations; the abdomen became much distended and very tender, and the bowels were constipated. All the organs were normal, as was the urine. Vomiting did not begin till near the end, when the tongue first became coated and then dry. Hiccough intervened before death on the thirteenth day. Treatment was without success in any way, and an exploratory laparotomy revealed no abnormality beyond bowels distended with gas. On post mortem examination, no pathological phenomena were seen, except hæmorrhages into both suprarenal capsules, and, judging by the histology, this may have been a case of localized malarial infection without any sign in the blood.

THE THYMUS SYSTEM.

The normal weight of the thymus at birth is 13·26 grammes, and it should increase till between eleven to fifteen years of age it should weigh 37-52 grammes according to Hammar, after which it decreases, until after sixty-six years it only weighs 6·0 grammes, and is then principally composed of adipose tissue. In 1858 Friedleben published the only monograph on this gland in health and disease. The gland is supposed in some unknown way to be associated with certain cases of sudden death (*mors thymia*), especially when there is the so-called *status thymicolymphaticus*, in which a much enlarged thymus is associated with hyperplasia in the lymph glands and lymphoid tissues all over the body.

Only once have we encountered a persistent thymus gland with some enlargement of the lymphatic glands, and this was in a case of sudden death.

OTHER DUCTLESS GLANDS.

We are not acquainted with observations referring to the other internal secretion [illegible] human diseases of the tropics.

DIABETES.

This disease is extremely common in the tropics, but more especially in Asia, and particularly in Ceylon, though we have met with it in Africa.

In India, according to Waters, it has been known since the days of the Susruta Samhita, where it is called 'madhumeha.' It was said to be unknown among the Chinese and Japanese, but Reid has collected 207 cases in China, and in Korea the complaint is called ' weet water disease.'

West says that it is rare in Hindu women, but that it does occur even in Hindu widows, and in general [illegible] may be said to be much more common in men than in women, and is most frequently met with in the better or educated classes.

The disease is the same as in the Temperate Zone, and will not be further considered here, except to point out the frequency of boils and carbuncles due to it, and also the occurrence of Kussmaul's coma, which may be induced by a malarial infection.

Pentosuria.

As in the Temperate Zone, so in the tropics, pentosuria may occur, but is rare, though it is necessary to bear in mind the possibility of its occurrence when the diagnosis of diabetes is made on the reduction of Fehling's solution. A simple method of diagnosis is by using Castellani and Taylor's mycological method of examination of the urine (see Chapter LXXXV., p. 1934).

MACIES PERNICIOSA.

Dr. Ernest Black gives the following account of this disease, which occurs among the aboriginal natives in the north of the State of Western Australia. It has also been reported among the tribes of the Northern Territory of the Commonwealth, where it is called 'living skeleton' disease.

Though the white settlers regard it as a form of consumption, it is not tubercular, and it does not appear to be associated with any malignant growth. It does not correspond clinically with any known tabetic disease. In one case seen in the earlier stages the pancreas was most affected. There is a progressive enlargement of the liver and spleen, the abdomen becoming considerably distended. All the fat disappears and the muscles atrophy, but retain the power of movement. The appearance is quite characteristic—extreme emaciation of the whole body, with a protruding abdomen. Ultimately, through increasing weakness, walking becomes impossible, a serious matter with these nomadic people, which may account for the fact that the few cases of long duration which were observed had remained near white settlements. The course of the disease is slow, but, so far as could be ascertained, it always terminates fatally. Only one case was seen in a child, who died within a year, whereas in the case of a woman who appeared to be middle-aged it was said to have already lasted over two years.

The cause of the disease is unknown. No parasite has been found in the blood of patients examined in the endemic areas.

Further investigation is necessary to see whether this disease is a type of tropical splenomegaly (*vide* p. 1303).

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CHAPTER LXXXV

DISEASES OF THE URINARY ORGANS

General remarks—Bilharziosis—Urinary amœbiasis—Oxaluria—Urinary myiasis and canthariasis—Chyluria—Mycological urinary tests—Test for quinine in the urine—References

GENERAL REMARKS.

RENAL disease in all its forms is frequently met with in the tropics, where nephrolithiasis, pyonephrosis, and pyelitis, with all their associated phenomena, are by no means rare. Stone in the bladder is common in certain regions, as is prostatic hypertrophy. But the only disease which really concerns us in this work is urinary bilharziosis, caused by *Schistosoma hæmatobium*. Tumours of the bladder are not common in our experience. Prostatic abscess is met with at times. We have observed various mycoses of the genito-urinary organs due to fungi of the genera nocardia, aspergillus, monilia, cladosporium. Native children in some parts of Africa (Sudan) suffer very often from a complaint called by the Arabs 'har boul,' characterized by severe burning on passing urine. This condition is due to concentrated acid urine and the presence of gravel. Cystinuria is rare, but we have met with a case.

In the present war a form of nephritis has been noticed in soldiers in the trenches (trench nephritis).

BILHARZIOSIS.

Synonyms.—Urinary schistosomiasis, Endemic hæmaturia, Bilharzia disease.

Definition.—Bilharziosis is infection with *Schistosoma hæmatobium* Bilharz, 1852, the eggs of which irritate and invade the urinary tract, and cause hæmaturia and cystitis.

History.—The disease has been endemic in Egypt since ancient times, Ruffer having demonstrated calcified eggs of *S. hæmatobium* in mummies of the twentieth dynasty (about 1250-1000 B.C.). Hæmaturia was much noticed by the French army surgeons in 1799 to 1801; but it was not till 1851 that Bilharz made the discovery that the disease was due to *S. hæmatobium*.

Climatology.—Bilharziosis is prevalent in Africa, especially in Egypt and the Cape, but it is also met with in Asia, in India, Syria, and Mesopotamia, and in the West Indies. In Egypt, according to Sandwith, infection probably takes place in the early winter months when the floods have subsided.

Ætiology.—The cause of the disease is *Schistosoma hæmatobium.* The life-history is described in Chapter XXIV., p. 584. The method of infection is by the cercariæ penetrating the skin or mucous membranes and developing into adults, which live and copulate in the portal and vesical veins, while the eggs leave the body with the urine.

It occurs in any race and at any age, except infancy, but is more common in males than in females, due, it is thought, to the men washing in streams and working in the fields barefooted. According to Miss Elgood's investigations, the disease is common also in young girls, even in those who do not bathe, and who use filtered water. It is rare in Europeans, being much more common among the natives, in whom it is prevalent among the working classes, especially the field-labourers.

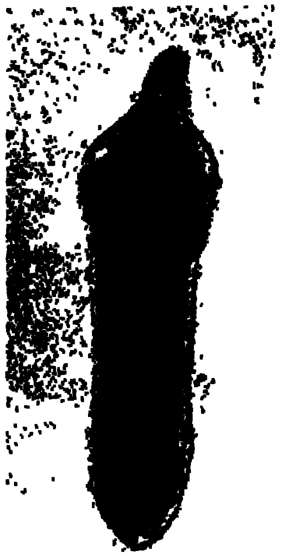

FIG. 778A.—MIRACIDIUM OF *Schistosoma Hæmatobium.* (× 300 DIAMETERS.) (Photomicrograph.)

FIG. IOTOGRAPHS OF *Bulinus contortus*.

Pathology. The worms live in the porta vein, but proceed to the venules of the bladder to lay the eggs. The irritation of these eggs excites a round-celled infiltration, sometimes of a very extensive nature, giving rise to a sort of bilharzial granulation tissue—that is, a tissue composed of round cells and eggs. Madden divides the pathological changes into two classes- the hypertrophic and the atrophic. In the former, which is more common in mucous membranes, there is proliferation of the epithelium, with the formation of flattened projections or papillomata, while vesicles may also form, and, according to Madden, by bursting, give rise to the ulcers which at times are seen.

The ova may escape from the mucosa, according to Looss, without the aid of ulceration, by working their way between the epithelial cells into the lumen of the viscus. Underneath the mucosæ the round-celled infiltration forms the typical bilharzial granulation tissue, and leads to much thickening of the wall of the viscus, and, proceeding to connective-tissue formation, may cause marked changes. Lesions may also be found from the pelvis of the kidney to the meatus urinarius, but are most common in the bladder.

Morbid Anatomy.—The earliest changes are found in the bladder in the formation of a general infiltration and thickening of the mucosa with bilharzial tissue. Over this thickened mucosa is a layer of adherent mucus, which is apparently protective. In this mucus numerous eggs are found. Later hyperæmic patches are found associated with vesicles, which are especially marked around the trigone, and contain a whitish fluid in which there are eggs. The hyperæmic patches increase in size and thickness, and the whole bladder becomes much thickened. Papillomata of all shapes and sizes are formed principally on the trigone and the posterior wall of the bladder. These papillomata bleed readily, giving rise to the hæmaturia.

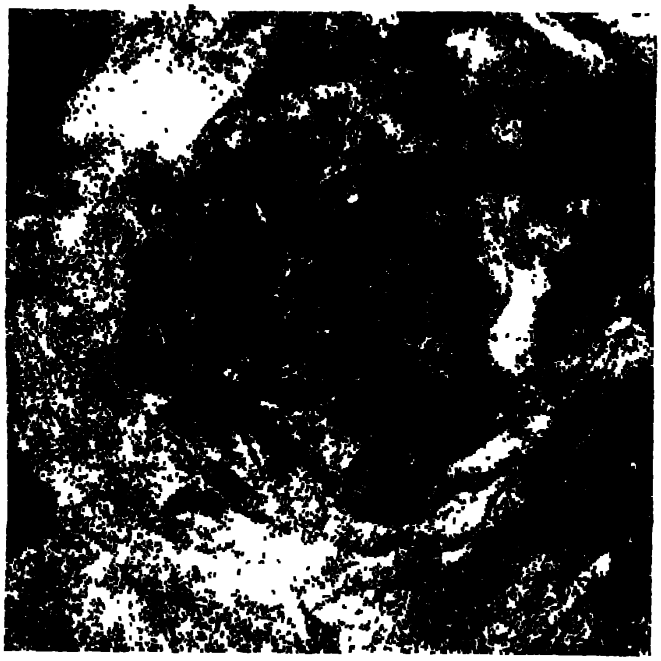

FIG. 778C.—BLADDER SHOWING LESIONS OF BILHARZIOSIS.

As the eggs increase in amount, connective tissue forms round them, and they die and become calcified, thus giving rise to brownish-yellow, sandy patches, not protected by mucus, and leading to an atrophy of the mucosa of the viscus.

The urine collects in the hollows between the papillomata, and, decomposing, gives rise to phosphates, which produce a whitish incrustation on the bladder wall. The orifices of the ureters may become obstructed, giving rise to backward pressure, causing hypertrophy of the ureters and hydronephrosis. Septic infection is very liable to spread from the bladder up the dilated ureters to the kidney. Bilharzial tissue may also form in the ureters and the pelvis of the kidney, and take the form of infiltrations and papillomata. Calculi may also form in the bladder, and interstitial nephritis in the kidney.

As the bladder becomes infiltrated it rises in the abdomen, and may be felt above the pubes, and in this situation infection may spread to the abdominal wall. In this case the typical bilharzial tissue forms in the subcutaneous tissue, and, working its way to the surface, forms a sinus lined with bilharzial granulations containing eggs and discharging pus. These sinuses may spread, and a large area of skin become involved.

Bilharzial tissue may also form in the prostate and urethra.

Symptomatology.—The incubation is not known, but, according to Sandwith, it varies from three to six months. At first no symptoms are exhibited, but in course of time frequency of micturition, with a sensation of burning in the perineum or along the urethra, may be noted, while there is some straining after passing urine. In due course hæmaturia appears, beginning with a few drops of blood either at the end of micturition or after the urine has been passed. Usually there are no symptoms with this hæmaturia, but there may be scalding. The urine is clear and acid, but some mucus may be passed, which, if centrifugalized or allowed to settle, shows the typical ova and, of course, red cells, leucocytes, and epithelial cells. Usually the general health is good, but pains in various directions may be felt—*e.g.*, in the back, the perineum, the gluteal region, or down the leg.

Sooner or later the urine begins to stagnate in the hollows in the mucosa formed by ulcers and by papillomata. When this happens, the urine becomes alkaline and turbid, containing pus and phosphates, as well as decomposing blood and ova. With this decomposition of the urine cystitis appears, and the sufferings of the patient begin in earnest, with at first increased, and later almost constant micturition, scalding pains in the perineum and the scrotum, together with tenesmus, which increase until he can rest neither day nor night. In order to add, if possible, to his miseries, the prostate may enlarge or a stone may form in the bladder, which may be composed of uric acid or oxalates covered with phosphates, or simply of phosphates. If the bladder is examined in this stage it will be found to be thickened, and may be felt above the pubes. Fistulæ may form in the abdominal wall above the pubes, or the urethra may be attacked. The urethral symptoms begin with localized pain and the formation of a lump which develops an abscess, and later urinary fistulæ.

The patient now becomes weak and anæmic, and begins to suffer from pyonephrosis. The enlarged kidneys, and at times even the ureters, may be felt through the abdominal wall. In course of time septicæmia sets in, and the patient dies. On the other hand, cases which have left the endemic area may slowly recover, the ova ceasing to be passed.

Complications.—Retention of urine from blocking of the urethral opening by papillomata or a stone may occur. Stone in the bladder as has already been mentioned, is an important factor in increasing the sufferings of the patient, but its symptoms may be masked by those of the disease. Urinary fistulæ has already been referred to, and cancer may also occur as a complication of the disease, but is said to be rare. Ankylostomiasis and pellagra and other diseases may also complicate a case.

Diagnosis.—The only certain diagnosis is by the discovery of the ova, but hæmaturia in the endemic area must always be regarded with suspicion. Centrifugalization is necessary when the ova are in small numbers.

Fairley recommends a complement fixation-test with an antigen prepared from livers of infected snails.

Prognosis.—The prognosis depends largely upon the possibilities of infection, and is therefore better if removal from the infected area is possible; for, according to Sandwith, most cases cease to pass eggs within three years of leaving that area.

FIG. 778D.—EGG OF *Schistosoma hæmatobium* IN URINE. (Photomicrograph.)

Treatment. McDonagh and Christopherson have recommended the intravenous injection of tartar emetic, which should be administered in the same way as for intestinal schistosomiasis (p. 1864). Various treatments, such as injections of sulphuretted hydrogen and carbon dioxide gases into the bladder, have been suggested. The drug commonly used in the past was liquid extract of male fern, in 5-minim doses, three times a day, continued for a long time. It is said to reduce the hæmaturia and lessen the discharge of eggs. Emetine has been recommended by several observers. Madden recommends the washing out of the bladder with injections of silver nitrate, beginning with 1 in 10,000, and increasing the strength gradually; or quinine in a 1 per cent. solution; or adrenalin in normal saline solution.

In addition, boracic acid, in 5-grain doses, three times a day, or helmitol, in 15 grain doses, three times a day, urotropine, salol, benzoic acid may be given, or the ordinary buchu and hyoscyamus mixture may be administered. Large quantities of water or Vichy water should be drunk to wash out the urinary passages.

If a calculus is present, it must be removed by lithotrity or by perineal, not suprapubic, cystotomy. Cock's operation of cystotomy and drainage of the bladder gives relief in the later stages, but Madden says that this only lasts for a few days, and then usually diarrhœa and septic infection set in, and the patient dies in about two weeks.

With regard to fistulæ, they ought to be thoroughly dissected out and this may mean a very prolonged operation if it is to do any good.

McDonagh, who first used antimony in bilharziosis in 1912, prefers colloidal antimony, which he gives intravenously and intramuscularly in doses of 0·5 c.c. to 2 c.c. of a 0·2 per cent. emulsion.

Salvarsan has been used by several observers, with doubtful results.

Prophylaxis.—As the method of infection is unknown, it can only be suggested that bathing in polluted or possibly polluted water is dangerous, and drinking-water must be carefully boiled and filtered. The urine of persons suffering from the disease should be mixed with some disinfectant before being disposed of.

URINARY AMŒBIASIS.

Definition.—Urinary amœbiasis is the infection of the urinary tract with amœbæ, which most commonly are *Loeschia histolytica* (Schaudinn, 1903).

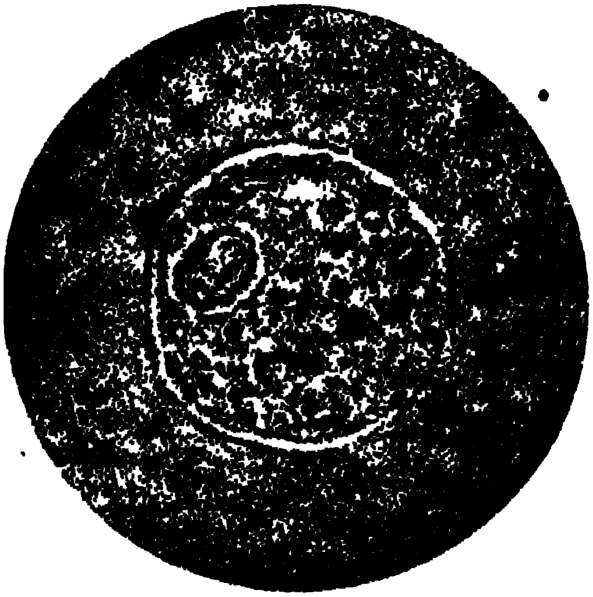

FIG. 779.—PRECYSTIC STAGE OF *Loeschia histolytica* (SCHAUDINN, 1903, *emandavit* WALKER, 1911), AS SEEN IN URINE IN A SUDAN CASE. FRESH AND UNSTAINED SPECIMEN. (× 1,500 DIAMETERS.)

(Microphotograph. This illustration may be examined with advantage by means of a reading lens.)

Historical.—In considering the history of urinary amœbiasis, it is convenient to divide the subject into infections low down in the urinary tract, into those which are situate high up, and into those of which the site is unknown.

Low Down in the Urinary Tract.—Amœbæ were first described in urine and in vaginal secretion by Baelz in 1883, when he named the particular species which he saw *Amœba urogenitalis* Baelz, 1883. This amœba was provided with a synonym by R. Blanchard in 1885, when he called it *Amœba vaginalis* R. Blanchard, 1885. It measured some 23-50 microns in diameter, was actively motile, extruded short and blunt pseudopodia, possessed granular cytoplasm containing a vesicular nucleus and phagocyted red blood-corpuscles, while cystic stages of the same organism were also observed. There is, in our opinion, no reason to doubt that this is the same species as the organism variously known at the present time as *Loeschia histolytica* (Schaudinn, 1903, *emendavit* Walker, 1911); *Entamœba histolytica* Schaudinn, 1903; *Entamœba tetragena* Viereck, 1907; *Amœba dysenteriæ* Councilman and Lafleur, 1891; and *Amœba coli* Loesch, 1875; and by various other names.

The unpleasant point is that if the rules of zoological nomenclature are pressed we ought to call the amœba of dysentery by Loesch's name.

The following cases are known to us: —

(1) Baelz's patient was dying from pulmonary tuberculosis, and it was only shortly before death that hæmaturia associated with severe tenesmus of the bladder set in, and Baelz considered that the bladder as well as the vagina was infected, but it is not evident from abstracts of his paper that any post-mortem examination was made.

(2) In Jurgens's 1892 case the amœbæ were found by post-mortem examination to come from mucous cysts in the bladder of an old woman who had suffered from cystitis, and in whose vagina they were also found.

(3) In 1911 Craig found *Loeschia histolytica* Schaudinn, 1903, in an infection of the bladder in which the autopsy showed a minute fistula between the ulcerated intestine and the bladder.

(4) Lynn's 1914 Costa Rica case seems to have been probably caused by a vesical lesion, as the patient is reported to have felt 'a pain in the trigonum vesicæ at the end of micturition.' He responded very well to emetine treatment, as it is stated 'in the course of five days the vesicle tenesmus was relieved and the urine cleared'; moreover, there was no return of the symptoms after one month.

(5) and (6) Scott Macfie' second case was probably a bladder infection associated with bilharziosis, while his third and fully described case was probably an infection of the genito-urinary tract in the neighbourhood of the seminal vesicles.

High up in the Urinary Tract.—In these cases the site of infection is probably in the pelvis of the kidney.

(7) Posner's 1893 Berlin case began with a rigor and the passage of urine tinged with blood, which, when examined, showed red and white blood-corpuscles, hyaline and granular casts, and large granular bodies 50 by 28 microns, which slowly altered their shape, and which contained, among other things, red blood-corpuscles and one or more nuclei and some vacuoles. Posner, probably correctly, came to the conclusion that the pelvis of the kidney was affected, but seems to have considered that this infection began in the bladder.

(8) A similar case exhibiting signs of pyelitis without any vesical symptoms has been recorded by Chalmers and O'Farrell in the Anglo-Egyptian Sudan.

Site in the Urinary Tract Unknown.—(9) We have been unable to refer to the original papers written by Wijnhoff, by Jeffries, and by Fisher, and are therefore unable to state where the infection was situate.

(10) The very brief note by Ward, Coles, and Friel arouses the doubt as to whether the amœbæ really came from the patient, because they do not state whether these bodies were merely seen once or whether they were of frequent occurrence. They call the organism *Amœba urinæ granulata*, but, as Fantham has pointed out, in no case can this name stand.

(11) Scott Macfie, owing to the non-return of the patient to the hospital, was unable to define the site of the infection in his first case.

All the cases which we have met with have been associated with symptoms which have pointed to the pelvis of the kidney as the probable source of infection.

Climatology.—Cases are known in Europe, Africa, and Asia.

Ætiology.—It is possible that all reported cases were due to *Loeschia histolytica*.

Symptomatology—*Amœbic Pyelitis.*—With or without the history of previous amœbiasis in the form of amœbic dysentery or other amœbic infection, a person is seized with an attack of lumbar pain associated with the passage of turbid urine, with or without blood, and slight fever, the temperature rising to 99°-100° F.

The urine, if collected and examined after centrifuging, will be seen to contain a deposit of red blood cells, leucocytes, and amœbæ in a precystic stage, and more or less degenerate.

The blood, when examined, has been found to show:—

Polymorphonuclear leucocytes	61·0
Mononuclear leucocytes	8·4
Large lymphocytes	22·4
Small lymphocytes	5·6
Eosinophile leucocytes	2·2
Mast cells	0·4
Total	100·0

Amœbic Cystitis.—In these cases there is pain and straining at the end of micturition. On examination the urine shows motile amœbæ.

Treatment.—The treatment is to give urotropine by the mouth and emetine intramuscularly.

OXALURIA.

Definition.—Oxaluria is the deposit in abnormal quantity of oxalate crystals in the urine, and should be restricted to cases which show an increase in the quantity excreted in the day.

Historical.—The crystals of calcium oxalate were discovered by Donné in 1838, and were much discussed for a time, being made the basis of the oxalic acid diathesis of Prout, Golding, Bird, and Begbie; but as a result of Smoler and Bacon's investigations, this theory fell to the ground. In 1896 Dunlop attributed them to the oxalates in the food, and in 1900 Baldwin conducted a series of experiments upon dogs, and showed that fermentative intestinal disturbances associated with the absence of free hydrochloric acid in the gastric juice were the causal agent.

Climatology.—It may occur in any part of the world, but is very commonly met with in the tropics, in Europeans and natives alike. With regard to its presence in natives, Burkitt's observations in Chandira in Eastern Bengal are especially interesting.

Ætiology.—The normal quantity of calcium oxalate to be excreted in the urine is 0·5 gramme per diem. It may perhaps come from certain vegetal substances in the diet, but it is more likely that it is in some way associated with either proteid fermentation in the alimentary canal or proteid metabolism.

Miss Baldwin's experiments tend to show that if the carbohydrate food of a dog is abnormally increased hypochlorhydria may result, and with it oxaluria. Burkitt's observations support this, as he shows that the Manipuris (of Mongolian origin) living round Chandira in Eastern Bengal, and consuming nothing but vegetables and fruit, suffer excessively from oxaluria. Certainly treatment based upon the idea of too little acidity in the stomach is most successful.

Symptomatology.—Dyspepsia, pain in the lumbar region, shooting down the ureter, burning during micturition, and even hæmaturia, are signs of oxaluria. These symptoms may or may not be associated with signs of mild neurasthenia. If unchecked, oxaluria may lead to the formation of an oxalate calculus in the kidney or bladder, accompanied by the ordinary signs of stone in the kidney or bladder.

Treatment.—The treatment is simple and certain. A few minims of the dilute pharmacopœial preparation of nitrohydrochloric acid combined with ½ drachm of the compound tincture of cinchona bark and 1 ounce of the compound mixture of gentian, given three times a day before meals, is the best remedy.

URINARY MYIASIS AND CANTHARIASIS.

See Chapter LXVII., pp. 1628 and 1640.

CHYLURIA.

This is generally due to filariasis, and is described on p. 1608. Cases of schistosomic origin occur, and Remlinger has placed on record two cases due to hydatids, with hydatid membrane in the urine. Quarelli, in 1918, drew attention to a *malarial chyluria* associated with malarial parasites in the blood, and cured by quinine therapy, occurring in a person who had never left Italy.

URINARY TESTS.

Castellani and Taylor's Mycological Method for the Detection of Glucose, Lactose, Maltose, and Other Carbohydrates in the Urine.—The tropical practitioner generally bases the diagnosis of diabetes on the reduction of Fehling's solution by the suspected urine. Fehling, however, may be reduced by a number of other substances in addition to glucose—for instance, by lactose, galactose, maltose—and the detection of such substances by chemical procedures is long and requires much practice. Castellani and Taylor's mycological method will often be found simpler and easier. Castellani and Taylor thought that, just as various carbohydrates and other carbon compounds are used in the identification of certain bacteria and higher fungi, the reverse process might also be carried out—viz., bacteria and higher fungi might be used for the detection and identification of certain chemical substances. For many years ordinary baker's yeast (so-called German yeast) has been, of course, used to detect glucose, but this is the only sugar for which a purely mycological method has been used in pathological work, and, as a matter of fact, it is an unscientific method, as ordinary baker's yeast very often ferments galactose, maltose, saccharose, and other sugars, in addition to glucose. If a urine, therefore, is fermented by baker's yeast, this does not mean with certainty that it contains glucose, as stated in so many textbooks. Castellani and Taylor determine whether a substance is or is not a certain carbohydrate by testing on it whenever possible the action of two germs known to be identical in all their biochemical reactions, except on that particular carbohydrate. For instance, in order to see whether a certain chemical substance reducing Fehling is maltose or not, the substance is tested with two germs which are known to be identical in all their biochemical reactions, except on maltose, such as *Monilia krusei* Castellani and *Monilia pinoyi* Castellani. The procedure to detect, for instance, maltose in the urine is as follows. The urine is collected aseptically, or, if this is not feasible, is distributed in sterile tubes (each containing a small fermentation tube) as soon as passed, and then sterilized in Koch's stove for thirty minutes on two or three consecutive days. It should never be autoclaved, as autoclaving may alter the composition of the sugars and other carbohydrates present. Two tubes of the aseptic urine to which one-third or the same amount of sterile, sugar-free, peptone water has been added (to facilitate an abundant development of the organisms) are inoculated—tube No. 1 with *Monilia krusei* and tube No. 2 with *Monilia pinoyi*. The two tubes are incubated at 35° C. for twenty-four to forty-eight hours, and then examined. If No. 1 does not contain gas, while No. 2 contains gas, the urine, according to all probability, contains maltose.

To understand and properly carry out the method one must have, of course, an exact knowledge of the biochemical reactions of a certain number of bacteria and higher fungi which can be found at pp. [illegible] and 1082. The working and results of the method are seen at a glance in the following mycological formulas:—

URINE FEHLING-REDUCING.

1.	*Monilia balcanica* Castellani .. .	Gas	= glucose.
2.	*Monilia balcanica* Castellani .. .	O	= levulose.
	Monilia krusei Castellani	Gas	
3.	*Monilia krusei* Castellani	O	= maltose.
	Monilia pinoyi Castellani	Gas	
4.	*Monilia pinoyi* Castellani	O	= galactose.
	Monilia metalondinensis Castellani ..	Gas	
5.	*Monilia metalondinensis* Castellani ..	O	= pentoses.
	Bacillus coli sensû stricto Escherich .	Gas	
	Bacillus paratyphosus B Shottmuller ..	Gas	
6.	*Bacillus coli* Escherich	Gas	= lactose.
	Bacillus paratyphosus B Shottmuller ..	O	

URINE NOT FEHLING-REDUCING.

1.	*Monilia pinoyi* Castellani	O	= saccharose.
	Monilia rhoi Castellani	Gas	
2.	*Bacillus coli* Escherich	O	= saccharose.
	Bacillus pseudocoli Castellani	Gas	
3.	*B. paratyphosus B* Shottmüller var. M. ..	Gas	= inosite.
	B. paratyphosus A Shottmüller	O	

URINARY TEST FOR QUININE ELIMINATION.

At times it is necessary for the physician to be certain that quinine is being absorbed by the patient, and at others that the patient is really taking the quinine which has been ordered. Under such conditions a simple easy urinary test which will indicate the presence of the drug in the urine is of value. Such a test can be performed as follows:—

A. To 2 cubic centimetres of the *filtered* urine contained in a *clean* test-tube add ½ cubic centimetre of *Tanret's reagent*. This reagent is a mixture of 3 grammes of iodide of potash, 1 gramme of corrosive sublimate, and 20 cubic centimetres of glacial acetic acid, in such a quantity of distilled water as will produce in all 60 cubic centimetres.

B. If the patient has been taking quinine, or if he has albumen in his urine, the operation described in the preceding paragraph will give rise to *a faint opalescence* or *a white cloud*, depending upon the quantity of either present.

C. Next add a few drops of *absolute alcohol*, when the precipitate if due to quinine will disappear, while that caused by albumen will remain.

This reaction appears in about two hours after taking a dose of quinine, and will persist for twenty-four hours after a dose of 5 grains, and for forty-eight hours after that of 20 grains of the drug.

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CHAPTER LXXXVI

DISEASES OF THE GENERATIVE SYSTEM

General remarks—Male generative system—Endemic funiculitis—Female generative system—Tropical puerperal fever—Sutika—References—Addendum—Ante- and post-natal pathology—Addendum references.

GENERAL REMARKS.

In this chapter we propose to include a few general remarks upon the male and female generative systems. The subjects will be merely touched upon, as space forbids anything else.

MALE GENERATIVE SYSTEM.

In Chapter III., p. 77, we have invited attention to the effects of climate upon the generative organs, and have noted that they act more vigorously than in the Temperate Zone, and that venereal excess is distinctly more deleterious in the tropics than in temperate climates. We have also noted that puberty in boys appears at an earlier age in the tropics than in other climates.

In Chapter V., p. 118, we have touched upon the subject of Eugenics, and have mentioned the ill-effects of *alcoholism*, *syphilis*, *gonorrhœa*, and *tuberculosis*, the effects of which are much the same as in other climates, but as regards the first we have set forth its evils in Chapter X., p. 175. In reference to syphilis, it is very common, and its primary, secondary, tertiary, and inherited effects can be abundantly seen among natives, as may be judged from Chapter XCVII. *Gonorrhœa* is very common among all classes of the population and all races. The clinical features are the same as observed in temperate zones, but complications are much more frequent, owing to the native patients consulting a doctor only when the disease is of long standing. We have seen several cases of gonococcus septicæmia with endocarditis ending fatally, and also several cases of so-called 'gonococcus rheumatism.' It may be noted that among certain natives there is a general belief that the disease is not of sexual origin. African porters firmly believe that it is due to prolonged marching. There are also various curious superstitions in connection with it. In Abyssinia, according to Annaratone, natives believe it is contracted by passing water on the ground illuminated by moonshine, or by passing water where dogs have previously urinated. Occasionally true cases of non-gonorrhœic urethritis are met with (p. 1943); in a few of these cases chlamydozoa-like bodies have been described. Rare cases of urethritis, with black discharge due to the presence of *Aspergillus fumigatus*, and cases of balanoposthitis due to monilias, are observed. *Neglected strictures* are by no means uncommon, and, as we have already stated, one of these apparently caused intestinal obstruction and death. Extravasation of urine is not rare—at all events, in Africa—as the result of neglected stricture. *Elephantiasis of the generative organs* is common in Africa, and in many parts of tropical Asia and America. *Hydroceles, chyloceles, hæmatoceles, orchitis,* and *epididymitis* are all common, and bilharziosis has been already noted by us. Epithelioma of the penis is associated with phimosis and the accumulation of irritating secretions, which may cause balanitis. In these circumstances, if no treatment is carried out, epithelioma may result. Certainly epithelioma of the penis is rare in races in which circumcision is performed.

Castration and circumcision are still performed in many tropical countries. As regards the former, it may be restricted to the simple removal of the testes, but more generally the penis also is cut away. This operation is usually performed upon small boys. Circumcision usually takes place about puberty, but in some races it is performed at an early age. It is usually associated with some semi-religious rites intended, in the case of the older boys, to be an initiation to sexual life, as may be found detailed in works upon anthropology. Christopherson has drawn attention to the mutilations performed by the Abyssinians upon their conquered foes in times of war. This consists of a complete castration—*i.e.*, the removal of the penis and testes—and, as may be imagined, but few survive such a mutilation performed on the field of battle. The result of these operations and mutilations is the formation of much scar tissue surrounding the orifice of the urethræ and the pubes.

With regard to the *breast*, we have seen extraordinary hypertrophy of the male breast.

ENDEMIC FUNICULITIS.

Synonyms.—Suppurative phlebitis of the spermatic cord, Suppurative corditis, Cellulitis of the spermatic cord, Cirsoitis (Pfister).

Definition.—Endemic funiculitis is an acute specific suppurative inflammation of the spermatic cord, of which the ætiology is not firmly established.

History.—For many years medical men practising in Ceylon have noticed the occurrence of a peculiar form of acute suppurative inflammation of the spermatic cord, which occasionally takes a true epidemic character, numerous cases occurring within a short period. References to this affection may be found in almost all the medical reports for the colony during the last twenty years, the disease being variously indicated by the name of phlebitis of the cord or corditis. It was considered by some to be of traumatic origin, by others of venereal origin. Some practitioners considered it to be a malarial affection. The disease was investigated by Castellani first in 1904, and more completely in 1907. He came to the conclusion that it had nothing to do with either malaria or gonorrhœa. He thought the malady had sufficiently characteristic symptoms to be ranked as a separate disease, and suggested the name 'endemic funiculitis.' The affection is not limited to Ceylon, as cases occur in Southern India, and an identical pathological condition has been described in Egypt by Madden in 1907 under the name of cellulitis of the spermatic cord. The condition described by Wise in the West Indies is probably the same pathological entity. Of great importance are the investigations by Coutts

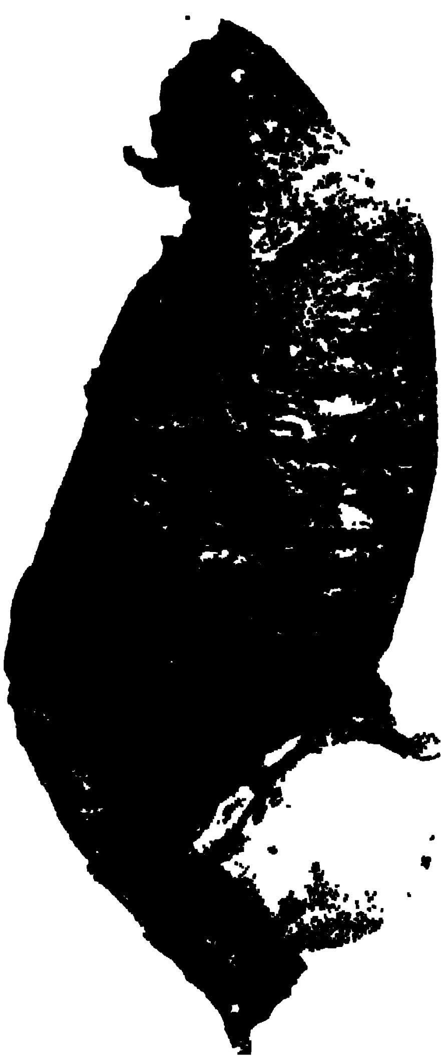

FIG. 780.—ENDEMIC FUNICULITIS, SHOWING LONGITUDINAL SECTION OF THE CORD.

The testes and epididymis are normal

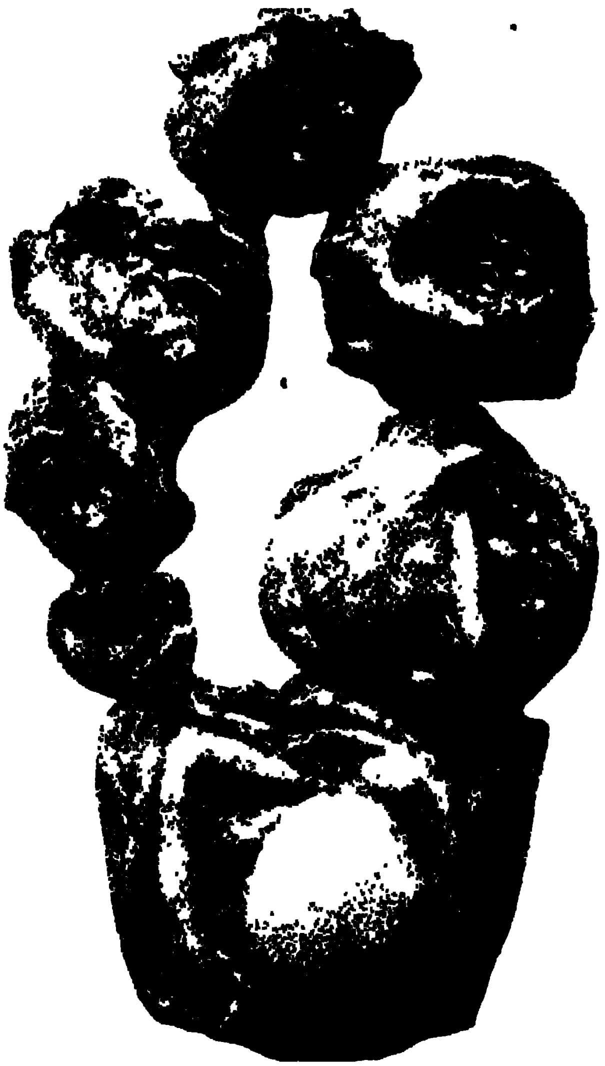

FIG. 781.—TRANSVERSE SECTIONS OF THE CORD IN ENDEMIC FUNICULITIS.

The testes and epididymis were normal, but the tunica vaginalis held a small quantity of fluid. The sections of the cord are arranged in an arch from right to left. The dilated veins, which were filled with pus, are clearly visible.

Ætiology.—Among Ceylon practitioners the disease was considered by some to be of traumatic origin; others believed it to be of venereal origin, and yet others to be a malarial affection. Castellani found in all the cases virulent diplo-streptococci, and in some cases, one in 1904 and the others in 1909, and later, a microfilaria. This microfilaria is morphologically identical with *Microfilaria bancrofti*, but in our cases, though provided with a sheath, it showed translation movements. The cocci are practically indistinguishable from the ordinary streptococci but for the fact that some decolourize by Gram in sections of the tissues and in smears from the pus, while they are Gram-positive in cultures. According to Coutts these micrococci are often found in the urethra of natives. He regards the suppurative condition of the cord as due to the extension of an infection from the urethra by way of the vas deferens. Wise has found in his cases *F. bancrofti* and numerous streptococci. Pfister believes the disease to be connected with bilharziosis. We are inclined to consider the malady to be a filarial condition with a superadded streptococcus infection The filaria probably plays the more important or only rôle in the subacute or chronic cases, while the streptococcus is probably the causative agent of the acute symptoms and the suppuration, and of the symptoms of septicæmia.

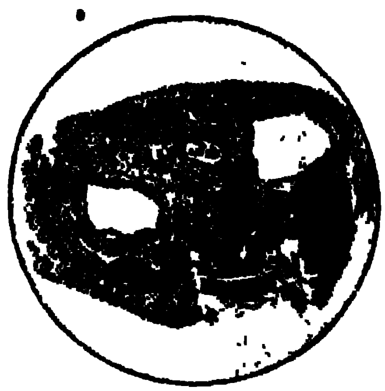

Fig. 782.—Transverse Section Inflamed Cord. (Actual Size.)

Predisposing Causes. A certain importance must be given to a sudden chill or to some form of traumatism. In nearly all the Ceylon cases the disease begins abruptly after taking a cold bath when feeling tired. In some cases the patient gives a history of having made an effort, such as in lifting a weight, etc

Pathology. The whole of the spermatic cord is highly inflamed and infiltrated. The circumference of the cord may be as much as 3 to 3½ inches. The tunica vaginalis is hyperæmic, but in most cases there is no collection of fluid. On making a transverse section of the cord, yellow creamy pus will exude from the opened veins of the pampiniform plexus, as well as from the vas deferens. The inflammation is not localized to the cord only; it ordinarily extends to the epididymis. In two very recent cases of ours, however, the epididymis was normal. The testicle proper remains generally unaffected; there is occasionally some effusion of clear fluid into the tunica vaginalis. The histological lesions are, briefly, the following: The veins of the pampiniform plexus are much dilated, and present a cellular infiltration of all the coats, the lumen of some veins being occupied by pus cells or thrombi. The vas deferens also presents a well-marked cellular infiltration of its mucous membrane and various muscular coats. The type of cellular infiltration as noted by Coutts and Castellani is mostly mononuclear.

Morbid Anatomy.—At the post-mortem examination of the cases in which an operation has not been performed in time, the lesions found are those of a septicæmic process. The skin is jaundiced, and may present petechiæ; the lungs often show hypostatic congestion: the heart is flabby, and subpericardial hæmorrhages are often seen. The spleen is enlarged and soft. The liver is generally enlarged, and may show fatty degeneration or cloudy swelling. The kidneys are often congested.

Symptomatology.—The disease begins suddenly, generally after a hard day's work or severe exercise. In Ceylon the usual history is as follows: The patient, after an extra hard day's work, comes home in the evening very tired, but not feeling unwell, and takes a cold bath as usual. After the bath he is suddenly seized with a shivering fit, the temperature rising very high. He feels very sick, and there is often actual vomiting. At the same time he complains of pain along the cord and the epididymis. The condition becomes rapidly worse, and the patient is generally taken to hospital on the second or third day of the illness. On admission, it is usually found that the general condition is grave. There may be continuous vomiting, and occasionally hiccough; the temperature is generally above 102° F., and the pulse small and frequent. At the physical examination it will be seen that the inguinal region is occupied by a large cylindrical swelling in the direction of the cord. The swelling is very tender on pressure, and hard; the skin is not affected. Generally the epididymis is somewhat enlarged and tender, though in some very recent cases it may not appear to be affected. In all cases the testicle proper appears to be normal; there is, as a rule, no effusion in the tunica vaginalis. The affection is generally localized to one side only, but occasionally attacks both sides. On examination of the penis and scrotum no ulcers will be found, no signs of gonorrhœa, and no signs of any traumatic lesions, though in several cases the patient gives a history of having made an effort of some sort. As a rule, the disease has no tendency to spontaneous recovery. If an operation is not performed in time, signs of general septicæmia usually set in. In such cases the skin of the patient often becomes jaundiced, cutaneous hæmorrhages

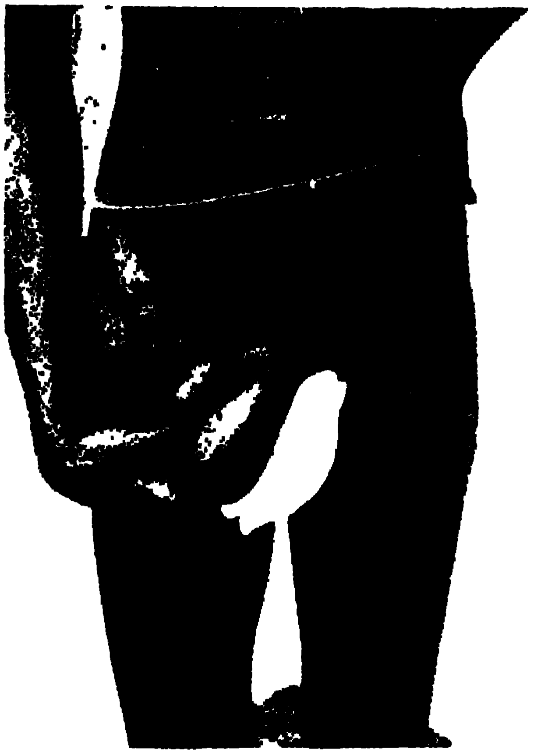

FIG. 783.—ENDEMIC FUNICULITIS IN A SINHALESE MAN.

may appear, the fever is of an intermittent or remittent type, the pulse becomes extremely small, there is often hiccough, and the patient dies in a few days.

Varieties.—A mild form, with thrombosis of the veins, but without suppuration, is at times met with. According to Coutts, a chronic form, also without suppuration, may occur.

Prognosis.—This is serious in the ordinary acute form. If an operation is not performed in time, symptoms of general septicæmia set in, and the case, as a rule, ends fatally.

Diagnosis.—The disease is apt to be confused with strangulated hernia and an acute elephantoid condition of the testicle and cord. From the former endemic funiculitis may be differentiated by the history, the high fever, and the course, which is somewhat less acute. In some cases, especially in the fulminating forms, operative treatment alone will clear the diagnosis.

From an acute elephantoid condition it may be differentiated by the absence of the erysipelatous-like redness of the skin.

Treatment.—Except in the rare mild forms, when lead lotion and ichthyol ointment, with or without ice application, may be sufficient, the only effective treatment is surgical, and orchiotomy, with section of the inflamed cord as high up as possible, is imperative. Coutts recommends exposure of the inflamed cord by a free incision through the skin and external oblique, to be followed by numerous incisions into the tumour. The wound is left open, and fomentations applied till the surface is clean. The wound is then left to heal by granulation. Coutts considers that in this way, though the testis loses its generative function owing to the obliteration of the spermatic duct caused by the inflammation, its internal secretion is unimpaired.

When the disease has extended beyond the internal abdominal ring, orchiotomy must be performed and the veins left unligatured while fomentations are applied.

NON-GONORRHŒAL URETHRITIS.

Urethral muco-purulent discharge is as a rule of gonorrhœal origin, but Castellani has called attention to a number of forms of quite different ætiology, which may be classified as follows:—

A. Traumatic Mucous Urethritis.

This occasionally arises after long and violent continued physical exercise. One is rather sceptical in admitting such a type of urethritis, and practically all the cases of so-called 'porter's urethritis' we have seen were gonorrhœal infections. Still, there cannot be any doubt that in soldiers and native porters doing long marches day after day a slight urethritis with scanty mucous discharge may occasionally develop, even in individuals who have never suffered in the past from gonorrhœa. The secretion, however, in our experience is never frankly purulent.

B. Urethritis of Hyphomycetic Origin.

The following clinical varieties may be differentiated:—

1. The discharge is black, greenish-black, or brownish-black, generally due

to fungi of the genus *Aspergillus* Micheli and *Cladosporium* Link. One of us has described some of these cases in Ceylon.

2. Discharge whitish or yellowish. Generally fungi of the genus *Monilia* and of the genus *Oidium* are found.

3. Red discharge. Generally due to a red pigment-producing monilia or cryptococcus, or to a non-pigmented monilia, and associated with red pigment-producing bacilli or cocci.

C. Urethritis associated with Animal Parasites: I. With Protozoa; II. With Animal Parasites Higher than Protozoa.

I. **Urethritis of Protozoal Origin.** - The following varieties may be distinguished:—

(1) *Urethritis associated with Flagellates.*- The flagellates found belong to the genera *Trichomonas* Donné, *Cercomonas* Dujardin, *Prowazekia* Hartmann and Chagas. In one of our cases a flagellate with four flagelli was observed. It is doubtful, however, whether the flagellates found are the true ætiological agents of the discharge.

(2) *Urethritis associated with Ciliates.*- In a case of urethral discharge in a native man we observed the same ciliate we have fairly often noticed in Ceylon in the vaginal secretion of native women.

(3) *Urethritis associated with Amœba*. We have seen several such cases. The amœbæ were of different type; in one case it closely resembled *Loeschia histolytica*.

(4) *Spirochætic Urethritis.*- This type of urethritis due to *S. urethralis* Macfie is occasionally met with. The discharge may be abundant and frankly purulent, and contains an enormous number of spirochætes. It must be noted, however, that spirochætes are not rarely found in the normal urethra, as shown by many observers and in the tropics by Mendelson.

(5) *Treponema urethritis.*- The discharge is muco-purulent and contains a large number of treponemas (*Treponema urethrale* Castellani). The organism is very delicate, stains purplish or pinkish, has numerous small spirals, all practically of the same size; length of the parasite [illegible] to 12 microns. The patient has no sign of syphilis, and Wassermann is negative. Urethral irrigation of a 1 in 20,000 solution of hyd. perchlor. cures the condition.

II. **Urethritis associated with Animal Parasites Higher than Protozoa.** —These are generally due to larvæ of flies and chance parasites setting up an inflammation of the urethra.

Balanoposthomycosis.—In 1881 Simon of Breslau first described a balanoposthitis due to fungi, and occurring in persons suffering from diabetes. It is probably the same disease as that referred to by Rollo in 1798, by Bardsley of Manchester in 1807, by Friedreich in Hanover in 1864, by Hassal in 1833, and by de Beauvais in 1874. The symptoms consist of slight itching and burning on the glans penis and on the inner aspect of the prepuce, and is associated with erythema, followed by superficial ulceration and a yellow purulent discharge, while the margin of the prepuce may become irritated and phimosis set in. On examining the discharge fungal hyphæ of a moniliform character may be seen. Castellani has described several such cases due to fungi of the genus Monilia.

FEMALE GENERATIVE SYSTEM.

Circumcision is exceedingly common among native races—*e.g.*, among the semi-civilized Arabs and the Sudanese of Kordofan and other parts of the Sudan every young girl when aged five or six years undergoes one of two varieties of this operation. The milder operation, called 'sunna tahuret,' or circumcision according to religious law, consists of the removal of the clitoris and labia minora, while the more severe cutting, called 'Pharaoh's tahuret,' or the old

Egyptian circumcision, entails in addition the removal of the upper two-thirds of the labia majora. The result of these operations is the formation of scar tissue, and hence it is almost always necessary to enlarge the vulvar orifice by means of a razor, not merely at the time of marriage, but again at the birth of a child, when, otherwise, it would be difficult for the head to emerge. The enlarged orifice is again partially closed some little time after birth of the child, and therefore incision has to be repeated at every succeeding birth.

In 1910 Wilson studied the peculiar elongation of the nymphæ found in Hottentot women, and came to the conclusion that it was largely produced artificially.

In 1917 Neve drew attention to the fact that rickets is rare in Kashmir, but that osteomalacia was common in multiparous women, in whom the first symptoms appear in pregnancy and cause the characteristic deformity of the pelvis.

We have discussed the question of the onset of puberty and the climacteric in Chapter III., p. 77, to which reference may be made. Displacements, inflammations, and tumours of the female generative organs are quite common, especially *uterine fibromata* and *ovarian cysts*. Cancer of the uterus is not rare.

VULVO-VAGINITIS.

Every type of vulvo-vaginitis met with in temperate zones is also found in the tropics, and gonorrhoeal infections are very common. It is interesting to note that we have found in the vaginal secretion practically all the organisms we have mentioned under the heading Pseudo Gonorrhoeal Urethritis, and that there are forms of vulvo-vaginitis associated with flagellates, ciliates, amoebæ, spirochætes, treponemata, and fungi, and hence it is quite possible that a certain number of cases of protozoal and hyphomycetic urethritis in man are contracted in reality by sexual intercourse.

Vulvo-vaginitis associated with hyphomycetes is far from rare, and such cases may be separated into two principal groups:—

I. Associated with fungi of the genus Aspergillus, Sterigmatocystis, Penicillium, Cladosporium, with discharge, which may be dark-brownish or black.

II. Associated with fungi of the genus Monilia and the genus Oidium, with white or yellow discharge. These cases may present two different clinical appearances: some are characterized by the presence of thrush-like membranes on the vaginal mucosa (*vaginal thrush*); others do not show any membrane on the mucosa, but the discharge is purulent and very thick. In the tropics Castellani has found fungi principally of the types *Monilia pinoyi* Castellani, *Monilia tropicalis* Castellani. In temperate zones the same observer with Taylor have found *Monilia pinoyi* Castellani, *Monilia londinensis* Castellani, *Monilia metalondinensis* Castellani, and other species.

VAGINAL PROTOZOA.

The vagina of native women may be the habitat of numerous protozoa apart from *Treponema pallidum* and spirochætes. We record the presence of the following:—

Sarcodina :—

Loeschia histolytica (Schaudinn, 1903).
Loeschia coli Loesch, 1875.

Mastigophora :—

Oicomonas vaginalis Castellani and Chalmers, 1908.
Prowazekia vaginalis Castellani and Chalmers, 1918.
Trichomonas vaginalis Donné, 1837.
Tetratrichomonas vaginæ Castellani and Chalmers, 1918.

Ciliata :—

Balantidium vaginale Castellani and Chalmers, 1918.

TROPICAL PUERPERAL FEVER.

Synonym.—Puerperal septicæmia.

Definition.—Tropical puerperal fever is an infection of parturient or puerperal women with various germs, which may cause a local septic condition or a general septicæmia.

History.—It is probable that puerperal fever has been prevalent throughout the world in all ages wherever man has roamed, but as it is conveyed from infective sources, living or dead, autogenetic or heterogenetic, by instruments or by the hands of the attendants, to the uterus of the parturient woman, it is obvious that, in those primitive tribes in which little or no aid is given to the woman in childbirth, there will be little puerperal fever, notwithstanding that her immediate surroundings may be insanitary.

Usually in non-civilized races there is less difficulty with child labour, and hence less damage to the organs of generation, and consequently a less number of portals of septic infection.

The reasons for this easier childbirth are not well known, but may possibly depend upon two factors—*i.e.*, the mother and the child. With regard to the mother, the fact that pregnancy takes place at an earlier age in the uncivilized than in the civilized, and the fact that the woman of non-civilization, from spare and hard living, is often thinner than the woman of civilization may help, even if her pelvic measurements are relatively smaller; while it is often alleged that the head of the uncivilized child is smaller than that of a civilized race, and it has even been asserted by Brooke that on an average the child weighs 1 pound lighter in uncivilized races. If these statements are correct, they will help to explain the easy child labours and the less amount of puerperal fever in those races.

When we consider old native civilizations and the Caucasian races, we find that child labour is difficult, and that assistance has had often to be rendered to the parturient woman from time immemorable, and that puerperal fever in isolated cases and in epidemics has been known for ages.

Turning to one of the old civilizations of the tropic—viz., that seen in Ceylon—these facts are well borne out by the researches of one of us in 1907 into the vital statistics of the various peoples inhabiting that island.

These inquiries showed that the deaths of women in childbirth were higher than those in Europe, and that the principal cause was puerperal fever.

When the racial incidence was investigated it was found that the sociological and hygienic factors influencing this incidence were marked, as the percentage of the total annual racial deaths attributable to childbirth and principally caused by puerperal fever was only 0·1 per cent. for Europeans, while it was 1·2 per cent. for Sinhalese, who form the bulk of the population, 0·8 per cent. for Tamils, the next largest native community, 1·1 per cent. for a mixed native and European race known as burghers, under which heading also come those inhabitants of pure Dutch descent from the settlers of two hundred years ago. Many of these burghers are very poor, and nearly all inhabit towns and mostly live under more insanitary conditions than the average European. The Mohammedan communities of Arabs and Malays have a mortality of 1·2 per cent. and 1·1 per cent. respectively.

The disease is known to have been not uncommon in Bengal since Twining wrote in 1833, while its death-rate in Calcutta for 1906-07 was 1·2 per cent. of the total deaths.

With regard to Egypt, the first medical accounts of the fever are contained in Pruner's writings published in 1847, where it is stated that it was not so common as in Europe, but an epidemic, extending from Alexandria to Luxor, is mentioned as taking place in 1844.

The peoples of the Anglo-Egyptian Sudan are peculiarly interesting from the point of view of our present study, because they contain very primitive tribes, semi-civilized natives, and civilized peoples.

As examples of the primitive tribes we may consider the Nyam-Nyam, who live in the southern part of the Bahr-El-Ghazal Province, and the Jur or Gour tribe, which occupies a limited area of that province between the River Gell and the Rumbek-M'volo road. In these tribes, according to Anderson, childbirth is usually a simple physiological process taking place for the first time when the woman is in her teens, and managed by a midwife, who is simply any other woman who has given birth to a child, and who sees that everything connected with the parturient woman is strictly clean, and placing her on a bed of freshly cut leaves, allows Nature to do the rest, with the sole exception of such rare cases as require assistance, when, according to the same authority, she calls in the aid of some small boys. Under these primitive conditions puerperal fever must be rare. The same easy childbirth can be observed among the Bedouins of Syria.

Among the semi-civilized Arabs and Sudanese of Kordofan and other parts of the Sudan every young girl is circumcised as described above. This procedure, as already stated, is followed by the formation of scar tissue, which renders it almost always necessary to enlarge the vulvar orifice by means of a razor, not merely at the time of marriage, but again at the birth of a child, when otherwise it would be difficult for the head to emerge. The enlarged orifice is again partially closed some little time after the birth of the child, and therefore the incision has to be repeated at every succeeding birth.

If this second cutting is performed carelessly and the resulting wound becomes septic, then fever ensues, and in a case of this nature we have found streptococci and other organisms. 'These people are well acquainted with puerperal fever, which they call 'el jarat,' or sometimes 'humma nafas,' or when slight they term it milk fever, or 'humma laban,' and which they consider to be transmitted from one case to another.

The civilized peoples of Khartoum and Omdurman, more especially the Greeks, Syrians, and better-class natives, suffer from *febris puerperalis* and *febris in puerperio*, but no statistics are available to show the incidence of the disease.

As regards Zanzibar, the deaths from puerperal fever are given as eight out of a total mortality of 1,022, of which 572 are female deaths at all ages.

In none of the above statistics is it possible to compare the puerperal deaths with the number of births, as these were not accurately known.

In the West Indies and in Central and South America the fever is not uncommon, and Brooke, writing in 1908, with his experience of the West Indies and Singapore, says:

> 'The mortality and morbidity from puerperal sepsis and the infantile death-rate among native communities are enormous.'

He blames the village midwife or handywoman, who he says, is a prejudicial, ignorant, and dirty person, and summarizes his remarks by stating:

> 'We see that, for the n [illegible] woman under her native skies, want and poverty may play havoc with t [illegible] uld that is to be, but there is often a physical environment of ignoranc [illegible] sepsis during labour which demands the attention of public opinion.'

Our experience in various tropical and subtropical regions supports these statements made by Brooke.

Ætiology.—Early in the seventeenth century there appeared the idea of a double origin for the fever—viz., the autogenetic and the heterogenetic—and also that the disease was microbic in origin (Kircher, 1671).

In 1788 Denman observed that the disease was carried from cases of puerperal fever to healthy lying-in women by doctors and midwives, which view was strongly supported by the work of Alexander Gordon in Aberdeen in 1795, and by Oliver Wendell Holmes in America in 1843, the last-named observer asserting that not merely could it be conveyed in this manner, but that it could come in a similar way from a case of erysipelas or from a post-mortem, and that it was necessary for the physician to disinfect his hands and to change his clothes after leaving a case of puerperal fever. This work was ably supported and put upon a sound basis by Semmelweiss, whose brilliant researches are too well known to require recapitulation.

With these investigations the heterogenetic origin of the disease was firmly established, and it now remained for the bacteriologists to show the nature of the infective material which, when carried from the sick to the healthy, produced the disease.

In 1871 von Recklinghausen found micrococci in the bodies of persons dying from puerperal fever. The next important step was the discovery by Pasteur in 1878-79 of his 'microbe en chapelet' in the blood of puerperal fever patients.

As this organism belonged to the genus named streptococcus by Billroth, in 1874, Arloing gave it the name *Streptococcus puerperalis*, in 1884, apparently believing that it was distinct from the organism named *S. erysipelatos* Fehleisen, 1883, which is more popularly known as *S. pyogenes* Rosenbach, 1884. Later Furneaux-Jordan and Mackay have revived *S. puerperalis*, but Arloing's name has priority and stands for a synonym of *S. erysipelatos*.

A new phase of the bacteriological history was opened in 1893 by Veillon finding an obligatory anaerobic micrococcus in such diseases as Ludwig's angina, suppuration of Bartholin's glands, phlegmonous perinephritis, etc. This organism, which he called *Micrococcus fœtidus* Veillon, 1893, though usually a diplococcus, can exist in short chains, and therefore may well be a streptococcus. Hallé, in 1898, found it in the secretions of the normal vagina as well as in pus from Bartholin's glands and in the exudate of retained placentæ. It was next observed by Jeannin in 1907 to be present in numerous cases of putrid puerperal infection, and is thought by Veillon's pupils to be the same organism as the anaerobic streptococcus found in vaginal secretion in 1897 by Menge and Kroenig, whose work had been questioned by Koblank but supported by Natvig, Schottmüller, and Hamm.

In 1907 Gioelli reported the presence of a coccus, thought to be a staphylococcus, which he found in a peri-uterine abscess and named *Coccus anaerobius* Gioelli, 1907, while in 1908 he dealt with the question of the bacteriology of puerperal infections. As this coccus produces fœtid gas it may well be the same as Veillon's organism.

In 1910 Schottmuller increased our knowledge as to the streptococci in puerperal fever by finding a new obligatory anaerobe, which he called *Streptococcus putridus*, and which he found not merely in puerperal fever, but also in otitis media, meningitis, cysto-pyelitis, abscess of the lung, gangrene of the lung, and empyema, and he followed this up in 1911 by two papers upon the ætiology of *febris puerperalis* and *febris in puerperio*.

In fifty cases of *febris puerperalis* he found the following organisms to be present thirty-three times—*i.e.*, in 66 per cent., and in all severe and fatal cases:—

S. erysipelatos Fehleisen, 1883, in fifteen cases in the uterine discharges and in two of these also in the peripheral blood. *S. putridus* Schottmuller, 1910, in fifteen cases in the uterus, including five blood infections. *S. erysipelatos* with *S. putridus* three times in the uterine discharge, with both together in the blood once and separately in the other two cases.

He also met with *Streptococcus mitior seu viridans*, an aerobic organism first described by himself in 1903, in the uterus and blood of one case.

He considers that there are two distinct methods of infection: the first is the autogenous, caused by organisms, like *S. putridus*, which lives in the normal vaginæ of pregnant and puerperal women, and are capable of being carried from the vagina to the uterus by means of instruments or by the hand. This form he considers to be non-contagious.

The second method of infection is the heterogeneous, caused by *S. erysipelatos*, and brought from an external source of infection to the puerperal woman as just described.

Von Lingelsheim, in 1912, considered that the importance of *S. putridus* must, for the time being, remain undecided, as it lacked confirmation, but it is obvious that the gas production alone differentiates this streptococcus from *S. erysipelatos* Fehleisen, and it appears to us that there is a general agreement between Schottmüller's organism and that described by Veillon. They both produce fœtid gas, they both are obligatory anaerobes, and they are both found in the vagina and also in association with puerperal fever, and they have both been found in severe infections in other parts of the body. They are probably the same organism as the anaerobic vaginal streptococcus described by Menge and Kroenig, and also that found by Gioelli in 1907.

All these organisms, in our opinion, should be classified under the name of *S. fœtidus* Veillon, 1893.

In 1901 Lewkowicz found an obligatory anaerobic streptococcus, which he named *S. anaerobius micros*, in the mouths of sucklings. In 1907 Jeannin reported that it was present fairly frequently in puerperal infections. It is described as being lanceolate and usually disposed in diplococcal forms, and only occurring in short chains.

In 1812 Furneaux-Jordan published an important lecture upon 'Puerperal Infection.' He and Mackay examined the uterine discharges of twenty-one cases of puerperal fever, and found streptococci in seventeen cases—*i.e.*, 80 per cent. This streptococcus was identical in all cases, and was said to be quite distinct from other streptococci, and so the name *Streptococcus puerperalis* Furneaux-Jordan and Mackay, 1912, was given to it; but we have noted that Arloing had already applied this name in 1884 to a streptococcus which he obtained from cases of puerperal fever, and which he believed to be distinct from *S. erysipelatos* and *S. pyogenes*, the only named forms at that time, but at present all three are considered to be one and the same organism.

In 1916 Chalmers and Atiyah found that *S. salivarius*, *S. bovis* (synonym, *S. bovinus*), and *S. versatilis*, were causal germs in the Anglo-Egyptian Sudan, and traced the origin of these germs to human saliva (*S. salivarius*), zibla—*i.e.*, horse-dung used for walls and floors—bovine fæces, and equine fæces, etc. (*S. bovis* and *S. versatilis*).

The known puerperal streptococci are therefore:—

1. *S. erysipelatos* Fehleisen, 1883.
2. *S. fœtidus* Veillon, 1893.
3. *S. anaerobius* Lewkowicz, 1901.

4. *S. mitior* Schottmüller, 1903.
5. *S. puerperalis* Furneaux-Jordan and Mackay, 1912.
6. *S. salivarius* Andrewes and Horder, 1906.
7. *S. bovinus* Broadhurst, 1915 (synonym, *S. bovis* Chalmers and Atiyah, 1916).
8. *S. versatilis* Broadhurst, 1915.

Other Organisms.—Streptococci are, however, by no means the only organisms found in puerperal fever, as the following have also been recorded: *Aurococcus aureus* (Rosenbach, 1884); *Albococcus tetragenus* (Gaffky, 1884); *Diplococcus pneumoniæ* (Weichselbaum, 1887); *Diplococcus gonorrhœæ* (Bumm, 1885); *Bacillus coli* (Escherich, 1886); but *Bacillus typhosus* (Zopf, 1885) (Eberth's bacillus) only rests under suspicion, while *B. pseudodiphtheriticus* has also been reported.

Among the anaerobic organisms other than streptococci the following have been met with in puerperal infections: *Bacillus emphysematosæ* (Fränkel, 1893); *Bacillus tetani* (Flugge, 1886); and a vibrio described by Curtis in 1913, and probably by Kroenig in 1895, which, though deserving of a definite appellation, is still unnamed.

Abortion.—A very interesting point is the question whether the same organisms are found *post abortum* as *post partum*. This was investigated by Schottmuller in 1911, more particularly in criminal abortions, with the result that he found the following organisms arranged in order of frequency to be present: *S. putridus*, a *Staphylococcus*, *B. coli*, and *B. emphysematosæ*, while *S. erysipelatos* was relatively rarely met with.

Febris in Puerperio.—Another point of interest is the organisms causing *febris in puerperio*—*i.e.*, the slight fever known by Willis' name of lacteal or milk fever, which is frequently met with *post partum*. This has also been investigated by Schottmuller and Heymann, who found the following germs to be present: *S. putridus*, a *Staphylococcus*, *B. coli*, *B. erysipelatos*, *B. vaginæ*, and *B. emphysematosæ*, arranged in order of frequency.

Thus it would appear that the same organisms occur in the mild and in the severe infections, a fact which places on a sound basis Willis' observation that the mild lacteal may become the severe putrid fever.

Methods of Infection.—Adverting to the methods of infection of the parturient woman, we note that Geddes in his 'Statistics of Puerperal Fevers,' published in 1912, says that he believes 99 per cent. of the cases are due to those conducting the labour. A statement of this nature makes it imperative to possess some knowledge as to the presence or absence of bacteria in the normal vulva, vagina, and uterus.

This has been investigated by many workers whose researches make apparent that the vulva at birth is germ free, but after seven to eight hours it contains micro-organisms which have probably been acquired from the secretion of the mother's vagina, the air, and the water of the first bath. As a rule the following organisms are described as being present in the normal vulvar secretion: *Obligatory aerobes*: *Albococcus tetragenus*, *B. coli*, and *B. pseudodiphtheriticus*. *Aerobes and facultative anaerobes*: *Albococcus albus* and *B. vaginæ*. *Obligatory anaerobe*: a *Streptococcus*, probably *S. fœtidus*.

With regard to the vagina this appears to be free from micro-organisms at birth, at which time its secretion is acid, which is said to be due to carbonic acid, and is also bactericidal, an action which cannot be due to leucocytes, which are normally absent.

Some twelve hours after birth the first bacteria can be found therein. The secretion remains acid during life, but is now due to lactic acid, which is said to be present in a strength of 0·4 per cent., and appears to be associated with an organism, *Bacillus vaginæ* Döderlein, 1893.

The normal adult secretion has a bactericidal action when tested against staphylococci, streptococci, and bacteria, but saprophytic organisms can grow therein and may be obligatory or facultative anaerobes, but are generally characterized by having acidophile tendencies. Anaerobic organisms are common, but obligatory aerobes are not frequently met with. Pathogenic organisms are relatively seldom found in the normal secretion, being generally *Staphylococci*, *B. coli*, and *B. pseudodiphtheriticus*.

With regard to the normal vaginal secretion during the puerperium, its bactericidal powers are markedly increased by the lochia, and they do not return to normal until several days after the birth of the child. Notwithstanding this fact, obligatory and facultative anaerobic streptococci, staphylococci, and bacteria are to be found, as has already been indicated, and this fact appears to us to be of the greatest importance when considering the method of infection of puerperal fever.

The secretion of the normal uterus is, by a consensus of opinion, considered to be sterile.

It would thus appear as though Geddes was correct in throwing the responsibility of puerperal infection upon the attendants, as both autogenetic and heterogenetic infections are probably due to them in some way, but the former is much more difficult to prevent than the latter.

With regard to the latter, the researches of Chalmers and Atiyah have thrown suspicion upon cow and horse dung as sources of infection, and this has been confirmed by the work of Chalmers and Marshall, who found the same organisms in bovine and equine fæces.

There are three native uses of cow and horse dung, and they are:—

1. *Cow-dung Poultice.*—This is commonly used by natives throughout the Sudan, and is placed on any painful region of the body, and is, at times, applied to the lower part of the abdomen and even to the external genitalia of the pregnant woman, and in this way may bring about an infection of the vagina with bovine types of streptococci.

2. *Cow-dung Wash.*—In many parts of the tropics it is not uncommon for the natives to use a cow-dung wash for the floors and walls of dwelling-rooms for the purpose of keeping away biting insects and also white ants, and although the practice does occur in the Anglo-Egyptian Sudan it is not so common as in other parts of Africa and in parts of Asia.

Cow-dung, however, is used in Khartoum and Omdurman as a wash for the tops of ovens, and especially of those used for baking bread, and also for the walls of outhouses, especially those used for storing grains.

3. *Zibla.*—It is also used at times in lieu of horse-dung as a constituent of a mixture called zibla which is applied to roofs and walls.

As this wash dries it must form dust, which must pollute the air and be driven hither and thither by the strong winds, which are often present in certain areas of the Sudan, and as the researches of Andrewes and Horder have demonstrated that streptococci are resistant to desiccation, it is possible that the dust derived from dried cows' dung may contaminate the sterile instruments and hands of the attendants on the parturient woman, and so bring about puerperal infections, which would belong to the heterogenetic type.

Once the disease has been started it is always possible for new cases to be infected from previous cases by the agency of attendants, and in this way an epidemic may arise at any time, or, failing this, the infections may be kept up indefinitely by the same means.

Pathology.—The post-mortem anatomy shows some of the features well known in Europe.

Symptomatology.—There seems to be no doubt that the same organisms can cause the mild 'febris in puerperio,' and the severe 'febris puerperalis.'

Why there should be such a difference is not clear, and must depend in some way or another upon the general bodily condition of the patient, and perhaps upon the strength of the streptococcal strain, which, as is well known from laboratory experiments, varies considerably.

Be this as it may, there can be no doubt that one and the same organism infecting the uterus can cause the mild 'febris in puerperio' or 'milk fever' and the more severe and even fatal 'febris puerperalis,' the symptoms of which vary according as to whether there is a local, more or less extensive infection, or a septicæmia.

Prognosis.—A prognosis may be arrived at by observing improvement or the reverse in the clinical symptoms, but more accurate decisions may be deduced by a study of the opsonic indices taken daily, provided that the causal organism is known and is available in pure culture, the index, as already stated, remaining low or sinking in serious or fatal cases, but rising as improvement sets in.

Diagnosis.—It is of the utmost importance that any fever attacking a puerperal woman in the tropics should be assumed to be puerperal fever until it is proved to be something else.

The presence of one of the varieties of puerperal fever can be confirmed:—

1. By microscopical examination of stained smears of the intra-uterine exudate taken aseptically by a sterile swab passed through a sterile speculum inserted into a previously douched vagina.
2. By cultural examinations in ascitic broth of the same exudate taken in the same way, and incubated aerobically and anaerobically at 37° C. and examined at the end of twenty-four and forty-eight hours.
3. By a low opsonic index in the case of the streptococcal infections as tested against the causal organism. This of course is especially applicable in small or large local epidemics, when the causal organism will be available in pure culture in the local bacteriological institute.

With regard to the differential diagnosis, the most important fever which requires attention is malaria occurring in the puerperium, and this should be capable of easy differentiation by:—

1. An examination of peripheral blood smears for the parasites, or, if they cannot be found, by—
2. A differential leucocytic count, with the discovery of a distinct mononucleosis which cannot be explained by other protozoal infections, such as amœbic dysentery, kala-azar, etc.
3. Enlargement of the spleen, not due to one of the forms of tropical splenomegaly.

If these three tests fail to decide the presence or absence of malaria, then a few doses of quinine should be administered, and can do no possible harm, and may even benefit the patient if a puerperal infection due to streptococci or bacteria is present. In our experience this quinine is best administered by intramuscular injections, with or without oral administration, and should, in nervous patients, be associated with a dose of sodium bromide. If the temperature rapidly declines and the symptoms improve with the quinine therapy, then the diagnosis of malarial fever may be made, but if, as has more often happened in our experience, the fever continues, then the disease is not solely caused by malarial parasites. If there is reason to suspect that the puerperal fever is septicæmic in type, or if early enteric fever in its broadest sense is feared, then the diagnosis can be effected by removing aseptically 1 c.c. of peripheral blood from a vein and immediately adding this to nutrient broth medium contained in a flask, half of which is then incubated aerobically at 37° C., while the other half is incubated anaerobically at the same temperature, and both are examined at the end of twenty-four and forty-eight hours.

By these methods, and by these alone, as far as our experience goes, can a case of puerperal fever be accurately diagnosed.

Treatment.—The aim of the rational treatment of puerperal fever must be to:—

1. Kill the causal organisms.
2. Neutralize their toxic effects.
3. Promote the normal action of the patient's organs.

In order to kill the causal organisms they must be attacked in the positions in which they are living, and as this is usually the wall of the uterus, it is necessary to give the patient an anæsthetic as soon as possible and to thoroughly investigate the walls of the uterine cavity in order to discover any portions of placenta, membranes, or blood-clot, and at the same time to observe whether there is any abscess formation in the vicinity of the uterus and also whether there is any inflammation of the tubes, both of which conditions being treated if present.

Usually all that is necessary is the removal of offending substances from the uterus by means of a mild and modified form of curettage, followed by a thorough antiseptic irrigation of its cavity, which is then drained.

After this the vagina and uterus should be irrigated twice or three times a day with an antiseptic solution in bad cases, and less frequently in mild cases.

With reference to the second heading, viz., the toxic effects of the organisms, if these are at all marked they should be combated at once by means of injections of antistreptococcal serum if these are the causal organisms, and by saline, subcutaneous, or intravenous injections, which should be given early and not reserved until too late for beneficial results to follow.

The third point is a matter of common knowledge, and need not delay us here.

SUTIKA.

Synonym.—The puerperal diarrhœa of Bengal.

Under the above term Dr. Pearse, the Medical Officer of Calcutta, gives an account of a chronic diarrhœa associated with fever which causes a death-rate of 1·3 per cent. in the total number of registered births in Hindu and Mohammedan puerperal women of all ages in that city.

The disease begins with diarrhœa some two or three weeks after delivery, there being five to fifteen watery, frothy, fermenting motions per diem without blood or mucus. Along with the diarrhœa there may be loss of appetite and dyspeptic symptoms, rarely vomiting, but no griping pains or abdominal tenderness. The temperature is raised, and an irregular fever lasts throughout the illness. There is no vaginal discharge; œdema of the feet is noted as a late symptom. The course of the disease varies. Sometimes it is rapid, and kills the patient in a few months: more usually it lasts five to eight months, and less usually it continues for more than twelve months. Towards the end the patient becomes weak and emaciated, and dies of exhaustion. The case-mortality is not known.

The nature of this disease is obviously obscure, and requires investigation.

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ADDENDUM.

REMARKS ON ANTENATAL AND POSTNATAL PATHOLOGY.

General remarks—Antenatal pathology—Postnatal pathology—References.

General Remarks.

We think that perhaps a few remarks concerning antenatal and postnatal pathology may be of interest.

Antenatal Pathology.

Much useful work has been done of late in Calcutta and other tropical towns by means of *lady health visitors*, by the training and provision of *midwives*, as well as by the training of school-teachers and school-girls in matters connected with hygiene. The effect of skilled attention at the time of birth has been indicated by the entire absence of *tetanus neonatorum* amongst babies delivered by the municipal midwives in Calcutta, and by the extraordinarily low death-rate under similar conditions during the first week of life, as related by Miss Lewis.

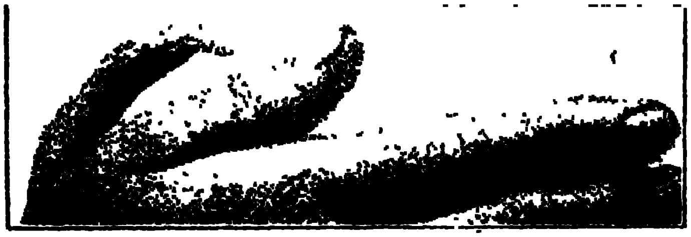

FIG. 784.—POLYDACTYLISM.

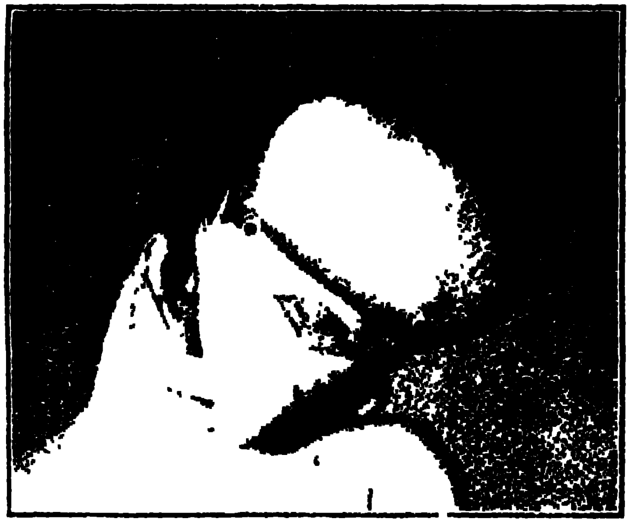

FIG. 785.—CYCLOPS.
(From a photograph by Sambon.)

There can be no doubt that this is the right step to combat such diseases as puerperal fever and infantile mortality, but in order to insure the birth of a healthy child the mother should be medically advised in the early days of pregnancy, and suitable medicines given, if necessary, as so many monstrosities and abnormalities appear in the tropics that some care is required to diminish their numbers.

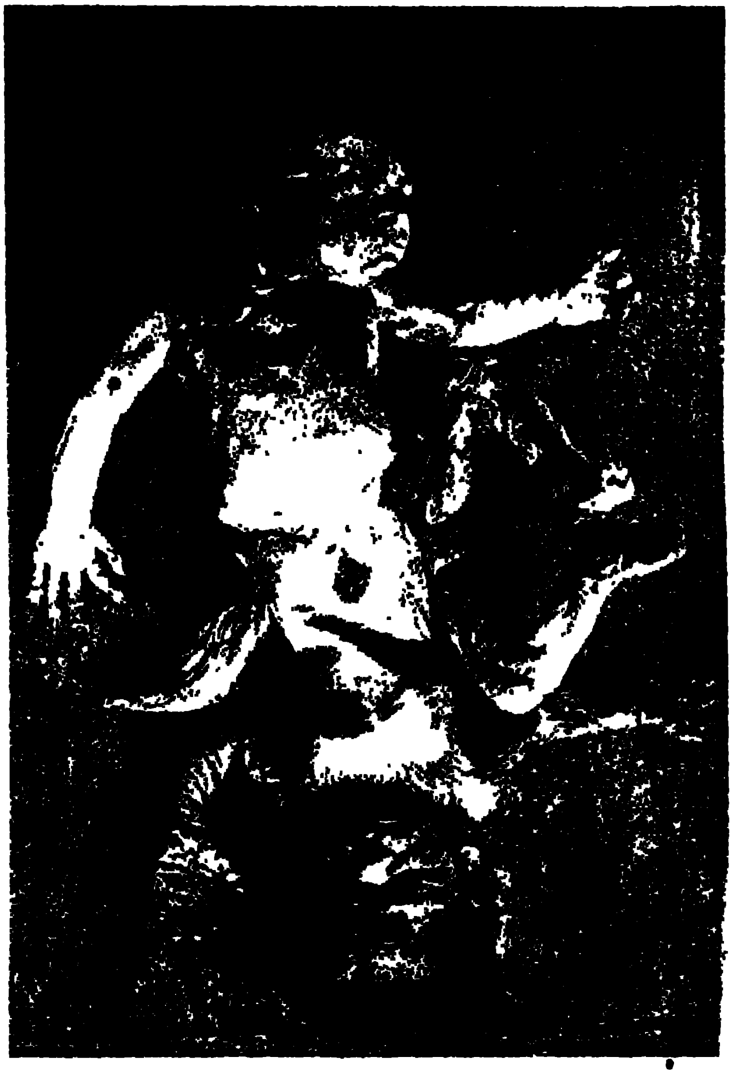

FIG. 786.—ISCHIOPAGUS TRIPUS.

Since the days of Licetus many attempts have been made to classify monstrosities by such authorities as Buffon, Blumenbach, Meckel, Bischoff, Foerster, Fischer, Ahlfield, and others, while Ballantyne has written a most interesting book on the subject.

We have always used the classification introduced by Hirst and Piersol in 1892, and have found it useful. It is as follows:—

Hemiterata.—Anomalies of volume, form, colour, structure, disposition, number, and existence.

Heterotaxis.—Splanchnic inversion and general inversion.

Hermaphrodites.—True, including bilateral, unilateral, and lateral, and false —*i.e.*, with double sexual external genitalia, but unisexual glands.

Monsters.—These are divided into:—

A. *Single monsters* :—

I. Autositic:—Ectromelus, Symelus, Exencephalus, Pseudencephalus, Anencephalus, Cyclocephalus, and Otocephalus.

II. Omphalositic:—Paracephalus, Acephalus, Asomata, and Anideus.

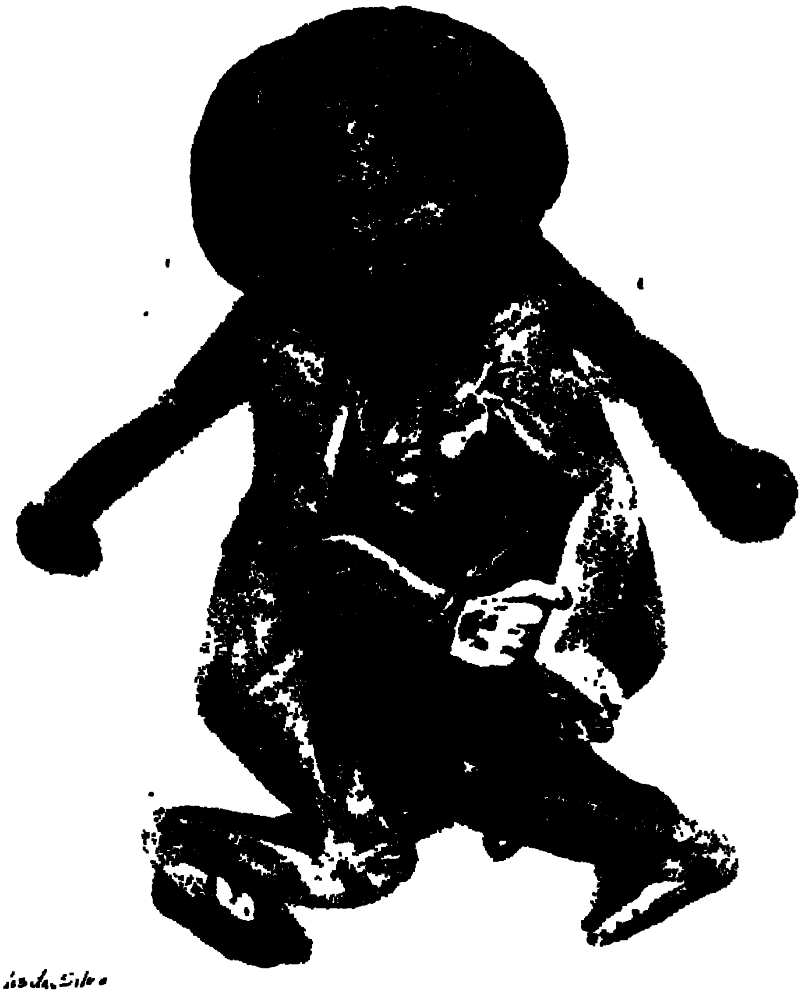

FIG. 787.—SYNCEPHALUS OR JANUS.
(This form of monster is fairly common in Ceylon)

B. *Composite monsters* :—

I. *Double autositic* :—

(*a*) *Terata katadidyma* :—Diprosopus, Dicephalus, Ischiopagus, Pyopagus.

(*b*) *Terata anadidyma* :—Dipygus, Syncephalus, Craniopagus.

(*c*) *Terata anakatadidyma* :—Prosopothoracopagus, Omphalopagus, Rachipagus.

II. *Double parasitic* :—Heterotypus, Heteralius, Polygnathus, Polymelus, and Endocyma.
III. *Triple monsters.*

Fœtal monstrosities and *abnormalities* appear to be much commoner in the tropics than in the other parts of the world, or else we have been singularly fortunate in meeting with them. This is hardly the place to give a detailed account of these abnormalities, but we should advise the tropical practitioner to have some elementary ideas, at all events, on the subject, and therefore we indicate in the above classification the varieties known and in the references the works dealing with this subject. We have met with the following:—Fœtus papyraceus, cyclops, agnathia; several double monsters of both general types, including a specimen of symmetrical janus; acephalic monsters; and rachischisis, meningocele, non-development of the eye, coloboma iridis, hare-lip, cleft palate, branchial fistula, non-development of the thigh. Macrodactylism has been reported from the Philippines, and pes gigas from China.

Further, McCarrison and others have shown that endemic cretinism is brought about by goitre in the mother, combined with psychic impressions or illnesses during the pregnancy, as well as with nutritional difficulties and difficult labour; and it should be the duty of the Government of districts in which goitre is endemic to take steps to combat these factors.

Postnatal Pathology.

The infantile mortality of the tropics is much higher than that in the Temperate Zone, and must be combated by 'Baby Welfare Work,' as in Europe, with a 'Baby Clinic' in all the hospitals. In Calcutta daily visits are paid by the midwives during the puerperal period, and then the work is carried on by the lady health visitor by weekly visits until the child is three months old. Among other matters, the feeding of the mother is attended to by organized private charity. A pure milk supply is an essential in every community, and should be under Government control and at a cheap rate.

Meningitis is rare among the newborn, and seems, according to Barron, to be mostly associated with spina bifida and to be caused by *Bacillus coli*, *staphylococci*, *streptococci*, and more rarely by the *pneumococcus*, the *meningococcus*, *B. lactis aerogenes*, or *B. pyocyaneus*; but of all, *B. coli* is the most important according to him. Breast-feeding is most important, and it may be that it helps to raise the resistance of the infant against disease.

Weaning is a difficult and dangerous period in the tropics, and it is considered that if possible a child should not be weaned in the very hot weather.

In calculating out the dilutions necessary for cow's milk it will be remembered that the milk of the *Bos indicus*, the humpbacked cow, is very rich in fat, attaining generally about 5 per cent. thereof.

The great danger of this period is diarrhœa or dysentery from infections with amœbæ or bacilli.

All the diseases which attack adults in the tropics may affect the child after birth, and the special features which they show have already been recorded, as well as the treatment, in the chapters on the various diseases, and need not be repeated; but the danger of the child being infected with tuberculosis is very great, especially in the slums of large towns

Dosage of Drugs.—As we have often been asked for the dosage of drugs in young children, we give the following rules:—Several drugs, but especially opium, require to be given with caution, as children are especially susceptible to them; but excluding these, the best method so far published for the determination of dosage by age is Cowling's rule with Brunton's modification.

In brief, it is to take the full adult dose and divide it by a factor obtained by placing the child's age at its next birthday over twenty-four if the ordinary British weights and measures are used, and over twenty-five if the metric system be employed. For example, suppose that the full adult dose is 6 grains and the child's age next birthday is four years, then the factor is $\frac{4}{24}$ (*i.e.*, $\frac{1}{6}$) and the dose is 1 grain.

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CHAPTER LXXXVII

DISEASES OF THE LYMPHATIC SYSTEM

General remarks—Climatic bubo—Volvulosis—References.

GENERAL REMARKS.

The lymphatic system is affected in many general diseases—as, for example, in plague and trypanosomiasis—and in cosmopolitan affections like septic disease, syphilis, tuberculosis, etc. In addition, there is the enlargement of the glands in the inguinal region called 'climatic bubo,' and the various pathological phenomena caused by *Filaria bancrofti*. These morbid changes are varices of lymph-channels, inflammations, and elephantiasis, and have already been discussed in the chapter on Filariasis. The pathological changes caused by *Onchocerca volvulus* must be mentioned here.

With regard to the serous membranes, pleurisy and empyema are common, while peritonitis from the perforation of a typhoid ulcer or the perforation of the bowel by an *Ascaris*, as has been recorded by Ziemann in the Cameroons, or from the extension of some septic area—*e.g.*, a gonorrheal salpingitis—are all met with. Chylous ascites is rare.

CLIMATIC BUBO.

Synonym.—Glandula idiopathica (Brooke).

Definition.—Climatic bubo is the enlargement of the inguinal glands associated with pain and fever, the cause of which is unknown.

History.—The history of this disease only dates back to 1896, when Ruge reported several cases suffering from inguinal buboes, in which the usual causes of such an adenitis were all absent, and he was therefore inclined to consider the disease a separate entity dependent probably on climatic influences. About the same time Goding, independently of Ruge, published a series of observations apparently of the same nature, while more recently cases have been reported by many observers.

The disease has been recently investigated by many observers—*e.g.*, Rüffer, Luzzatti, Vanzetti, Rost, Nattan-Larrier, Letulle, Ley, and others.

Climatology.—The chief geographical distribution of climatic bubo is the East Coast of Africa, the West Indies, the Straits Settlements, and China, but it may be met with in any tropical and subtropical region. Le Dantec quotes cases occurring in Mauritius, Tonkin, and Madagascar. Low and Castellani have described a case in Uganda, while Luzzatti has met with several cases in Chili. We have observed cases in Ceylon, and Skinner has described numerous cases in Bengal. Climatic bubo may also occur in the Temperate Zone, for Scheube has come across several cases in Japan, Gabbi in Sicily, and Rost in other Mediterranean districts.

Ætiology.—Though various micro-organisms have been described, the ætiology of the disease is still obscure.

Ferraro, from one of his cases, isolated an organism practically identical with *Bacillus pestis*. Hewlett isolated from the affected gland a bacillus not decolourized by Gram, the characters of which were somewhat similar to those given by Kitasato in his first description of *B. pestis*; for Kitasato stated at first that the *B. pestis* was not decolourized by Gram. Low and Castellani were not able to grow any organism from their case. Some authors have isolated the ordinary pyogenic cocci.

Martin, Suger, Le Sueur, and Fleurant consider climatic bubo to be a manifestation of malaria. Schumm believes the bubo to be secondary to some intestinal infection G. Rost believes the affection to be of sexual origin, and due to a micro organism living in the vaginal mucosa of native women.

According to Cantlie, climatic bubo is a form of attenuated plague—*Pestis minor*—basing this opinion on the fact that in Hong Kong he observed several cases of so-called climatic bubo to precede the outbreak of an epidemic of true plague. He has been confirmed in his opinion by Hewlett's discovery mentioned above. Cantlie's theory is supported by Luzzatti, who considers the climatic bubo to be a form of *Parapestis*. Ernest Black suggests that the disease may be due to an insect bite.

Letulle and Nattan-Larrier have seen in the cells of the capillaries minute bodies which they believe to be parasitic

In our opinion, climatic bubo is a disease *per se*, and is not related to plague.

Predisposing Causes.—The condition is apparently most commonly met with in sailors and stokers. It occurs chiefly in young adults, and is said never to be found in children.

Pathology.—The results of our histological researches agree better with those obtained by Vanzetti in Italy on the material collected in South America by Luzzatti than with those of other authors.

The capsule of the affected gland is much thickened, and the interstitial tissue is very abundant. There is great proliferation of lymphocytes, and hæmorrhagic foci are noticeable here and there. Very characteristic is the presence of numerous typical plasma cells, while the so-called retractile Recklinghausen cells found in plague are absent. The histological structure of climatic bubo is, therefore, totally different from that of the plague bubo, in which, as was shown by the classical histological investigation of Duerck, plasma cells are absent or extremely rare, while the so-called retractile Recklinghausen cells are numerous.

Symptomatology.—The length of the incubation is not known, but according to some observers it may be prolonged. Ley and Rost believe that it can extend to many weeks. The onset is generally gradual; after perhaps two or three days of vague malaise and slight fever, the patient complains of pain in one or both of the inguinal regions, which increases on walking. On examining the parts, one or more inguinal glands, or occasionally the crural glands on both sides, or more frequently one side only, will be found to be enlarged, very painful on pressure, and hard. The swelling may be as large as a goose's egg. There will be no signs of lymphangitis present. The glands may become greatly enlarged, reaching the size of a hen's egg or larger, but in most cases do not suppurate. Aspiration by means of a syringe will draw only a little gland-juice, occasionally blood-stained, but no pus. The liquid will be found to be sterile.

Fever is often present of an irregularly remittent or intermittent type. It rarely exceeds 102° F.; and is higher at night than in the morning. The duration of the disease is variable, from a few days to several weeks, and rarely months. In time the pain in the affected region gradually disappears, the size of the enlarged glands decreasing. As a rule, the affected glands remain larger than normal, but not painful, long after the illness is over. Occasionally a relapse occurs. The general health is not much affected, though the patient may be very weak and unfit for work. The spleen is not enlarged. The examination of the blood may reveal a slight leucocytosis; Wassermann's reaction is negative; the urine is normal. Occasionally a trace of albumen may be present.. Intestinal symptoms are generally absent.

Clinical Varieties.--In our experience an acute, a subacute, and a chronic type of climatic bubo may be distinguished. *The acute type* is always accompanied by fever and severe pains in the affected glands. All the symptoms disappear within five to ten days. In *the subacute and chronic type* lasting from a few weeks to several months the onset may be insidious, without any local pain at first, and fever may be absent altogether. Moreover, in some cases the periglandular tissues become inflamed, suppuration may take place, and fistulous tracks may develop.

Diagnosis.—The absence of soft chancre on the genital organs will exclude *venereal bubo;* the absence of lymphangitis, infected wounds, insect-bites on the legs and feet will exclude the ordinary symptomatic bubo. In contrast to *plague*, the patient does not look very ill, but the only satisfactory way to differentiate acute climatic bubo from a mild case of plague is the puncture of the affected glands and the bacteriological examination of the gland-juice. To do this the skin of the inguinal regions is thoroughly cleansed with spirit and ether, then disinfected with a perchloride (1 in 1,000) or carbolic lotion (5 per cent.), then washed again with ether or spirit, or more simply the skin may be painted with tincture of iodine. One of the enlarged glands is then aspirated with a sterilized syringe. The gland-juice which is drawn off is then examined microscopically and by culture method in the ordinary way for the presence of the plague bacillus.

Climatic bubo is generally easily distinguishable from attacks of *filarial lymphadenitis*, which is generally accompanied by very high fever and severe lymphangitis, and an erysipelatous-like condition of the leg. During and after various *intestinal infections*—as, for instance, typhoid and paratyphoid—occasionally a suppurative inflammation of some lymphatic glands—sometimes the inguinal glands—occurs. In such cases the history of the case—the fact that the bubo comes, as a rule, to suppuration—and the bacteriological examination of the gland-juice, which in true climatic bubo is sterile, will clear the diagnosis.

Prognosis.—The prognosis is favourable, though in some cases the affection may last for several months. A relapse may occasionally occur shortly after the first attack is over, sometimes on the side previously affected, sometimes on the other side.

Treatment.—The treatment is merely symptomatic, consisting of complete rest, application of lead lotion on the affected region, or an ichthyol and belladonna ointment, together with the administration of a mild aperient, and, if there is much pain, a hot fomentation locally together with small doses of opium by the mouth. In the rare cases, where signs of suppuration are noticeable, incision of the glands is necessary, using the ordinary aseptic precautions. In protracted cases complete surgical removal is the best treatment. When the glands remain enlarged after the acute stage has passed off, local applications of tincture of iodine, iodine valsol, or an ointment composed of 30 grains each of lead iodide and potassium iodide to 1 ounce of vaseline may be of benefit. X-ray treatment has been recommended by G. Rost.

VOLVULOSIS.

Definition.—Volvulosis is a disease caused by *Onchocerca volvulus* Leuckart, 1893, and characterized by the formation of fibrous, cutaneous, or subcutaneous tumours.

History.—As already mentioned on p. 649, these tumours were discovered by a German medical missionary to contain worms, which were described by Leuckart in 1893, and subsequently the disease and its causative worm were studied by Labadie-Lagrave and Deguy in 1899, Prout in 1901, Brumpt in 1904, Ziemann and Védy in 1907, and Fülleborn in 1908, the last paper being a most valuable contribution to our knowledge of the subject.

Climatology.—The disease is found in Africa, at Sierra Leone, on the Gold Coast, and in Dahomey, Cameroons, and the north-east of the Congo, where it is variously stated to affect from 1 per cent. to 10 per cent. of the population, being distributed along the banks of rivers. Brumpt found it along the Welle, Cooke in Uganda, and Parsons in Northern Nigeria.

Ætiology.—The disease is caused by *Onchocerca volvulus* Leuckart, 1893, but the method by which this worm is introduced into the human body is quite unknown, as is also its life-cycle outside human beings.* Brumpt has, however, suggested that it will probably be found in a tsetse-fly, because of its riverine distribution and the fact that microfilariæ have been found in the peripheral circulation by Fülleborn, Rodenwalt, and others.

Pathology.—The adult worms lie in lymphatics, the anterior end of the female being in close approximation to the posterior end of the male, because the apertures of the genital apparatus lie in these positions. By some means—possibly by the presence of the *Microfilaria*, or possibly by toxic waste-products—these worms irritate the lymphatics, causing lymphangitis and perilymphangitis. These inflammatory processes eventually lead to the formation of a fibrous capsule around the worms, which then lie in a portion of a vessel cut off (?) from the rest of the lymphatic system, and which forms a fibrous subcutaneous nodule containing male and female worms and *Microfilariæ*.

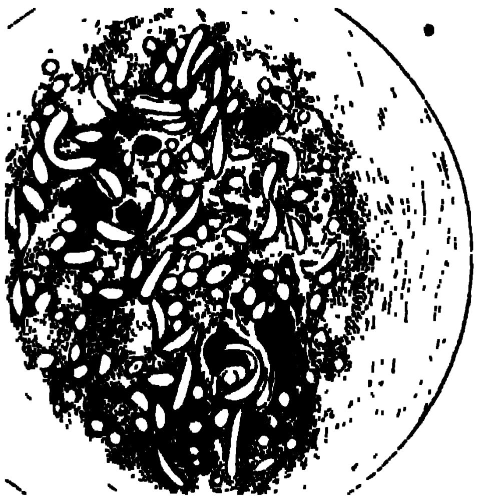

FIG. OUR CONTAINING *Onchocerca volvulus* L

(After Fülleborn.)

On opening one of these tumours it is seen to consist of a capsule of fibrous connective tissue, beneath which is some soft caseous material composed of endothelial cells, granular débris, and *Microfilariæ*, and to enclose a central space containing a greenish, semi-purulent fluid. The worms, which are usually cut across in several places when opening the tumour, lie partly in this central cavity and partly in narrow twisted tunnels, which ramify through the walls of the fibrous capsule, giving it a network-like appearance. Sometimes the central cavity is not obvious, and only the network of tunnels is seen ramifying through the connective tissue.

Symptomatology.—The disease, as a rule, begins insidiously with malaise, weakness, vague pains in various regions of the body, and irregular fever, but it is said that at times attacks of lymphangitis may be noticed. In due course a tumour is discovered in the sub-occipital region, the elbow, axilla, side of the chest, iliac region, gluteal region, or popliteal space. These tumours vary in size from a pea to that of an egg, and lie in the skin or subcutaneous tissue, in which they are freely movable. They may be elastic if they contain fluid, or firm if composed mainly of fibrous tissue. They usually remain quiescent for years, and but seldom ulcerate.

Bernard and Ouzilleau believe that *Onchocerca volvulus* may also give rise to true elephantiasis in certain parts of Africa.

Diagnosis.—The presence of an elastic tumour somewhat resembling a lipoma, or of a firm fibrous tumour in any part of the body of a person who has resided in the endemic region, should arouse suspicions as to the presence of *Onchocerca volvulus*.

When the nodules are in the proximity of articulations the condition may closely resemble the 'juxta-articular nodules' (see p. 2260). The microscopical examination of the contents of the nodules obtained by tapping with a syringe or by excision will clear the diagnosis.

Prognosis.—These little tumours are not in any way dangerous to the life or health of the patient.

Treatment.—Removal by incision and enucleation is quite easy, and devoid of danger.

Prophylaxis.—As the life-cycle of the parasite is unknown, nothing can be said as to prophylaxis.

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CHAPTER LXXXVIII

DISEASES OF CONNECTIVE TISSUES, MUSCLES, BONES AND JOINTS

General remarks—Somatic tæniasis—Subcutaneous filariases—Dracontiasis—Dermo-conjunctival filariasis—Lōiasis—Calabar swellings—Dubini's filariasis—Myositis purulenta tropica—Goundou—Boomerang bones—Pes gigas—Endemic enlargement of the os calcis—References.

GENERAL REMARKS.

THE diseases of the connective tissues which concern us are mostly parasitic, being caused by the cysticerci of tape-worms, but round worms are also commonly met with, especially the guinea-worm.

With regard to muscles, a disease which must be mentioned is *trichiniasis*, which is said to be far from rare in Northern India. *Necrosis, caries, and tumours* of bone are not uncommon, but *rheumatoid arthritis* is rare, and *tubercular disease*, at present, is very rare. *Gonorrhœal* and *post-dysenteric arthritis* are met with, and *filarial synovitis* of the knee-joint has been described by Maitland. *Gout* is rare, but we have seen a typical case in a native who had never left Ceylon

A peculiar condition called 'trench foot' has been met with in war zones in the winter, and is therefore not a tropical disease. It is a painful congestion of the foot, sometimes leading to gangrene, and associated with the presence of spirochætes and other organisms in the bullæ (see p. 2110).

DISEASES OF CONNECTIVE TISSUES.

SOMATIC TÆNIASIS.

By somatic tæniasis is meant the invasion of the body by the cysticercus of cestode worms. The subject is, therefore, divisible into—(*a*) *Cysticercosis*, or infection with the larvæ of *Tænia solium*, which occurs now and again in the connective tissue of muscles, fasciæ, and in the brain; (*b*) *Echinococcosis*, which is the infection of the body with the hydatids of *Echinococcus granulosus*, and of which we have only met with one example in the tropics, and even then it was imported; but, judging by Begbie's observations, it would appear as though the disease was endemic in Ceylon; (*c*) *Sparganosis*, which is the invasion of the body by *Sparganum mansoni*, *S. baxteri*, or *S. prolifer*, all of which have been sufficiently described in Chapter XXV., p. 596.

THE SUBCUTANEOUS FILARIASES.

Definition.—The subcutaneous filariases are infestations of the subcutaneous tissue by the adult worms of species belonging to the Filariidæ other than *Filaria bancrofti* Cobbold, 1877.

Remarks.—The form of filariasis caused by *F. bancrofti* is detailed in Chapter LXVI., and now we consider those in which the adult worm lives in the subcutaneous tissue. The varieties of this form of filariasis are dracontiasis, or guinea-worm infection, and dermo-conjunctival filariasis.

DRACONTIASIS.

Synonyms.—Dracunculosis, Turkish disease.

Definition.—Dracontiasis is the infection of man with *Dracunculus medinensis* (Linnæus, 1758), the guinea-worm (p. 651).

History.—The disease has been known from very remote periods, and it is probable that the fiery serpents which attacked the Israelites in the desert were guinea-worms, and that the serpent on the stick was an illustration of the method of extraction advised.

Plutarch (A.D. 50-117) gave an account of the disease as seen on the shores of the Red Sea, while Galen (A.D. 131-210), who never saw a case, called the disease 'dracontiasis.' Oribasius also mentions it and the worm, and Aëtius, quoting from Leonides, says that it occurs in the legs and arms of people in Ethiopia and India. Paul of Ægina stated that in India and in the upper part of Egypt there was a class of worms called 'dracunculi,' formed in the muscular parts of the body such as the arms, thighs, and legs, and under the skin in the sides of children, which moved, and after a time the skin opened and the head came out. He advises that this be fixed with a piece of lead, the part placed in hot water, and the worm gently pulled, when it will come out by degrees; but if during this process it breaks, there will be much pain. Pollux calls it a corrupted nerve, and Actuarius writes about its presence in Egypt. Avicenna calls it *Vena medina*, after Medina, where it was common. He notes the bleb which it makes in the skin, and its protrusion after the bleb bursts. He recommends ligatures above the worm and baths to make it come out. Haly Abbas says that it occurs in India, Egypt, Ethiopia, and Libya, while Avenzoar notes that it is most common in negroes. Albucasis, Rhases, Bertapalia, and Guy de Cauliac, all mentioned the disease, and the last named calls the worm *Vena civilis vel medina*, while Audry considers it to be an animal. Other writers on this subject are João Rodrigues de Castell Branco (1511-1568), Linscholeri (1599), and De la Motte Lambert (1666). In 1674 Velsch wrote a book on the subject and saw guinea-worms everywhere.

The scientific study of the disease and its parasite dates from the work of Fedschenko in Central Asia, in 1870, when he discovered its development in the cyclops, the integument of which he believed the young worms pierced.

Fedschenko's observations were confirmed by Manson, Blanchard, and by Wenyon working in the Sudan. The cyclops swallow these embryo worms as food, and Indian observers have noted that the worms are at first coiled up in the stomach, but later they pierce the wall of this organ and escape into the body cavity, and may kill the cyclops. In the body cavity they shed their cuticle about the seventh day and undergo developmental changes, and will remain alive in this cavity for some fifty-three days.

In 1907 Leiper proved that the infection of man was *per os*, the cyclops being swallowed in water. In the stomach the crustacean is killed, but the worm escapes through the digested integument of the cyclops, bores its way through the wall of the vertebrate stomach, and in about eight to twelve months becomes the adult female, measuring some 30 inches, but during this process she moves about and finally produces the blister, where water can be touched, and so gets her young into water.

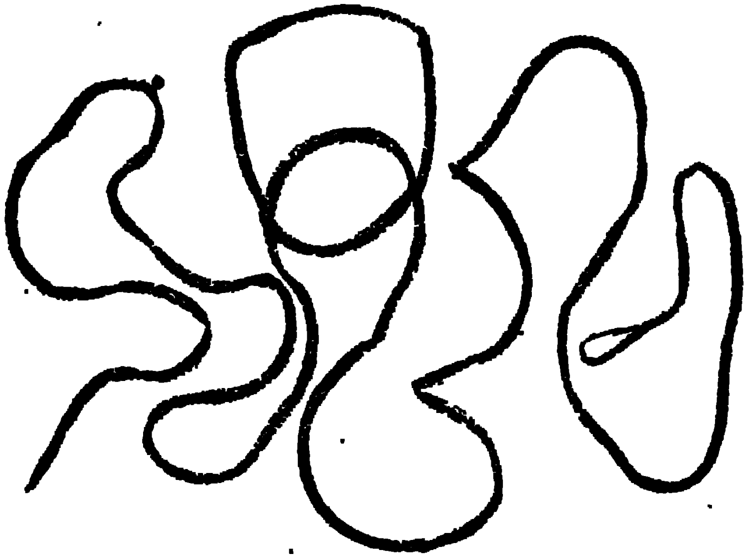

FIG. 788A.—GUINEA WORM SOMEWHAT SHRIVELLED FROM ACTION OF PRESERVING FLUIDS. (HALF NATURAL SIZE.)

In 1913 Turkhud extended our knowledge considerably, and has shown that a man who drank water containing infected cyclops on April 5, 1913, showed the worm on March 18, 1914—*i.e.*, 348 days later. He also demonstrated that the worm would not develop in *Macacus sinicus*.

Whether there is more than one kind of guinea-worm is not known, but Scheube says that Cholokowski has described an unclassified filaria, several inches in length, which causes ulceration of the fingers, and even gangrene, in Tiver, in Russia, which may or may not be the same worm.

Climatology.—Dracontiasis is a disease of the tropics, especially of tropical Africa, and particularly of the West Coast. It is also known in Asia Minor, Persia, and India. Although coolies infected with the worm frequently pass from India to Ceylon, we have no evidence that the latter island has so far become infected. It is also known in the Fiji Islands. It was introduced into America by the negro slaves, and has become endemic in British Guiana and Brazil.

Ætiology.—The causation of the disease is *Dracunculus medinensis* Linnæus, 1758, taken into the body by drinking water containing infected cyclops, which are most abundant during the dry season, and which mostly live near the bottom of wells and collections of water.

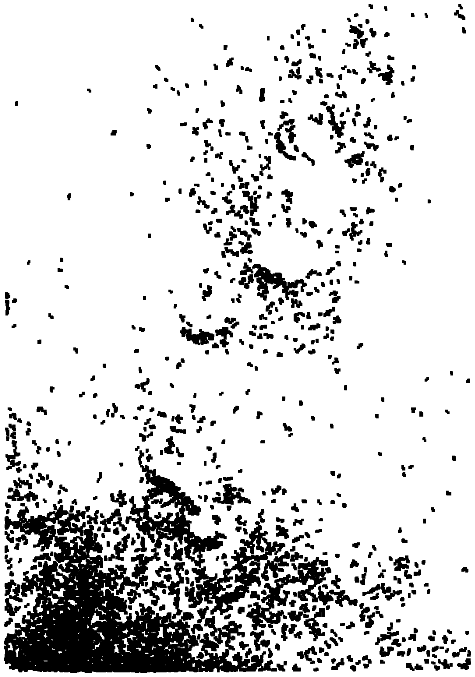

FIG. 789. GUINEA WORM UNDER THE SKIN.

(From a photograph by Christopherson.)

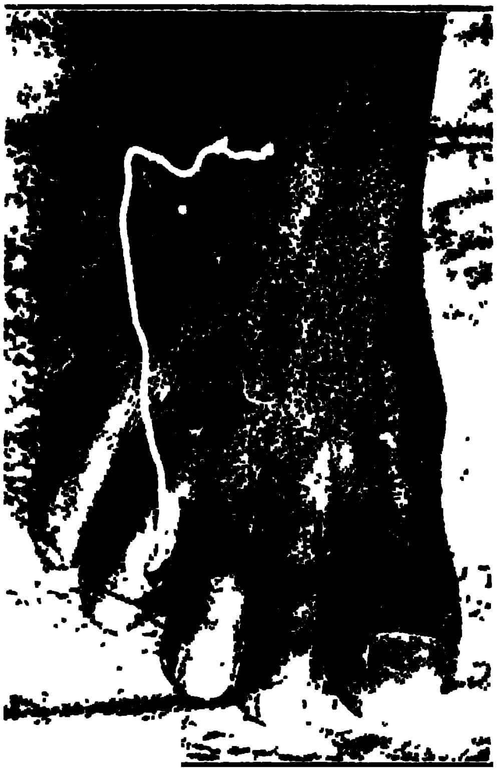

FIG. 790. GUINEA-WORM IN PROCESS OF EXTRACTION.

(From a photograph by Christopherson.)

Pathology.—On entering the stomach the cyclops is killed by the action of the acid of the gastric juice but the *Dracunculus* is stimulated, and, dashing about energetically, effects its escape from the cyclops, and, piercing the walls of the stomach, enters the connective tissue of the mesentery and becomes an adult.

After a time the fully-developed female begins to travel in search of a means of depositing the larvæ in water, and therefore usually wanders into the leg, and forming first a vesicle and then an ulcer in the skin, discharges the larvæ.

Symptomatology.—The worm as a rule produces no symptoms until a little vesicle appears on the skin, or the outline of the worm is noticed under the skin, but urticarial eruptions have been observed by several authors and ourselves. The little vesicle bursts, leaving a round hollow, out of which exudes a clear fluid full of larvæ, and at the bottom of which lies the vaginal orifice of the worm. After discharging a certain amount of fluid, the anterior end of the worm extrudes through the skin opening, and is either twisted on a stick or fixed in position by a piece of string by the native patient. It is not advisable to pull vigorously on the protruded piece of worm, as it is liable to break, and if this happens a serious inflammation of the affected area may result. The wound usually quickly heals after the worm has finally been extracted. The usual site for it to appear is about the feet or legs, more rarely the hands or arms, and still more rarely the head or trunk.

But all cases are not so simple, and aching or dragging sensations, sometimes accompanied by rigors and fever, may occur. Rarely it enters a knee-joint and causes synovitis or arthritis. Usually there is only one worm, but there may be more.

Blood.—Dudgeon and Child have investigated the blood in this disease, and find a marked eosinophilia. The average differential count was as follows: Polymorphonuclears, 63·6 per cent.; lymphocytes, 18·4 per cent.; large lymphocytes, 2·8 per cent.; mononuclears, 1·6 per cent., eosinophiles, 13 per cent.

Diagnosis and Prognosis.—There is no difficulty in the diagnosis, and the prognosis is good.

The X rays are useful in detecting encysted calcified worms, which may cause obscure purulent conditions

Treatment.—It is a good plan to massage the area above the vesicle, and try with a little patience to get the worm out whole, or, if it is visible under the skin, to make an incision and remove it. Natives extract the worm by twisting the protruding portion on a stick, every day giving a turn or two. A better plan is to douche frequently with water the part occupied by the worm until she gets emptied of all the embryos, which generally takes place in from two to three weeks. When all the embryos have been exuded, the worm is either absorbed or tends to emerge, and, no longer resisting extraction, can be easily removed. It has been advised (Emily) to inject a 1 per 1,000 solution of perchloride of mercury into the swelling caused by the worm. But this is very painful, and does not appear to be very successful. Some authors have advised the injection of 10 to 15 minims of a 2 per cent. solution of cocaine into the protruding portion of the worm.

Prophylaxis.—The prophylaxis is very simple—viz., the drinking of only boiled and filtered water. Another simple method suggested by Leiper is to pass steam into the wells.

THE DERMO-CONJUNCTIVAL FILARIASES.

These are Löiasis, Calabar swellings, and Dubini's filariasis.

LÖIASIS.

Definition.—Löiasis is a subcutaneous and subconjunctival filariasis caused by *Loa loa* (Guiyot, 1778).

Remarks.—*Loa loa,* which is carried by a species of Chrysops, as discovered by Leiper, has frequently been noticed in the ocular and palpebral conjunctivæ crossing the bridge of the nose, in the skin over the sterno-mastoid muscle, or that of the scalp, the fingers, the penis, etc., and much more rarely in the anterior chamber of the eye, though accounts of its presence in the vitreous humour require confirmation. For description of the worm see p. 645.

Climatology.—The geographical distribution of the worm is confined to the West Coast of Africa from Sierra Leone to Benguela, but is most particularly Old Calabar, the Cameroons, and the Ogomé River. It penetrates some six hundred miles or more into the interior of Africa.

Symptomatology.—In our experience it usually causes but little disturbance, but at times, when in the conjunctiva, it is associated with piercing and lancinating pains, uncertain vision, and swelling of the eyelids. It is probably the cause of the Calabar swellings mentioned below.

Treatment.—It can be removed by an incision and careful traction. Hot fomentations, as noted by Elliott, cause the worm to come to the surface.

CALABAR SWELLINGS.

Synonyms.—Kamerungeschwülste, Tropical swellings, Ndi-töt = swelling (Calabar).

Definition.—Calabar swellings are smooth, temporary, slightly raised tumours on the head, arms, hands, ankles, and feet, probably caused by the presence of *Loa loa* (Guiyot, 1778), and possibly other species of filaria or allied genera in the subcutaneous tissue.

History.—For many years it has been known that peculiar swellings occurred in the people living in Old Calabar, and in due course accounts appeared in works of travels in West Africa, but it was not till 1895 that Argyll Robertson described them as a distinct disease, using their popular nomenclature. In subsequent years he published several accounts of his cases. In 1898 Plehn drew attention to the complaint, and in 1899 Thompstone published an account of a case, while Habershon and Kerr in 1904, Wurtz and Clerc and Stephens in 1905, and Ward in 1906, have all added to the literature of the subject.

The paper by Ward is, however, of especial interest, as it deals fully with the history of the disease.

Climatology.—The disease is only known on the West Coast of Africa, particularly in the regions of Southern Nigeria and the Cameroons. We have seen, though rarely, a similar condition in Ceylon, where the existence of *Loa loa* has not been reported.

Ætiology and Pathology.—There is a consensus of opinion that in some way these swellings are caused by *Loa loa* Cobbold, 1864, but this has never been definitely proved.

The way in which the worm induces these peculiar lumps is a matter of conjecture, Argyll Robertson assigning them merely to the movements of the parasite. But this cannot be so, otherwise the swellings would occur as they cross the bridge of the nose, which they can do without any such disturbance.

The next theory is that the parasite irritates the skin, causing the patient to rub the affected area, which in this way becomes mechanically inflamed. This theory was originally propounded by Manson, who has relinquished it in favour of another and better explanation.

Two other theories suggest that the parasite, by irritating the nerve endings, either directly or by reflex action, causes the swelling; but this does not appear likely, as they ought to occur wherever the worm travels. Manson in 1903 suggested that they might be brought about by the expulsion of the microfilariæ from the uterus of the parent worm, and this appears not unlikely, and would explain their evanescent character.

Ward is not satisfied with Manson's theory, and suggests that they may be due to the expulsion of waste products from the worm.

Age, sex, and employment have no influence in the causation of the complaint.

Symptomatology.—Sometimes without prodromal symptoms, or at times after some nausea and headache, swellings appear on the head, face, arms, wrists, hands, fingers, ankles, or toes, less commonly on other parts of the body. The reason of this distribution, according to some authors, is believed to be the small amount of connective tissue in those regions. The swellings are smooth, firm, slightly elevated areas, generally about the size of half a goose's egg (5 to 8 centimetres), often painless, though this is not invariable. There is either absence of or only very slight pruritus. They are hot, and do not pit much on pressure. They appear quickly, last for two or three days, and disappear gradually or rapidly, and are always associated with an intense eosinophilia. In many cases only one swelling appears at a time.

Stephens gives the differential count of his case as—Polymorphonuclears, 26 per cent.; lymphocytes, 23 per cent.; mononuclears, 1 per cent.; eosinophiles, 50 per cent.

Diagnosis.—There is no difficulty in recognizing these fugitive swellings in persons who have resided in the endemic region. The presence of extremely well-marked eosinophilia may help in the diagnosis.

Prognosis.—They have never been known to cause serious symptoms, but may recur for many years after the patient has left the tropics.

Treatment.—This is unsatisfactory, but cool applications such as diluted liquor plumbi (5 per cent.) may be made to the swellings, and an ichthyol ointment or lotion applied.

Prophylaxis.—As our knowledge of the life-cycle of *Loa loa* is very incomplete, it is not possible to lay down rules for the prophylaxis.

DUBINI'S FILARIASIS.

Definition.—Dubini's filariasis is a dermo-conjunctival filariasis caused by *Filaria conjunctivæ* Addario, 1885.

History.—The immature female worm was originally discovered by Dubini in the subconjunctival tissue of a man in Milan, and is possibly the same as that described as *Agamofilaria oculi humani* von Nordmann, 1832, and as *Agamofilaria palpebralis* Pace, 1867, *nec* Wilson, 1844. In 1880 Babès found another immature female worm in a calcified nodule in the gastro-splenic omentum of a woman in Budapest. He named it *Filaria peritonei hominis*. In 1885 Addario named a female worm extracted by Vadela from the conjunctiva *F. conjunctivæ*. Vadela's case was a woman from Catania in Sicily. In 1887 Grassi gave a full description of the female worm, calling it *F. inermis*, because of the absence of papillæ on the head. In 1906 Alessandrini found it in an abscess in subcutaneous tissue of the arm; and in 1918 Graham Forbes met with two cases in the subcutaneous tissue of the forearm and of the nose, and was the first to describe the adult male.

It is the same as the worm called *Filaria papillosa* Rivolta, found in the eye of an ass at Pisa, and also *F. apapillocephala* Condorelli-Francaviglia.

Climatology.—The worm is found in Italy, Sicily, Hungary, Macedonia, and Roumania. It is a parasite of the horse and ass, and but rarely of man.

Ætiology.—It has been suggested that the worm is introduced by the bites of *Chrysops excutiens*.

Morbid Anatomy.—The nodule containing the worm consists of fibrous connective tissue with round-celled infiltration and traversed by lymph spaces.

Pathology.—It is thought that the worm enters a lymphatic canal, which becomes cut off and is surrounded by an inflammatory reaction. No microfilariæ can be found in the blood or in the nodules.

Symptomatology.—Marks of a bite have been seen in only one case. Usually it is a small tumour in some area of the body which is the first sign to attract attention.

The differential blood count is as follows:—

	Per Cent
Polymorphonuclear leucocytes	47·0
Mononuclear leucocytes ..	10·5
Small lymphocytes	38·0
Eosinophile leucocytes ..	3·5
Basophile leucocytes	1·0

As time progresses the little lump may become hot and swollen, but not painful. After these inflammatory symptoms have lasted for some three days they subside, only, however, to recur again in about ten to fourteen days, and this cycle recurs and recurs. Sometimes an abscess forms in which the worm or its remains can be found.

Treatment.—The correct treatment is to excise the nodule.

Prophylaxis.—Nothing can be said under this heading, as the method of infection is unknown.

DISEASES OF MUSCLES.

MYOSITIS PURULENTA TROPICA.

Synonyms.—Muma fever (Samoa), Bungpagga (Northern Gold Coast).

History.—This condition has been observed in various parts of the tropics, including the northern territories of the Gold Coast, by several observers, among whom Van Polak, Ziemann, Külz, may be mentioned. The last-named author has given a good general account of the malady.

Climatology.—The disease is found in tropical Africa and Samoa.

Ætiology.—Some authorities suggest that it is due to a *Filaria*

Symptomatology.—The patient complains of rheumatoid pains in the limbs associated with fever of a remittent or intermittent type. Abscesses form in the muscles in various parts of the body.

Treatment.—This is surgical, the abscesses being evacuated.

DISEASES OF BONES.

GOUNDOU.

Synonyms.—Anákhré big-nose; Henpuye = dog-nose.

Definition.—Goundou is a disease of unknown causation, characterized by a bony swelling, usually bilaterally symmetrical, situated on either side of the nose.

History.—The disease was first described by Macalister in 1882, under the term of 'the horned men of Africa.' Lamprey in 1887 also referred to the disease under a similar term, and Strachan drew attention to it in a West Indian child in 1894. Maclaud in 1895 described the disease which he saw on the Niger under the terms 'goundou' or 'anákhré.' In 1900 Chalmers gave an account of the disease as seen on the Gold Coast, and Renner as seen in Sierra Leone. Later Braddon recorded a case in Malaya, and others found the disease in Sumatra and in China. Friedrichsen gave an excellent description of it as seen in East Africa, and Nell gave an account of his cases on the Gold Coast, while Cantlie records a case of unilateral goundou in a European. Lastly, Roques and Bouffard, and more recently Roubaud, Blin, Marchoux, and Mesnil and Léger, have recorded cases in monkeys—*Papio anubis*, *Cercopithecus* sp. ?, and *Callitrichus*.

The first three observers found that the condition affected many bones of the skeleton, besides the nasal bones. Letulle has noticed a somewhat similar condition in the skull of an ancient Inca found in a Peru necropolis.

Climatology.—The disease is most commonly met with in West Africa, but has been reported from East Africa, Malaya, Sumatra, South China, and the West Indies. It usually affects native races, but has been reported in one European. Usually it begins in the first two decades of life.

Ætiology.—This is unknown, though the association with yaws gave rise to the suspicion that this was the ætiological factor. Cantlie's European, however, had not suffered from yaws, and monkeys do not suffer spontaneously from yaws.

Occasionally in yaws patients a bilateral or unilateral swelling of the nose is present (pseudo-goundou of Brumpt), but it quickly disappears along with the other symptoms of yaws under treatment with potassium iodide or salvarsan, which has no effect on true goundou.

Other theories have been that it was a racial trait, or that it was due to a larva of a fly, but these are certainly not correct. As far as we know, it is never congenital. Braddon thinks that it is a disease *sui generis*, and in our opinion is probably right.

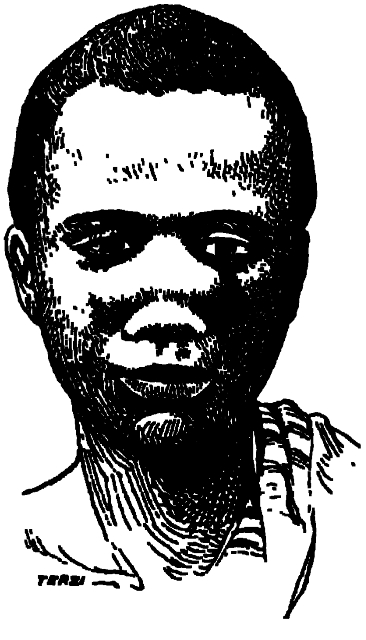

FIG. 791.—GOUNDOU IN A NATIVE OF THE GOLD COAST.

Pathology.- Whatever the cause may be, there seems no reasonable doubt that the infection begins in the nose; for although we were unable to find any abnormality in the nose of the cases we have seen, still, there was always a history of some obstruction, pain in the nose, and often of a bloody discharge. Moreover, Friedrichsen describes a swollen condition of nasal mucosa with almost polypoid excrescences. Léger has noted microscopically a proliferation of embryonal cellular elements derived from the bone-marrow infiltrating the bone-tissue. This is followed later by a true process of cicatrization or osteosclerosis. If this is correct, it is quite easy to understand that the vessels passing from the nose through the *sutura notha*, in the nasal process of the superior maxilla, can carry that infection to the periosteum, which, being irritated, proceeds to an excessive formation of bone in the area of that suture. This results in the formation of a bony swelling, composed on the outside of a thin shell of compact bone, underneath which is spongy, bony substance continuous with that of the bone from which it is arising. The *sutura notha* is, of course, found in all human skulls, and is not peculiar to the negro race.

The bony growths are attached to the nasal bone, the nasal process of the superior maxilla, and at times to the maxilla itself. The periosteum strips off readily, but usually shows no signs of recent inflammation.

Symptomatology.—Generally the disease begins with pain in the nose, or headache, which may be severe, and a bloody nasal discharge, which may continue for some six to eight months. When this is disappearing, it is noticed that there is a swelling, usually symmetrically placed on either side of the nose, in the region of the nasal bone and nasal process of the superior maxilla. Slowly and steadily these lumps increase in size, interfering with vision (it is said at times destroying the eyes), and giving rise to a hideous deformity rather like a *Cynocephalus* monkey, and hence called 'dog-nose.' When fairly well developed, an oval, bony swelling, with its long axis directed downwards and outwards, is seen symmetrically placed on each side of the nose; the skin over the tumour is never affected, being freely movable; and usually, when examined, the nasal mucosa is found to be normal, and the nasal ducts are patent, but there may be swelling and even polypoid-like excrescences. Occasionally a similar growth may invade the nose, partially blocking the nasal cavity. The growth, however, may stop at any stage of it's development, and proceed no farther. Some authors describe a curvature of the tibiæ as being associated with the disease.

Varieties.—Instead of being bilaterally symmetrical, the bony lump may develop only on one side of the nose. Orpen has described, in addition to the two usual tumours, a third in the malar region.

Diagnosis.—The symmetrical bony swellings at the root of the nose are characteristic, but must be distinguished from Brumpt's pseudo-goundou of framboesial origin by the history and by the inutility of salvarsan and potassium iodide.

Treatment.—Medical treatment is useless, and removal is not merely easy, but most effective, as the disease is known not to have returned some six or seven years after the operation.

Prophylaxis.—As the causation is doubtful, nothing can be said under this heading.

BOOMERANG BONES.

Synonym.—Boomerang leg.

Definition.—A disease of the long bones commencing gradually, and associated with pain, tenderness, and longitudinal bowing of the bones, which remain permanently deformed after the acute symptoms have disappeared. Several conditions are apparently covered by this term.

History.—The disease was first described in the second edition (1913) of this work from information received from Ernest Black. He described it as seen in the aboriginal natives of the north of Western Australia and the Torres Straits Islands. In 1915 Breinl and Priestley gave an account of the disease as seen in Northern Queensland and Western British New Guinea. In 1918 Christopherson described a similar condition as seen in the Anglo-Egyptian Sudan.

Climatology.—The disease is known in the northern portion of Australia, the islands of the Torres Straits, in the Sudan, in British New Guinea.

Ætiology.—This is unknown. It is not syphilitic, tubercular, osteomalacic, nor due to rickets. Black considers the condition to be due to hypofunction of the thymus gland. A clinically similar condition is undoubtedly a late manifestation of yaws.

Pathology.—The disease is believed to begin as a rarefying osteitis which causes softening and permits the bending of the bones. This is followed by a condensing osteitis and formation of periosteal bone fixing the deformities.

Morbid Anatomy.—The bending in the tibia takes place at the junction of the upper with the middle thirds. The bone is heavy, and compact in the centre and freer at the ends. The narrow cavity is almost filled in with compact bone.

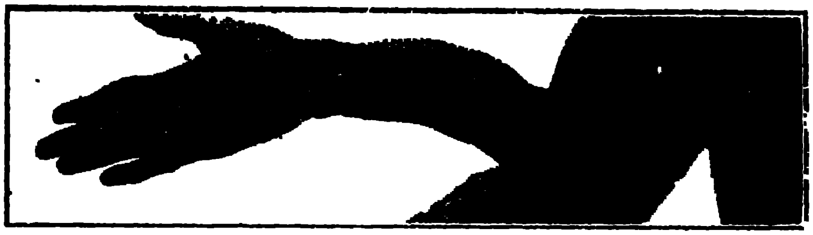

FIG. 792.—BOOMERANG DISEASE.
(From a photograph by Christopherson.)

Symptomatology.—The onset is gradual in young natives during the period of growth. There are pains in the shins, severe enough to prevent walking, and the skin over these bones is tender. The subcutaneous tissues become inflamed, and there is some febrile disturbance. After the acute symptoms and pain have subsided the children start to walk, and the bones bend forward gradually, thus giving rise to the characteristic deformity, which becomes permanently fixed.

Other bones may become similarly affected.

Treatment.—This is nil at present.

Prophylaxis.—Unknown.

PES GIGAS.

Synonym.—Congenital partial hypertrophy of the foot.

Definition.—Hypertrophy and fusion of the inner metatarsal bones, with club formation of the ends of the toes.

History.—Cousland, in the *Journal of Tropical Medicine* for January, 1900, gave an illustration of the disease as seen in a young Chinaman. Raynaud saw the disease in a Kabyle and Legrand in a European.

Symptomatology.—The condition is congenital, and may be studied by the X rays, when it will be seen that the three inner metatarsal bones are hypertrophied, and the second and third united, while the terminations of the toes are club-like. In Cousland's case there was marked hypertrophy of the calf muscles.

Treatment.—It has not been treated so far as we know.

ENDEMIC ENLARGEMENT OF THE OS CALCIS.

Definition.—Endemic enlargement of the os calcis is a disease of unknown causation, characterized by fever, pain, and tenderness over, and subsequently enlargement of, the os calcis.

History and Climatology.—This disease was first described by MacLean in 1904 in Fantis and Krooboys in the Gold Coast Colony, and subsequently in 1905 by Maxwell in natives of Formosa.

Ætiology.—The ætiology and pathology are obscure, but in some way it is connected with the wet season, as attacks and recurrences take place then.

Symptomatology.—The disease begins suddenly with fever, great tenderness over the os calcis, with local pains so severe as to prevent sleeping and walking. In three to seven days the outer surface of the bone begins to increase in size, and continues to do so for some two weeks, during which time the pain lessens and the temperature falls to normal.

In about a month the swelling reaches its maximum size, at which it may remain for about one to two months, during which time the pain is moderate and walking is possible. After this the bone diminishes to about half the maximum size, but sometimes considerable enlargement persists. Usually the disease is bilaterally symmetrical, but it may occur on one side only. It affects the outer surface as a rule, but may also attack the posterior third of the bone.

Rarely it attacks other tarsal bones, but has never been reported as affecting a joint. Yearly recurrences during the wet season are common.

Treatment.—Medical treatment is useless, but relief is given by cutting down on to the affected area and trephining a hole into the bone.

Prophylaxis.—Concerning this nothing is known.

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CHAPTER LXXXIX

DISEASES OF THE NERVOUS SYSTEM

General remarks—Endemic paralytic vertigo—Lâtah—Banga—Schamanismus—Âmok—Tropical neurasthenia—Endemic peripheral neuritis—Erythromelalgia tropica—Desert hallucinations—Emotional excitement—Delusions—Auto-suggestion—References.

GENERAL REMARKS.

The nerve diseases of the tropics include many general diseases already dealt with e.g., pellagra, leprosy, beri-beri, etc. But apart from these conditions, *meningitis, cerebral tumours, cerebral hæmorrhages, spastic paralysis, alcoholic neuritis*, and, more rarely, *arsenical neuritis*, are all well known. *Locomotor ataxia* and *general paralysis*—the so-called parasyphilitic affections are rare, though syphilis is rampant. The *cerebral tumours* which we have most commonly met with are endotheliomata and tubercular or syphilitic lesions. *Hysteria* is common among the better-class natives, especially among the young women educated according to Western ideas.

As regards insanity, *mania* and *melancholia* are the most usual; but *dementia, idiocy*, and *epileptic insanity* are not uncommon. According to Spence, the burden of lunacy in Ceylon is light as compared with England, Scotland, or Ireland, and it is possible that this applies not merely to Ceylon, but to other countries. But apart from these diseases, there are some curious nerve or mind affections which must be considered at greater length.

Sexual perversions are not uncommonly met with in native races.

Homicidal tendencies are generally due to alcoholism, or to long brooding over real or fancied injuries. *Suicide* is not rare, and may be approved by local custom.

Tropical 'kohler' has already been mentioned (p. 76), but tropical neurasthenia, endemic vertigo, and other conditions must be briefly touched upon.

War Zone Neuroses.—The recent war has greatly improved the general knowledge of neurotic conditions. It has been shown that congenital nervous conditions, concussion, chronic alcoholism, and sexual troubles are predisposing causes; while *exhaustion* due to mental or physical strain, toxæmia, insufficient food, pain, excessive heat, or *emotion* due to horrors or constant pain, *traumatism*, particularly concussion, are the exciting causes. The neuroses produced by the above-mentioned causes, according to Hurst, are neurasthenia, soldier's heart, stupor and amnesia, psychasthenia, hysteria, exaggerated defensive reflexes, hyperthyroidism, hyperadrenalism, and shell shock.

The pathology of some of these conditions has been carefully investigated by Mott. Many persons suffering from shell shock have been permitted to go on duty to the tropics, with often unpleasant mental results. These persons are especially liable to be influenced by the sun's rays.

ENDEMIC PARALYTIC VERTIGO.

Synonyms.—Vertige Paralysante, Vertige Ptosique Gerlier's disease, Kubisagari, Tourniquet.

Definition. Endemic paralytic vertigo is characterized by eye symptoms, such as ptosis, dimness of vision, and by paralysis of the neck and extremities.

History.—The disease was first described, in 1884, by Gerlier in Ferney, in Switzerland, in 1886, and by Miura, in 1894, in Japan.

Climatology. It is known in France, Switzerland, and Japan, where it is found in the northern provinces and in the island of Shikoku. It begins in spring, attains its greatest numbers in summer, and ends in autumn.

Ætiology.—The ætiology is entirely unknown, and hence there are many theories, which suggest alcohol, poisoned bread and lentils, and latent malaria; but the one which is favoured by both Gerlier and Miura is the association of the disease with stables. Gerlier says that in the valley of the Lake of Geneva it is not unusual for people to sleep in the stables; and Miura says that in the regions affected in Japan it is usual to have the house so arranged that a part is used as a stable, while the remainder is occupied by the family.

Further, it is associated with warm weather. Miura gives as exciting causes bodily exertion while hungry or after a full meal, writing, reading, steady attention to anything, uniform movements, or mixing with crowds; while the attacks are diminished by rest and change. Couchoud and Shionoya found a Gram-negative coccus in the cerebro-spinal fluid. This they grew artificially, and stated that they reproduced the disease by injecting this into cats.

Pathology.—This is quite unknown.

Symptomatology.—An attack begins with a blurring of objects, everything appearing as if in a fog, together with ptosis, and, less frequently, a diplopia due to paralysis of the internal rectus, with sometimes photophobia, disturbances of colour vision, and hyperæmia of the optic disc. Then follow disturbances of speech and loss of power in mastication, and, in bad cases, of deglutition. At the same time paralysis of the muscles of the back of the neck, the back, and the extremities are observed. The head falls forward, and is only raised with difficulty; hence the name of the disease, 'kubisagari,' which means 'he who hangs his head.' If the muscles of the back are paralyzed, there may be difficulty in raising the body from a stooping posture. Weakness in the hands, arms, and legs is often observed, and is first noticed in the muscles connected with symmetrical repeated movements. An attack lasts from ten to fifteen minutes, and varies in severity, in mild cases there being only ptosis and dimness of vision. Between the attacks the patient is perfectly well in every respect. After severe attacks there may be a little ptosis, or weakness of the muscles of the back, neck, hands, or legs, and increased reflexes.

Diagnosis.—The characteristic symptoms are: Ptosis and the falling forward of the head and neck. These symptoms differentiate it from the other forms of vertigo.

Prognosis.—The disease is never fatal, though it may last for many years.

Treatment.—The first requirement is removal from the endemic area and from living in close proximity to stables. Medicines are not of much use, but a combination of potassium iodide and arsenic is recommended.

LÀTAH.

Synonyms. Echomatism Mimicismus, Sakitlatah, Jumping, Bahtschi, Myriakit, Menatscheme.

Definition. Lâtah is a mental condition in which suggestion is at once followed by uncontrollable action in the form of echolalia or echokinesia, of which the mind is usually, but not always, conscious.

History.—The convulsive tics have been carefully studied in Europe by Charcot, Gilles de la Tourette, and Guinon, but the allied condition 'lâtah' found in Malaysia, as well as similar conditions found in other parts of the world, have as yet not been fully investigated. Thanks to the labours of O'Brien in 1883, Gilmour in 1892, Van Brero in 1895, Ellis in 1897, Gerrard in 1904, Manson in 1907, Fletcher in 1908, Plan in 1911, and Abraham in 1912, a fair amount of definite information with regard to lâtah is available.

Climatology.—Lâtah is found principally in the Malay Peninsula, Java, Sumatra, and is also known in Siam, in Burma, in the Philippines, Siberia, and among the Jumpers of North America. Fletcher has rightly drawn attention to the fact that, while the disease is very common in the Malay States it is, apparently, rare in the Malays who have emigrated. Thus, for example, it does not occur among the large colony of Malays in Ceylon, which may be due to the fact that they originally came from Batavia in Java, and not from Malaya, but it is said by Fletcher to occur in Chinese, Tamils, and in Europeans living in Malaya. The Ikota or Samoyeds, and the Tigretier of Abyssinia, are said to suffer from similar symptoms. In children the disease is milder than in adults.

Ætiology.—The exciting cause appears to be any sudden start, producing some peculiar movement, after which any unlooked-for action may be imitated, and is generally accompanied by bad language. The mildest form of the disease is merely an exclamation or a scream when startled, but in severe cases the patient will imitate any sudden motion or obey any suggestion made to him.

Fletcher relates that in some parts of the Malay States it is occasionally impossible for a judge to examine the witnesses, as they can do nothing but imitate and repeat the questions put to them.

According to Abraham, the exciting causes are: (1) Auditory—*e.g.*, an unexpected noise behind the person; (2) visual—some unlooked-for movement; (3) tactile, such as a sudden touch.

The predisposing cause would appear to be racial.

Symptomatology. On hearing an unexpected noise, seeing or performing a sudden movement, or being surprised by a touch, the patient repeats either the action seen or the words uttered, and at the same time may use foul language. The unfortunate victim is generally conscious of his words and actions, of which he may be ashamed, but he is quite unable to control them. The most graphic account of the symptomatology of the fully-developed complaint is that given by Sir Hugh Clifford in his 'Brown Humanity,' from which we are kindly permitted to give an extract. The disease is best seen in the Malays, and as no white man knows these people as Sir Hugh Clifford knows them, the following is of peculiar value:—

> 'The most typical case of lâtah within my experience was that of a Selangor Malay named Sat, who, in 1887 and 1888, cooked the rice for me and for ten, twenty, or thirty Malays who were then living in my house at Pekai. He was a great big, heavy-featured, large-boned, clumsily-built fellow, very solid, very stupid, very phlegmatic—the last person in the world one would have thought to be the victim of any nervous disorder. To the lay mind any abnormal degree of sensitiveness should be accompanied by a somewhat ethereal physique, a delicate skin, a blue-veined forehead, tiny hands and feet, and a highly-strung organization. To none of these things could poor Sat lay any sort of claim; and though, no doubt, doctors will say that these are by no means invariable accompaniments of a highly nervous temperament, I must own that Sat looked vastly improbable as the possessor of anything so rarefied. All the other Malays in my household were accustomed to put upon Sat most unmercifully, making him do almost the whole of the work that should rightly have been shared between them all. Sat never appeared to resent this arrangement, and he never made any complaint to me then, or at any later time, of the manner in which his fellows treated him.
>
> 'He spent almost the whole of his day in the great ramshackle room, built out over the river on supporting piles of nibong, in which the large wooden box, filled with baked clay, which served as our simple cooking-range, occupied the chief place in the centre of the tala floor.
>
> 'When the others were most noisy, Sat was still silent. When some of my men boasted of the great deeds they had performed in the old days in Selangor, Sat would listen obediently to the thrice-told tales, stolidly, but without excitement. Most of the other men had their own particular chums, but Sat was always solitary, and he never appeared to have any ideas in that great bullet-head of his which he desired to exchange with his neighbours.
>
> 'He had been an inmate of my hut for nearly a year before anyone discovered that he was lâtah. The fact came to light quite accidentally, Sat being startled out of his self-possession by the sudden capsizing of a cooking-

pot over which he was watching. A boy who chanced to be alone in the cook-room with Sat made an instantaneous grab at the fallen rice-pot, and in an instant Sat's hand was in the fire, grasping the burning hot metal. He withdrew his flayed fingers quickly, as the pain brought to him consciousness of what he had done, and he carried them at once to his head—that queer, groping, scratching motion which is an invariable accompaniment of lâtah—and the boy at his side needed no man to tell him that Sat was a victim to that extraordinary affliction.

'With the wanton cruelty and mischief of his age, the boy once more made a feint at the smoking rice-pot, and again Sat's fingers glued themselves for a moment to the scalding metal, and returned aimlessly to his head.

'I do not know how many times this was repeated, but Sat's fingers were in a terribly lacerated condition when at last someone chanced to enter the cook-room, and interfered to prevent the continuation of Sat's torture.

'After that, though I did all I could to protect him from molestation, Sat was never, I fancy, left in peace for long by the other men of my household. Gradually, in the course of a couple of months or so, this man, who for nearly a year had shown no signs of being the victim of any nervous disorder, was reduced to a really pitiable condition. The occasional lâtah seizures, which were at first induced by the persecutions of his fellows, ceased to be abnormal phases, and became the chronic condition of his mind. If one spoke to him, with no matter how much gentleness, he would repeat the words addressed to him over and over again, aimlessly, unintelligently, without, apparently, comprehending their meaning, and that wandering, groping hand of his would steal to his head, and scratch helplessly at his close-cropped hair.

'"Sat, listen, Sat!" I would say to him as quietly and as reassuringly as I knew how. "Listen! no man is worrying thee. Try to listen to what I say to thee." Sat would make answer, and then, very low, in a whisper under his breath: "Listen, listen, listen, listen, listen what I say to thee."

'I instituted a fine for anyone who was found annoying Sat, but it was impossible to get a conviction, for the unfortunate victim could never say who the man was who had teased him into a more than usually severe paroxysm of lâtah.

'It was about this time that a number of other people in my household began to develop signs of the affliction. I must not be understood as suggesting that they became infected with lâtah, for, on inquiring, I found that they had one and all been subject to occasional seizures when anything chanced to startle them badly long before they joined my people, but the presence of so complete a slave to the affliction as poor Sat seemed to cause them to lose the control which they had hitherto contrived to exercise over themselves. One of the older men among my people—Pa'Chim, we called him—a Malay by birth, and of some standing with his fellows, came to me and begged that I would see that no one did anything to give him a sudden start, since, he said, only a very little was needed to make him lâtah also. Yet this man, neither then nor later, showed any signs of the affliction. He probably exercised a considerable amount of self-control, but I always knew that in a moment I could have broken through his guard, and have startled him into as complete a seizure of lâtah as those of which Sat was the victim.

'One day a curious thing happened, which I will relate as it occurred, though I only witnessed the end of the incident.

'A Trĕnggânu Malay, who had a cousin among my people, came in to visit his relative, and chanced to find no one but Sat in the house. The latter invited the Trĕnggânu man to partake of sîrih, and they squatted down on the pĕntas, or raised eating-platform, in the centre of the house, with the sîrih-box between them. The villainous small boy, who had first discovered Sat's weakness was playing about in the room, and in some unholy way he had learned that the Trĕnggânu visitor was also a lâtah subject. He seized a long rattan, which, I think, was kept in the room by one of the older men for his occasional correction, and smote the sîrih-box as it lay between the two betel-chewers, making the wooden covering resound with the smart blow. The sudden and unexpected noise at once deprived both men of all power of

> self-restraint. Each gave a sharp cry and a " jump "—to use the colloquial expression—and, since there was nothing to distract their attention from one another, they fell to imitating each the other's gestures. For nearly half an hour, so far as I could judge from what I learned later, these two men sat opposite to one another, gesticulating wildly and aimlessly, using the most filthy language, and rocking their bodies to and fro. They never took their eyes off one another for sufficient time for the strange influence to be broken, and at length, utterly worn out and exhausted, first Sat and then the Trĕnggânu man fell over on the platform in fits, foaming horribly at the mouth with thin, white flakes of foam. Men came running to me for help, many having witnessed the end of this strange scene, and when I had doctored Sat and his companion back to consciousness, I tried to ascertain from them how they had come to fall victims to this seizure. They could tell me nothing, however, for they only remembered that before their trouble came upon them they had been chewing betel-nut. The matter was sifted out, none the less, and the small boy who had been the cause of the trouble again made the acquaintance of the piece of rattan, and, to judge by his cries, found the interview an unusually painful one.'

From the above account it will be seen that a sudden action will inhibit the higher centres and produce reflex movements in imitation of those performed by the exciting cause. The loss of memory of what has taken place and the peculiar movement of the hand to the head indicates the abrogation of the higher powers.

Varieties.—There are two varieties of the complaint—the impulsive and the mimetic. The former, produced by a sudden shock, results in violent action or bad language, of which the patient may be very ashamed. The mimetic is the form in which the sufferer, no matter how unwilling, is compelled to imitate.

Allied Complaints.—Lâtah must be closely related to those curious, psychical phenomena seen at times among different races, the afflicted people being variously known in Europe as ' the Jumpers,' ' the Barkers,' and ' the Jerks,' and must also be allied to those states of excitement into which people pass during times of religious revivals. In our experience it has also a certain resemblance to some cases of so-called ' Maladie de Gilles de la Tourette,' the main symptoms of which are echolalia and coprolalia.

A peculiar psychical outbreak took place in Madagascar in the years 1863-64 among the women of the lowest classes, consequent on the profound sensations caused by the violent death of King Ramada II., and the subsequent changes in the religion and laws. This outbreak is said to have been identical with the dancing mania of the Middle Ages. It is interesting to remember that there is a strong admixture of Malay blood in the natives of Madagascar, especially in the ruling classes.

It is thus seen that the condition, though at present most marked among the Malays, is, and has been, world-wide in its spread, and is really due to the possession of feeble higher centres which are easily upset, and then are unable to control the lower centres in the accustomed manner.

Diagnosis.—The diagnosis of lâtah is based upon the individual uncontrollably performing or imitating actions, often with echolalia or coprolalia.

Prognosis.—Lâtah is said never to end in insanity.

Medico-Legal.—With regard to the medico-legal aspect of lâtah, Fletcher has performed an experiment with a severely affected subject, proving that suggestion can compel a lâtah subject to commit a crime even against his will. He concludes that in lâtah crime is a possibility either as—

1. An act resulting from an imperfectly controlled inco-ordinate reaction to a sudden impulse; or as—

2. An act resulting from the suppression of volition in the severe forms, the determining cause of which is a criminal suggestion by a second person.

In evidence of the first, he cites two Malays going through a forest carrying their knives for cutting wood. A twig suddenly snaps, and the first man falls to the ground, which so upsets the second one that he also falls to the ground, and in so doing accidentally wounds the first man with the knife he is carrying. In evidence of the second, he places a dummy in a bed previously occupied by a friend of a lâtah person who had been removed without the latter's knowledge. Suddenly the lâtah person was ordered to take a knife which was placed in a handy position, and stab the dummy in the bed. The lâtah person tried not to do this, but was compelled to obey the suggestion. Thus, it would appear that there may be a near connection between lâtah and crime.

Treatment.—The treatment is most unsatisfactory, but auto-suggestion might be tried. Abraham states that some patients have cured themselves by determination not to succumb.

BANGA.

Definition.—A hysterical condition, chiefly influencing women above the age of puberty, but also occurring in men in the Welle District of the Belgian Congo.

Symptomatology.—Fright or anger may induce an attack, in which the body is shaken by convulsions, followed by wild cries and rushes out into the open country or forest away from frequented paths. Sometimes it is accompanied by aphasia.

Diagnosis.—It is said to be separable from hysteria by the absence of the stigmata of that disease.

Treatment.—Suggestion appears to cure these cases.

SCHAMANISMUS.

Schamanismus is the condition of excitement into which certain of the Dayaks and other peoples are able to throw themselves for religious purposes. This state of excitement seems to be attained by leading an extremely erotic life, and appears, by its singing, shrieking, and dancing to utter weariness, to resemble the dancing mania of the Middle Ages, and, therefore, to be related to lâtah.

ÂMOK.

Definition.—Âmok is a psychical disturbance, which, after a period of depression, suddenly develops into a violent attempt to kill people, of which no memory may be left, and after which a stuporous condition supervenes.

Remarks.—Âmok, which means 'an impulse to murder,' is a disease frequently found among the Malays, but also occasionally in other Oriental races. Abraham thinks that there may be some relationship between âmok and lâtah.

Climatology.—Âmok is found in Malaysia among the Bugis of Celebes, the Malays of Indo-China, Malacca, and the Malay States. It is also said to occur at times in Trinidad and among the inhabitants of India and Siberia.

Ætiology.—The exciting cause appears to be a strong emotion of anger, sorrow, or fear, after which a pause or incubation period of depression follows, which may last for days or weeks, during which the patient broods over his wrongs. The Dutch believe that it is induced by opium smoking, and Miall that it is due to smoking haschisch (*Cannabis indica*); but these causes are insufficient.

Symptomatology.—The attack is ushered in by colour sensations of red or black, with or without vertigo, and the patient complains of the appearance of devils, which he attempts to kill. The âmoker usually rushes out of his abode and attacks friends or foes, young or old, males or females, with his kris, or flame-shaped knife, or by firing on them with a gun. The attack usually lasts but a short time, and the deeds performed during that period are not remembered. After the attack the patient passes into a stuporous condition or deep sleep, which may last for a long time, after which he remains in a peculiar excitable condition for some months.

Allied Complaints.—This is a curious pathological entity, and may be a genuine psychical obliquity closely related to those epileptoid seizures investigated in Europe by Lombroso.

Medico-Legal.—If a case is considered genuine, the patient must not be regarded as responsible for his actions, but each case should be judged on its own merits.

Treatment.—No treatment has so far been tried in the prodromal stage, as far as we know.

TROPICAL NEURASTHENIA.

No disease among Europeans in the tropics deserves more careful study by the practitioner than neurasthenia, because, though not in itself fatal, still it leads to many of the petty worries felt and bad tempers exhibited, and, in worse cases, may seriously hamper good work being performed. The subject has been ably studied by Fales in Americans returning from the Philippine Islands.

Ætiology.—Tropical neurasthenia is apt to develop in white people in any part of the tropics, but especially in those which are subject to moist heat, and in some cases an important predisposing cause is the sun's rays, the effects of which are often disregarded. Moreover, the white man is generally compelled to work hard throughout the heat of the day, and is often exposed to the midday sun. The liability to the disease increases with the length of residence in the tropics. Predisposing causes are any previous illness, alcoholism, and overwork. Fales states that he found 30 per cent. of the men and 50 per cent. of the women who had resided for a year or longer in the Philippine Islands the subjects of such severe neurasthenia as to be semi-invalids. In our experience the disease is extremely common all over the tropics in Europeans as well as in the natives of the educated class.

Symptomatology.—In addition to the ordinary signs of neurasthenia, the tropical form seems to markedly affect the vascular system; palpitation is very common, and the patients suffer from various kinds of phobia, especially relating to diseases of the tropics.

Treatment.—The best treatment is rest and change of climate and mild hydropathic treatment. If this is not possible, hypodermic injections of sodium glycero-phosphate—0·1 gramme daily in bad cases—or some form of glycero-phosphate, with or without polyformates, by the mouth in mild cases, may be tried. The patient should discontinue cold baths, and should use warm baths, which should be taken at night if there is sleeplessness. Bromides are occasionally useful.

Prophylaxis.—As in some cases the disease is predisposed by exposure to the sun, protection is required against the sun's rays by topees lined with red, and, if necessary, by red underclothing or clothes made from the 'solaro' fabric already mentioned, and by avoidance of the midday sun as much as possible, and the total abstinence from alcohol.

Persons who are compelled to work hard under unfavourable conditions require change to the Temperate Zone at relatively short intervals—*i.e.*, about once in two or three years.

ENDEMIC PERIPHERAL NEURITIS.

Synonym.—Akatama.

Definition.—Endemic peripheral neuritis is a disease of unknown origin, characterized by numbness and intense prickling and burning sensations in the presence of cold or damp, which are temporarily relieved by the application of dry heat.

History.—The disease was first noticed by Wellman in Central Africa in 1896, and described by him in 1903. It affects 3 to 5 per cent. of the Bantu people, who are by profession porters, and are much impeded in their work by this complaint, which affects young and old, male and female alike. Their staple food is maize, which is eaten partially cooked.

Climatology.—The disease is found in that plateau of Africa which is 5,000 to 6,000 feet high, and is situated between 13° to 14° south latitude, and is inhabited by the Bihé, Bailundo, and Andulu peoples, all of whom are Bantus.

Ætiology.—Wellman was unable to find any causative organism in the blood or fæces. Some of the natives also suffered from filariasis, ankylostomiasis, and bilharziosis, but these were adventitious. His theories are that it may be caused by cold, fermented maize, or nerve-starvation; but he is not satisfied with any of these hypotheses.

Morbid Anatomy.—In bad cases there is some swelling, erythema, and slight œdema of the affected part; still, biopsies of the skin revealed nothing, and post mortem the nerves were found normal.

Symptomatology.—The disease usually begins with shooting, pricking, or crawling pains in the legs and forearms, accompanied by numbness, together with an erythematous rash and swelling of the affected area. All these symptoms are increased by cold and damp, and diminished by heat and dryness. They may also appear on the thighs and arms, and occasionally on any part of, or all over, the body. The gait is peculiar, the patient appearing to walk on the toes and heels. The disease may last for years, but spontaneous recovery is known.

Diagnosis.—The diagnosis is easy, for it is distinguished from beri-beri by the absence of pain in the calves, by the absence of the heart symptoms, and of the paralysis; from elephantiasis by the swelling being transitory; from malaria by an examination of the blood; and from pellagra by the symptoms improving during the warm season.

Prognosis.—This is good as to life and general health, though the course of the malady may be very protracted.

Treatment.—No method of treatment is known to do any good.

ERYTHROMELALGIA TROPICA.

Under this term Gerrard describes a nerve condition in which natives who work barefoot on roads and plantations in Malaya complain of a feeling of pins and needles in the soles of the feet, followed by an acute burning sensation, which prevents walking and sleeping. Malaria is assigned to be the cause. The treatment recommended is to place the feet in hot salt-water, which is said to give great relief.

DESERT HALLUCINATIONS.

Synonym.—Le Ragle.

D'Escayrac de Lauture describes hallucinations of the senses of sight, hearing, smell, or taste, or even of common sensations, which attack persons suffering from exhaustion in deserts. The causation is probably inanition. Generally the attack comes on at night, but it may occur in the day-time, when it is considered to be more serious. Usually hallucinations are visual, and thus stones look like buildings or large rocks, while caravans or files of soldiers may be seen which do not exist. It has nothing to do with true mirage.

Chalmers has met with a case which occurred in the Egyptian deserts, in which the attack at first only came on during the night, but once occurred in the day. Its causation appeared to be due to very hard work and mental worry. The symptoms quickly disappear under the influence of rest, better food, and cessation of worry.

EMOTIONAL EXCITEMENT.

Synonym. Misala.

Howard, in a very interesting paper, has recorded cases of emotional excitement called 'misala,' which vary from an attack of tropical anger to a condition almost bordering on mania, which can be controlled by authoritative commands, or which, left to themselves, pass off in a few hours or days. It occurs among the young adult males of Nyassaland.

DELUSIONS.

Delusions of poisoning and of bewitchment are common in Africa and Asia, and probably elsewhere, and are common explanations of various forms of disease or of hysteria.

AUTO-SUGGESTION.

Every practitioner in Africa and Asia is acquainted with the extraordinary ease with which a native can die if he makes up his mind to do so. The actual cause of death is often exhaustion due to starvation. It should be treated by suggestion.

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CHAPTER XC

DISEASES OF THE ORGANS OF SPECIAL SENSE

General remarks—Diseases of the eye—Diseases of the ear—Diseases of the nose—References.

GENERAL REMARKS.

It is not usual to consider the diseases of the organs of special sense in a work on tropical medicine, but all the diseases of the tropics are being carefully studied at the present time, and therefore we are of the opinion that a few cursory remarks on the above subjects, from the point of view of the general practitioner, may be of some interest.

DISEASES OF THE EYE.

The history of the study of eye disease in the tropics has still to be written, but anyone interested in the general history of this branch of medical science is referred to Hirsch, 'Geschichte der Augenheilkunde' (Leipzig, 1877), which, though issued as a separate little volume, was originally part of Graefe's and Saemich's 'Handbuch der Augenheilkunde,' vol. vii. In this book there is an account of the ophthalmology known in ancient Egypt and India, as well as the history before and during the Alexandrine period of medical development. It will suffice to say that eye disease is described and treated in the Ebers papyrus, and that Suśruta mentioned 76 diseases of the eye, of which 9 were of the joinings of the eye, 21 of the eyelids, 11 of the sclerotic, 4 of the black part of the eye, 17 of the eye in general, 12 of the true organ of vision, and 2 were injuries. In recent years the work of the ophthalmic surgeons of India and Egypt and elsewhere has been beneficial, not merely in an extension of knowledge, but more importantly in benefit to the communities of the lands in which they live. Excellent work has been done by the travelling ophthalmic hospitals, such as those provided by private generosity in Egypt, which go from district to district. By this means, natives at a distance from main hospitals are enabled to obtain expert advice and treatment, which can be carried on in the interval between a visit by the local hospital and dispensary.

Another excellent institution of more or less recent origin is the Central Ophthalmic Hospital, to which the patient can be sent or more prolonged expert treatment. A model hospital of this nature can be found in the Victoria Eye Memorial in Colombo, Ceylon. The prevalence and importance of eye disease in the tropics cannot be too strongly insisted upon. The cases of ophthalmia are so frequent that it has been stated that in no region of the world is conjunctivitis so common, which may be due to the high temperature which favours the growth of micro-organisms; to the overcrowded and filthy native dwellings, which favour their dissemination; to the dirty habits of the lower-class natives; and to the presence of large numbers of flies at certain seasons, which also materially assist in the spread of infection from the diseased to the healthy. Moreover, these factors are reinforced by the irritation caused by the glare of the sun, and by the dust. Blindness is also very prevalent in the tropics. Denham, in his report on the census in Ceylon in 1911, states that, in a population of 4,106,350 persons, there were 3,957 blind persons, which figures, when analyzed, showed that there were 11 blind men and 8 blind women in every 10,000 men and women in Ceylon. In India, in 1901, there were 12 blind men and 12 blind women per 10,000 of each sex; while in England, in 1901, there were 8 blind men and 7 blind women per 10,000 of each sex.

Dr. Andreas Nell, in his statistics of the Victoria Eye Memorial Hospital in Colombo, Ceylon, for the years 1906-1918, shows that the causes of blindness in Ceylon may be classified as follows:—

Congenital Causes.—These included malformations of the eyeball, and syphilis acting upon the optic nerve, retina, and choroid.

Local Eye Diseases.—Ophthalmia neonatorum, Purulent ophthalmia in adults, Catarrhal ophthalmia, Granular ophthalmia, Ulceration of the cornea, Severe paralysis of the ocular muscles, and Glaucoma.

Traumatisms.—Injuries from sticks, thorns, and edges of leaves in the jungle, from spikes in the paddy ear, from the tips of the blades of water-grasses. Some of these injuries are at first trifling, but may become septic, and so cause blindness.

Constitutional Diseases.—These include syphilis, malignant tumours, leprosy, tuberculosis, and enteric fever, but malarial cachexia was not met with as a cause of blindness, nor was ankylostomiasis.

Drugs.—Alcohol (most common); tobacco (rare); quinine and opium (very rare).

There can be no doubt that blindness arises from neglect of the trivial cases of eye disease, and from septic infection, and that, as medical aid becomes more readily available and hygiene is improved, this serious affliction will diminish in the tropics.

For the purposes of the few remarks which we propose to make it will be convenient to divide the subject into: A. Eye Diseases Proper; and B. Eye Complications of Tropical Diseases.

A. EYE DISEASES PROPER.

Œdema of the Eyelids.

Under this term Chalmers and Marshall mention the acute swelling of the eyelids in Europeans and natives in Khartoum. The affected area shows the mark of a bite, and may perhaps be due to an ant, perhaps of the genus *Monomorium* Mayr, 1855.

Congenital Defects.

These are by no means uncommon in the tropics, and our experience includes cases of apparent anophthalmus or microphthalmus, coloboma, and albinism.

Colour Blindness.

This is of importance, and natives who are to be employed as pilots or on railways should be examined as to their power of distinguishing colours; and, indeed, if this has been neglected, it is advisable to examine the existing employés, as the results of such examinations are sometimes surprising. In testing, only the Eldridge-Green lamp and method should be used.

Errors of Refraction.

A subject which has begun to attract a considerable amount of attention is the condition of the eyes of native children in the more modern and higher class native schools, as regards errors of refraction; but the medical inspection of native schools in the tropics is at present neglected, though the children suffer from what may be termed book hunger, and so strain their eyes excessively.

Foreign Bodies.

In addition to the usual foreign bodies met with in the Temperate Zone, small flies are apt to get into the eye in the early evening, and some of these are very irritating, and may cause congestion; or, by introducing micro-organisms, conjunctivitis. Chalmers and Marshall record the finding of a small ant, *Monomorium bicolor* var. *nitidiventre*, firmly fixed by its jaws on to the ocular conjunctiva in a person in Khartoum.

Pterygium.

In this disease the pinguecula, being irritated, spreads on to the cornea, and carries the conjunctiva with it, thus giving rise to triangular folds extending from the ocular conjunctiva to the cornea on the inner or outer aspects of the eye. It is very common in the tropics, especially among coolies in Indo-China.

The treatment is removal.

Hyperæmia of the Conjunctiva.

This is extremely common, being caused by the glare of the sun or by the dust, especially in sandy regions, and is especially apt to occur in persons who have some slight, and perhaps unnoticed, error of refraction. It is also more liable to occur in persons who have some congestion of the naso-pharynx, and is one of the symptoms of rhinitis spastica vasomotoria. Usually the symptoms are but slight, but the eyes are inclined to water; this is aggravated by exposure to light, while the patient may complain of a slight feeling of grit in the eye or of a burning sensation.

On examination, a portion of the palpebral and of the ocular conjunctiva is seen to be congested, while the secretion from the Meibomian glands is noticed to be increased in amount and the eyes to be watery. Treatment consists in bathing with warm 2 per cent. solution of boric acid, in giving the eye rest, and in wearing neutral-tinted or yellowish-tinted glasses (Xanthophylline), which can be obtained in three strengths—light, medium, or strong.

Conjunctivitis.

This is extremely common in the tropics among natives and Europeans, and may be clinically subdivided into—(1) Conjunctivitis catarrhalis; (2) Conjunctivitis gonorrhoica; (3) Ophthalmia neonatorum; (4) Conjunctivitis trachomatosa; (5) Epitheliosis desquamativa; (6) Conjunctivitis phlyctenulosa; (7) Conjunctivitis vernalis. Diphtheria is not common in the tropics, and diphtheritic conjunctivitis is rare, while conjunctivitis nodosa is extremely rare, but can be caused by caterpillar hairs, or plant hairs, becoming embedded in the conjunctiva.

Conjunctivitis Catarrhalis.

This may be subdivided into the acute, the ronic, and the follicular forms.

The Acute Variety.—This is very common in the tropics, where it may occur in epidemics. The most common cause is the Koch-Weeks bacillus, which may induce a very severe form of inflammation; while almost as frequently the Morax-Axenfeld bacillus causes a milder though more prolonged attack, often called angular conjunctivitis. Rarer causes are the pneumococcus and staphylococcus. The small eye fly of Ceylon is suspected by Castellani and Perry of being an agent in the spread of this disease in Colombo.

The disease begins with photophobia, burning and itching in the eyes, with a sensation of grit, all of which symptoms are more pronounced in the morning than in the evening, when the eyelids are often glued together by the dried conjunctival secretion.

On examination, the palpebral and ocular conjunctivæ are seen to be red and congested, and sometimes to be marked by red spots indicative of small hæmorrhages, while the conjunctival secretion is increased in amount and may have particles of mucus swimming in it, or it may be largely composed of mucus, or in severe cases it may be purulent. Usually both eyes are attacked. The disease may disappear in eight to fourteen days if untreated, but more usually it becomes chronic. The complications most commonly observed are corneal ulcer and iritis.

The best treatment in severe cases is to evert the eyelids, and to lightly mop the inflamed conjunctiva with 2 per cent. solution of silver nitrate, followed by a weak solution of salt, or by instilling a

10 per cent. solution of protargol, or 10 to 25 per cent. of argyrol. Ice compresses are very soothing. For the inflammation due to the diplobacillus of Morax and Axenfeld, the best treatment is to instil a 0·25 per cent. solution of zinc sulphate two or three times a day, or a 0·50 per cent. solution once a day. When the acute symptoms have subsided, a little adrenalin may be added to the zinc sulphate solution.

In order to prevent the sticking together of the eyelids, a 2 per cent. ointment of boric acid, or a ½ per cent. strength of white precipitate ointment, may be used.

It is almost unnecessary to state that no bandage should be applied to the eye, or that the disease is contagious, and that it is necessary to warn the patient's friends of the danger of the attack.

The Chronic Variety may be the sequela to an acute attack, or may be in the form of the angular conjunctivitis due to the Morax-Axenfeld bacillus, or due to eyestrain or local injury by wind, dust or foreign bodies, or the use of alcoholic liquors.

The symptoms are most marked at night, when the patient feels as though a foreign body was in the eye or has sensations of rainbow colours. The eyes are apt to burn and to be dazzled by light. In the morning the lids are stuck together. Sometimes there is excessive secretion, and sometimes there is lessened secretion. If neglected, this chronic variety may last for years, and may lead to epiphora, ectropion, or ulceration of the cornea.

The treatment is the same as for the acute stage, but the best therapy is the zinc sulphate drops in the form of a ½ per cent. solution applied night and morning.

The Follicular Variety may occur in epidemics, and may be acute, when it is usually of bacterial origin; or chronic, when it is usually non-bacterial. It is characterized by the formation of small, round, pale granules about the size of a pin's head, and is easily mistaken for conjunctivitis trachomatosa; but the granules are usually best marked in the inferior fornix, while those of trachoma are more marked in the superior fornix and tarsus, which must be most carefully examined by retroverting the lid and the retrotarsal fold in order to be certain that trachoma is absent. In the acute form the treatment is *the* same as for acute catarrhal conjunctivitis, but when chronic it is usual to apply copper sulphate treatment. An ointment of 1 in 1,000 copper sulphate or 1 in 100 copper citrate is recommended by some authorities.

Conjunctivitis Gonorrhoica.

This is so well known that no special reference need be made to it.

Conjunctivitis Neonatorum.

This is usually due to the gonococcus, but may be caused by a streptococcus or probably by a chlamydozoon.

Micrococci and Conjunctivitis.

The presence of Gram-negative micrococci may be due to infection from the generative organs by the gonococcus, but it may also be due to infection from the nasopharynx via the lachrymal ducts by the meningococcus and the *Micrococcus catarrhalis*, which is merely a term for a group of Gram-negative cocci. The Gram-negative cocci of the conjunctiva may be roughly separated from one another by cultivation in sugar media.

Organism.	*Glucose.*	*Maltose*
Gonococcus	+	–
Meningococcus	‡	‡
Micrococcus catarrhalis	–	–

Acid only, +; acid and gas, ‡; neither, –.

Conjunctivitis Trachomatosa.

Synonym.—Ophthalmia Ægyptiaca.

This is exceedingly common in China, where 70 per cent. of the children in Hong Kong are said to be infected. It is also common in many other parts of the tropics, especially in India, Japan, and South America; but it is also prevalent in North Africa, especially in Egypt, in South Africa, in Southern Europe, and in Porto Rico. It is an infectious disease, believed by many authorities to be due to a chlamydozoon described by Halberstaedter and Prowazek. A fungus—*e.g.*, the *Microsporon trachomatosum*—has been described by Noiszewski, which is only distinguishable from *Malassezia furfur* by the smallness of its conidia. With regard to the chlamydozoon, it occurs in the cytoplasm of epithelial cells as fine granules, which increase in size, and separate so as to enclose a cavity at first free from granules, in which subsequently very minute granules appear.

Probable Ætiology.—There is a growing suspicion that trachoma is essentially a disease arising from chronic urethritis in men and chronic vaginitis in women, because cell-inclusions of a chlamydozoan nature have been found by several observers in the discharge from the urethra of men suffering from gonorrhœa, while Castellani has found similar inclusions in a man in Colombo who is believed never to have had gonorrhœa. Further, similar bodies have been found in the vaginal discharge of women whose children have suffered from the form of ophthalmia neonatorum in which no gonococci or streptococci can be found. Further, Castellani has found similar bodies in a case which may have been one of the rare acute inflammations of a pure trachoma without granule formation, and which may have been induced in the acute form because the woman in question was run down owing to the acute attack of malaria from which she suffered. This case emphasizes the fact that these bodies should be looked for in those so-called attacks of malarial conjunctivitis which are found associated with attacks of malarial fever. Finally, Lander has produced a chronic conjunctivitis by transferring the secretion of vagina and urethra mentioned above to monkeys. This experimental conjunctivitis was associated with the formation of granules clinically and anatomically resembling the conjunctivitis trachomatosa of man.

Method of Infection.—The infection is carried by the hands, towels, handkerchiefs, etc., from the sick to the healthy. There is no evidence of aerial transmission. The agency of flies in the transmission of eye disease has long been known—for example, Budd, in 1862, considered it proven that they transmitted ophthal-

[illegible] trachoma [illegible]

[illegible] are supported by a [illegible] This is a layer of [illegible] and bloodvessels. [illegible]

[illegible] acute attack may begin [illegible] great swe[illegible] purulent [illegible] the typical no[illegible] at first be absent. [illegible] with [illegible] the [illegible] is dim[illegible] the disease [illegible] with photophobia, pain, and watering of the eye; the lids stick together in the morning, and there is diminution of visual acuity. The eye is not fully opened, partly because of the photophobia, and partly because the upper lid is swollen and heavy. On everting the lids, the tarsal and transitional conjunctivæ are found to be swollen and red, and either velvety in appearance, or with distinct nodules which are most marked on the upper lid. These nodules or granules are of considerable importance in the differentiation between trachoma and follicular conjunctivitis, and it is to be specially noted that those of trachoma are larger in the superior fornix than in the inferior fornix. It is therefore important to examine the superior retrotarsal fold very carefully. On the tarsal conjunctiva the granules are not so prominent, and are therefore less easily seen. A trachoma granule is typically a grey, roundish, translucent granule, comparable to a grain of boiled sago in appearance. Harston's sign is a linear groove running almost horizontally [illegible] external canthus. The hypertrophy of the co[illegible] increases until some indefinite [illegible] reached, when it ceases and [illegible]cicatrization [illegible]; but if the [illegible]trophy is excessive, it may last for [illegible] develop slowly but surely.

The cicatrization shows itself at [illegible] whitish striæ on [illegible] conjunctivæ, which, becoming more numerous, unite [illegible] network; the meshes of which are occupied by the [illegible] conjunctiva, which gradually diminish as cicatrization proceeds; until the conjunctiva becomes pale in colour. In some cases this cicatrization is very slight and hardly noticeable, while in others it may produce serious complications.

The loss of vision is due to pannus and ulceration of the cornea, the former being a deposit of vesicular gelatinous tissue on the cornea, which becomes uneven and raised in fine projections; while the latter may occur with the pannus or separately.

The sequelæ of trachoma may be classified into:—

(*a*) Corneal ulceration and pannus, leading to *opacities*.

(*b*) Cicatrization, leading to (1) *Trichiasis*, in which the cilia are turned backwards and may touch the cornea; (2) *Entropion*, in which the border of the lid is turned backward; (3) *Ectropion*, in which the lid is everted; (4) *Symblepharon posterius*, in which the fornix is diminished in depth, and the lid is tightly fastened to the eyeball.

[illegible] Conjunctival xerosis, in which the conjunctiva, owing to atrophy, loses its secreting powers, and becomes dry and shrunken.

Treatment.—The acute cases are to be treated with silver preparations, as described for conjunctivitis.

When the follicles are well developed it is usual to express them by means of a flat Grady's forceps or by the roller forceps of Knapp, but this must be performed under an anæsthetic. The ruptured surface is then painted with a solution of perchloride of mercury and after one or two days' interval the daily application of solid copper sulphate is commenced, which may be applied pure or as a Canestou's crayon, which consists of sulphate of copper, 1·0 gramme; orthoform, 0·5 gramme; holocain hydrochloride, 0·5 gramme; gum tragacanth, 0·1 gramme; and water as may be required. The above are the quantities required to make a pencil 5 centimetres in length.

Harston strongly recommends treatment by carbon dioxide snow, which has produced excellent results in many hands, and as it has only to be applied once a fortnight is useful for general out-patient work. It is, however, very painful, and this pain is not prevented by cocaine, which therefore need not be used.

Hegner and Baumm have advised treatment by quartz light, while other methods are Galezowski's excision of the retrotarsal folds, Kuhnt's removal of the tarsus, while treatment by Merk's extract of abrin, Mayon's X-ray method, and Treacher Collins's radium treatment may be mentioned.

Epitheliosis Desquamativa.

Synonym.—Samoan eye disease.

Under the name Leber and von Prowazek have described a form of conjunctivitis which they met with in Samoa, where they examined and treated seventy-nine fresh infections. They consider the causation to be a chlamydozoon—*Lyozoon atrophicans* Leber and von Prowazek, [illegible] which is found in the milky secretion in the form of trachoma-like bodies, which, when coloured by Giemsa, show blue poles and a central lacuna. These bodies are either intracellular or extracellular. The intracellular bodies form what is commonly called a 'cell inclusion of small granules,' which take on a violet-red colour when stained by Giemsa, and are called the 'elementary bodies' and lie in the centre, while the larger initial bodies lie at the periphery. These parasites cause a hypertrophy of the cell nucleus, which eventually leads to an atrophy of the cell. The disease was conveyed to guinea-pigs.

The symptoms begin with pain, photophobia, and livid coloration of the upper and lower lids, while a milky secretion is poured out, which is composed at first of epithelial cells only, but may become purulent. Granules similar to those of trachoma do not develop, but atrophy of the conjunctiva ensues. The treatment recommended is pyoktanin in the proportion of 1 in 1 000 to 1 in 10[illegible]

Conjunctivitis phlyctenulosa.

This is not very frequently met with in the tropics. It is usually found in scrofulous individuals, and is characterized by the presence of small vesicles, each surrounded by a reddened zone.

Conjunctivitis Vernalis.

Synonyms.—Conjunctivitis Æstivalis, Spring catarrh.

Definition.—A chronic form of conjunctivitis, resembling conjunctivitis trachomatosa, but occurring in the spring and summer, and disappearing in the autumn and winter.

Remarks.—Spring catarrh is apparently not so rare in the tropics as in the Temperate Zone, as Nell informs us that he has met with thirty-eight cases in Ceylon.

Ætiology.—The cause is unknown, but some authorities consider that it is due to sunlight, while others hold that it is an infection from the skin.

Symptomatology.—On the approach of the warm weather in spring the eyes begin to itch and water. The conjunctiva becomes red, and photophobia is experienced. On examination the conjunctiva is seen to be covered with broad, flattened papillæ, over which a bluish-white film is seen. The affection lasts during the summer, wanes in the autumn, and disappears in the winter, only to recur in the spring.

Diagnosis.—The diagnosis must be made by the history and by the bluish-white sheen over the papillæ. It resembles trachoma, but the granules are broader, harder, and paler, while the history is distinctive.

Treatment.—Protective glasses must be worn, and zinc sul[illegible] lotion (½ per cent.) dropped into the eyes. If the itching is [illegible] severe, it is recommended to apply a few drops of a very weak solution of acidium aceticum dilutum. Iron tonics are also advised.

Epithelial Xerosis of the Eye.

This condition has been recorded several times from the tropics. Archibald has recently described very carefully three cases in the Sudan. The xerotic patches were situated on the conjunctiva external and close to the corneal margin of both eyes (Fig. 793). The patches were greyish-white in colour and of a soft viscid consistency; the superficial layers were readily removed with a platinum loop; the deeper layers, however, were more adherent to the subjacent epithelium, which showed a brownish pigmentation. The bloodvessels in the vicinity of the patches were congested. There was no evidence of trachoma or inflammation of the eyelids. The whole bulbar conjunctiva was moist, and could be readily moved into folds by gentle pressure with a platinum loop. There was an absence of pain or discomfort associated with the lesions, which appear to have had a duration of several years. Vision was not impaired, and there was no evidence of night-blindness.

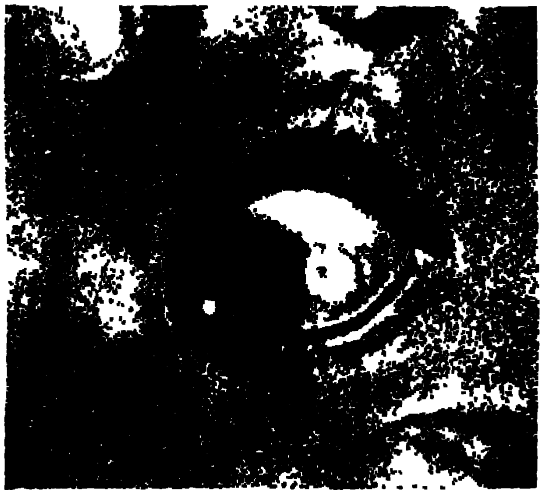

FIG. 793.—EPITHELIAL XEROSIS OF THE EYE.

(From a photograph by Archibald.)

Ætiology.—Scrapings from the xerotic patches showed the presence of a Gram-positive diphtheroid organism in large numbers which was obtained in pure culture from the cases. This organism (*B. xerosis* Neisser) differed from the true Klebs-Loeffler bacillus in its cultural reactions, and, moreover, was non-pathogenic to guinea-pigs.

Treatment.—Attention to general health and the administration of cod-liver oil internally is indicated. The affected eyes should be protected from light and daily douched with weak boric solution, followed by the application of a few drops of a 1 per cent. solution of protargol.

Lachrymal Sac.

The lachrymal sac, being in direct connection with the nose, is very liable to harbour micro-organisms and fungi, and is therefore a possible source of infection for the conjunctiva and cornea.

Cornea.

Phlyctenular keratitis is common as a sequela to conjunctivitis phlyctenulosa, both of which act as common predisposing causes to pterygium, which, according to Harston, is extremely common among the Chinese.

Ulcus Serpens Corneæ.

This appears as a greyish-white or yellowish slightly depressed disc near the centre of the cornea, the rest of which is clouded. It is associated with iritis and turbidity of the vitreous, hypopyon, and more or less œdema of the lids, with conjunctivitis, cyclitis, photophobia, and pain, except in the so-called 'torpid' cases. The ulcers increase in depth and extent; perforation occurs into the anterior chamber, which contains *sterile* pus, which now escapes, and at the same time prolapse of the iris may occur. The inflammation now comes to an end, but panophthalmia may occur. The most common cause in the tropics is the pneumococcus, which may often be found in the nose of the same patient. The prognosis is serious.

Treatment.—The cauterization of the ulcer and apparently clear border with the actual cautery is an imperative immediate treatment, followed by application of atropine, iodoform, or orthoform powder, or 1 per cent. xeroform ointment, or callaryol ointment 3 per cent., and moist and warm compresses. Harston recommends douching with hydrogen peroxide as an adjuvant to the usual treatment, while 1 in 40 formalin solution is also recommended, but must be preceded by cocaine, as it is very painful. Perforated ulcers are best treated by iridectomy on each side of the synechia. Harston operates on the worst eye of the two when both are involved, as operative interference is apt to set up a severe irido-cyclitis in the poorly-nourished Chinese coolie, with eventual loss of sight in the eye. The nasal infection must also be treated by antiseptic douches.

Iris.

Diseases of the iris are as common in the tropics as in the Temperate Zone. Those which are specially connected with tropical disease will be mentioned below, but it is well to remember that in native races the stroma of the iris is laden with pigment, which probably accounts for its slow reaction to mydriatics.

Cataract.

This disease is said to be on the wane in the Temperate Zone, but is very rife in the tropics. In fact, its home is said to be in India, the ophthalmic surgeons of which have a great reputation. Colonel Smith, of Jullundur, has perfected a complicated but most successful operation for intracapsular extraction.

Sometimes in the tropics it is impossible to wait until the cataract ripens, and operations may have to be performed on immature cataracts. To meet this difficulty, Nell has devised a modification of the usual procedure, which consists in performing a zonulotomy by means of a special hook introduced through the corneal wound made for a cataract extraction and under the iris. After this preliminary proceeding he completes the operation by intracapsular extraction of the lens.

Glaucoma.

Acute glaucoma is rare in the tropics, while chronic glaucoma is common; but the signs, symptoms, and treatment are the same as in the Temperate Zone. The Elliot operation of trephining, with or without subsequent iridectomy, is recommended.

Fundus Oculi.

The colour of the fundus oculi depends upon the amount of retinal pigment present and to a less degree upon the amount of the choroidal pigment visible. It therefore shows variations from the European standard in dark and yellow races. In these races the amount of retinal pigment is increased, and may completely conceal that of the choroid, and so produce a uniform yellowish colour, as seen in the Chinese; or a dark reddish, or even an almost greyish-red colour, as seen in the various negro races.

On the other hand, when the retinal and choroidal pigments are diminished, as in albinism, then the white sclerotic shows through, and the fundus becomes of a lighter red colour than normal.

Sunlight.

The effect of sunlight on the eyes has been studied by Sisson, who considers that there is ample proof that light injures the eye, and that it may possibly be the cause of some diseases of the eye, the ætiology of which is but little understood. Schmidt considers that nyctalopia and hemeralopia may be caused by excessive light. The use of protective xanthophylline glasses is recommended.

B. EYE COMPLICATIONS OF TROPICAL DISEASES

Malaria.

Malaria is held to be responsible for conjunctivitis, serpiginous corneal ulcers, malarial iritis, and retino-choroiditis, as well as amaurosis.

Until a few years ago, the majority of the fevers of the tropics, including enteric fever, were classified as malaria, and any local affection of an unknown nature was also classified in the same manner. The case of conjunctivitis in which one of us found cell inclusions would a few years ago have been named malarial. We are therefore of the opinion that the existence of malarial conjunctivitis has not been proved.

Keratitis Dendritica.—This keratitis is that variety of herpes corneæ febrilis (sometimes called 'herpes corneæ zoster') which gives rise to those ulcers (formed from the ruptured herpetic vesicles) which extend in certain directions only as grey forked striæ with lateral branches, which break down, thus forming a branched ulcer with grey margins. The ulcer then becomes clean, and heals after one to three months, leaving a branched opacity of the cornea. This is one form of corneal ulcer to which the name 'serpiginous' is given, but it equally applies to ulcus rodens and keratitis marginalis superficialis, which, as far as we know, have never been stated to be of malarial origin. Keratitis dendritica was first described by Kipp in America, who stated that nine out of every ten cases were malarial.

The treatment must be that described for malaria, as well as constitutional, and it is usual to recommend that the ulcers be treated by a piece of blue stone whittled to a fine point, and carried carefully along the furrow made by the ulcer, or by careful cauterization by the actual cautery.

Keratitis Profunda.—*Synonyms.*—Keratitis parenchymatosa circumscripta, or Central parenchymatous infiltration of the cornea.

This is said by Arlt, among other causes, to be brought about by chronic malarial cachexia. It begins with a grey opacity, situate in the middle and deep layers of the centre of the cornea, and over which the corneal surface is grey and punctate. Seen with a magnifying-glass, the opacity resolves into dots and maculæ, or grey interlacing striæ. After remaining four to eight weeks, it slowly abates without ulceration. The iris may be hyperæmic, and there may or may not be symptoms of inflammation of the cornea, which may recover completely, or with some opacity. The treatment would be the same as for malaria, but it must be definitely stated that the cause is unknown.

Iritis.—Secondary iritis is said to be very rarely caused by malaria, but even this is open to doubt.

Vitreous Opacities. Hæmorrhage and serous effusion have been described.

Amaurosis.—Malarial amaurosis is described in Chapter XI., p. 1181, under the term 'Amaurotic Pernicious Fever,' but may occur, not merely during an attack of malaria, but as a sequel, and as such was described by Jacobi in 1868, and later by Chiarini. It is due to atrophy of the optic nerve.

Retino-choroiditis.—This was first described by Poncet as occurring in chronic malaria, but it is also found in the acute and in the chronic forms. In the acute affection the vessels of the retina are filled with corpuscles, many of which contain malarial parasites. In the choroid the larger vessels contain pigmented leucocytes, many of which contain red corpuscles with malarial parasites. The retina is hazy, the papilla is obscured, and there are retinal hæmorrhages.

The amblyopia may be temporary or permanent. In the chronic condition there is atrophy of the capillaries of the choroid. The macular region shows small whitish dots, in the centre of which retinal pigment can be seen. These changes extend to the periphery. Pathologically, they are colloid masses in Bruch's membrane.

Suppurative Uveitis.—Suppurative choroiditis, leading to destruction of the eye, has only been described by Pennoff.

Accommodation Paralysis.—Accommodation paralysis and spasm of the muscles of accommodation have been described by Bull and Slitting.

Trypanosomiasis.

Choroiditis, cyclitis, iritis, and optic neuritis of a temporary nature are reported as occurring in sleeping sickness, as well as engorgement of the iris and loss of the light reflex, with wide dilatation of the pupil.

Relapsing Fevers.

Irido-cyclitis, or iritis, is a frequent complication of the relapsing fevers, and though it ultimately ends in a cure, it is usually protracted.

Plague.

Conjunctivitis is common in plague as an initial symptom; later a plastic uveitis with hypopyon and keratitis may occur, and call for special treatment by administration of mercury, local installation of atropine, and blood extraction by leeches.

Leprosy.

In tubercular leprosy yellowish translucent nodules of a nonvascular nature may develop in the conjunctiva near the cornea. Iritis and cyclitis, with or without the formation of nodules, may occur. According to Wood, more than half the anæsthetic lepers of South Africa suffer from eye complications—*e.g.*, paralysis of the orbicularis palpebrarum, ectropion of the lower lids, epiphora, corneal opacity, and ulcerations. Of the tubercular lepers he says 90 per cent. are affected in the first ten years of the disease, and if they survive they become blind. They suffer from invasion of the lids, conjunctivæ, sclerotic, cornea, and iris by the disease, and in addition may suffer from paralysis of the ciliary muscle and irido-cyclitis. Heymans finds lagophthalmos to be common. In 1915 Stanziale published experiments on the eye of rabbits, injecting leprotic material into the cornea.

Cholera.

Focal necrosis in the cornea and conjunctiva has been reported in convalescence from cholera, while a form of cataract depending upon the abstraction of water takes place at times in the last stage of the disease.

Dysentery.

Conjunctivitis, keratitis, iritis, and irido-cyclitis are reported in dysentery, both amœbic and bacterial.

Hikan.

Under this term a curious disease is described by various observers, among whom Jeanselme and Risb. The main symptoms appear to be hemeralopia, xerophthalmia, dryness of the skin, and diarrhœa occurring in young children in Russia, Brazil, and Japan. The causation is unknown, but treatment by cod-liver oil is said to be very efficacious.

Quinine.

Amaurosis associated with complete deafness may set in after doses of less than 1 gramme of quinine, though more usually after a dose of 3 grammes and upwards. The amaurosis gradually disappears, leaving an amblyopia with a much contracted field of vision. This result is due to a destruction of the ganglion cells of the retina by the quinine, after which a degeneration of the optic nerve sets in.

The symptoms are a blanching of the retina and disc, due to spasm of the vessels, and loss of the pupillary light reflex, the pupils being widely dilated. It should be differentiated from the malarial amaurosis. In the former the pupils are usually widely dilated, and do not react to light, while in the latter they do react to light.

The deleterious effect of therapeutic doses of quinine has often been exaggerated. Doses of 10 to 15 grains may usually be given three times daily for long periods of time without any damage to the eyes. Jamieson and Lindsay have noted that even when the visual field is found to be contracted, the prognosis is good and ultimate expansion of the field may be expected.

Atoxyl.

Sudden amaurosis may be caused by atoxyl.

Animal Parasites.

Ocular Paragonimiasis. Cysts containing *Paragonimus westermanni* have been reported as occurring on the eyelids and orbit, and so hindering the movements of the eyeball and obstructing the vision.

Ocular Filariasis. –*Loa loa* has been noticed in the ocular and palpebral conjunctiva (*vide* pp. 645 and 1972).

In addition to paragonimiasis and filariasis, the following parasites occur in the eye or its adnexa: *Agamodistomum ophthalmobium* Diesing, 1850; *Monostomum lentis* von Nordmann, 1832 (both of which may be stages of *Dicrocœlium lanceatum* Stiles and Hassell, 1896); *Sparganum mansoni* Cobbold, 1883: *Agamofilaria oculi humani* von Nordmann, 1832; *Agamofilaria palpebralis* Pace, 1867, *nec* Wilson, 1844; *Dermanyssus gallinæ* De Geer, 1778 (which may be seen as a dark spot embedded in the cornea): *Demodex folliculorum* Simon, 1842, which is found in the Meibomian glands, and may cause a blepharitis. The larvæ of *Dermatobia cyaniventris* Macquart, 1843, has been found by Malgahães under the palpebral conjunctiva and in the lachrymal sacs in Brazil. A larva of *Sarcophaga magnifica* Schiner, 1862, has been found in the anterior chamber of the eye, and a larva of a species of *Necrobia* in a sclerotic tumour; but for a fuller account of ocular myiasis see Chapter LXVII.

Cysticercus cellulosæ has been found in the choroid, which it may leave, and, passing under the retina, may cause detachment; later it may perforate the retina and enter the vitreous, or it may enter the retina or the ciliary region, and so pass directly into the vitreous, where it appears as a bluish-white bladder, with or without a protruded head. The eye may be destroyed by irido-cyclitis. Echinococcal invasion is very rare.

Ophthalmomycoses.

Definition.—Diseases of the eye and its adnexa caused by various fungi.

History.—The word mycosis was introduced by Virchow to signify a disease caused by fungi, being first used for aspergillosis of the lungs. The interest in fungi as causes of disease was first aroused by Gruby, who in 1847 appears to have noticed fungal structures in lachrymal concretions, although he did not publish his observations. Helmbrecht and Robin were the first to actually assign a disease of the eyes to the action of fungi. They observed a fungus, which they called *Leptomitus*, in a case of conjunctival inflammation associated with epiphora. In 1854 Graefe described the fungal nature of lachrymal concretions, and in 1874 Cohn showed that these fungi belonged to the genus *Streptothrix* (*Nocardia*). In 1879 Leber discovered the first case of keratomycosis caused by *Aspergillus fumigatus*. From this date until comparatively recently fungi went out of fashion, being replaced by interest in bacteria, but with the revival of interest created largely by Sabouraud eye diseases were again investigated, and in 1906 De Beurmann and Gougerot gave an account of ocular sporotrichosis, and in 1907 Danlos and Blanc of palpebral sporotrichosis, and Morax described a form of keratomycosis caused by *Glenospora graphii*, and Lagrange and Landrieu a form of conjunctivitis due to *Nocardia dassonvillei*, while in 1912 Landrieu reviewed the whole subject of ocular mycoses in a singularly able manner.

Fungi.—The following fungi have been recognized in various diseases of the eye:—

A. Order Ascomycetes.

- I. Suborder Gymnoasceæ.
  - (a) Family Saccharomycetes.
    - (1) Genus Cryptococcus.
      - *C. dermatitidis* Gilchrist and Stokes, 1898.
    - (2) Genus Saccharomyces several species.
  - (b) Family Gymnoasceæ.
    - (1) Genus Microsporon
      - *M. lanosum* Sabouraud, 1907
    - (2) Genus Trichophyton
      - *T. tonsurans* Malmsten, 1845, and other species of the same genus.
    - (3) Genus Achorion
      - *A. schoenleinii* Lebert, 1845
- II. Suborder Carpoasceæ.
  - Family Perisporiaceæ.
    - Genus Aspergillus.
      - *A. fumigatus* Fresenius, 1863

B. Order Hyphomycetes.

- (1) Genus Nocardia.
  - *N. bovis* Harz, 1877.
  - *N. israeli* Kruse, 1896.
  - *N. foersteri* Cohn, 1874.
  - *N. dassonvillei* Brocq Rousseau, 1907.
- (2) Genus Monilia.
  - *M. albicans* Robin, 1853, and other species of the same genus.
- (3) Genus Glenospora.
  - *G. graphii* Siebenmann, 1889.
- (4) Genus Sporotrichum.
  - *S. beurmanni* Matruchot and Ramond, 1905.

Pathogenicity.—The ocular diseases caused by the above fungi may be grouped as follows:—

Fungus.	*Disease.*
Cryptococcus dermatitis and various species of the genus Saccharomyces	Ocular Blastomycosis.
Microsporon lanosum Trichophyton tonsurans Achorion schoenleini	Ocular Tineæ.
Aspergillus fumigatus	Ocular Aspergillosis.
Nocardia bovis Nocardia israeli Cohnistreptothrix foersteri Nocardia dassonvillei	Ocular Nocardiases.
Monilia albicans and other species of the same genus	Ocular Moniliasis.
Glenospora graphii	Ocular Glenosporosis.
Sporotrichum beurmanni	Ocular Sporotrichosis.

Ocular Blastomycosis.

Ocular blastomycosis is seen in the form of **Palpebral Blastomycosis,** which begins as papules which increase in size and give rise to pustules covered with crusts, and, later, to a warty condition, which may become red, moist, and granular. In other cases a subdermal nodule is formed, which may ulcerate. The causal agent is *Cryptococcus dermatitidis* Gilchrist and Stokes, 1898. The diagnosis is made by culture of the fungus.

Ocular Tineæ.

Tinea palpebrarum may be caused by *Microsporon lanosum* Sabouraud, 1907, by various species of *Trichophyton*, of which that most commonly found is *T. tonsurans* Malmsten, 1845. These fungi may or may not attack the cilia. If they do so, then small yellow crusts will be seen surrounding a cilium. On the removal of these crusts, small pustules will be seen. When they do not attack the cilia, they give rise to herpetiform lesions on the eyelids proper. The diagnosis is made by culture of the fungus. The treatment consists in epilation, warm compresses, and tincture of iodine.

Achorion schoenleini Lebert, 1845, the fungus of favus, may also attack the eyelids.

Ocular Aspergillosis.

About two days after a slight traumatism to the eye, irritation is felt, followed by pains, and the formation of an abscess, and later an ulcer. The diagnosis can only be made by the microscopical or cultural examination of scrapings from the ulcer or of the pus from the abscess. The treatment consists in curetting and applying a lotion of silver nitrate and atropine drops.

Ocular Nocardiases.

Actinomycotic conjunctivitis was first described by Demichéri in 1899, actinomycotic corneal ulcers by de Bernardinis and de Donna in 1905, and miliary actinomycotic metastases in the choroid by Müller in 1903. Conjunctivitis due to *N. dassonvillei* has been recorded by Liégard and Landrieu in 1911.

Ever since the days of Céson in 1670 lachrymal concretions have from time to time been recorded, but their parasitic nature was not recognized until Gruby in 1848 found that they were really fungal in origin. This fungus is known to be *Cohnistreptothrix foersteri*. The concretions occur in the form of minute grains in the lachrymal sac, from which they can easily be removed.

Ocular Moniliasis.

Monilia albicans Robin, 1853, one of the organisms of 'thrush,' may very rarely attack the conjunctiva, as first described by Pichler in 1895. Cases due to *Monilia tropicalis* Castellani and other species have been seen by us in Ceylon.

Ocular Glenosporosis.

So far, only one case in the cornea is recorded. It was found in 1910 by Morax.

Ocular Sporotrichosis.

Sporotrichal infection of the eyelids, conjunctiva, lachrymal sac, and iris have been recorded, but are as yet rare. The first case was found in 1905 by Danlos and Blanc, the second case in 1908, the third in 1909. Four cases were recorded in 1910, and three in 1911, and several in 1912.

DISEASES OF THE EAR.

The diseases of the ear in the tropics require more attention than has hitherto been bestowed upon them. The majority are believed to resemble those found in the Temperate Zone. A few remarks will be offered with regard to the diseases of the auricle, of the external auditory meatus, and with regard to ear complications in tropical diseases.

The Auricle.

Deformities of the lobule are common among Indian girls and women, who drag the lobule into a long, pendulous loop by means of heavy golden ornaments, or, failing these, by pieces of other metals or even wood. A similar condition is reported by Castellani, Bland-Sutton, and others, as occurring among the Masai and the Kikuyu people of East Africa.

Nepaul Tumour.--In 1833, Campbell, and in 1835, Bramley, drew attention to a peculiar disease of the skin of the auricle which was endemic in the village of Nilkantha, situate in one of the Nepaul valleys, at the foot of the Sheopuri Hills. The disease begins as a small firm swelling of the skin on the external aspect of the auricle, which is elastic to the touch, and which increases until it reaches the size of a pigeon's egg in four to eight weeks. It is adherent to the subcutaneous tissues, but is slightly movable. If it grows rapidly, the superjacent skin becomes bluish, and a painful feeling of tension is produced. If the swelling is punctured, a thick whitish fluid exudes. It grows until it reaches the size of an orange or of a child's head, and it may attain such a size that it reaches to the patient's shoulder. After a time its contents soften and become absorbed, while the sac of the tumour shrinks, leaving the ear much thickened and shapeless. Usually both ears are affected, and sometimes a succession of tumours, one after the other, may take place. The causation is unknown. It is more common in women than in men. Campbell thinks that it occurs associated with goitre, which would suggest a parasitic causation, but Bramley is opposed to this view.

It is curious that there is so little literature on this subject, and that neither Scheube nor ourselves are acquainted with any further papers describing this disease.

Lipoma.—Lipoma of the lobule of the ear, often on both ears, is reported in Loango. This tumour may reach the size of a walnut or a child's head, and is thought to be due to the fact that the negroes bore their ears with thorns or with pointed strips of palm-leaves, which are retained in the lobe of the ear for some time.

Fibromata.—We have often met with soft small fibromata attached to the lobules of the ears of the negroes on the Gold Coast, which can readily be removed. Perhaps the lipomata of Loango are really soft fibromata.

Keloid.—Keloid is met with on the auricle in West African natives, arising after insignificant wounds, such as ear-piercing, etc., and may form large tumours.

External Auditory Meatus.

Foreign Bodies are commonly met with in the tropics, and may consist of animate objects, such as beetles, flies, etc.; or inanimate objects, such as pieces of wood, etc. Usually their presence can easily be determined by inspection, which should always be carried out before any treatment is resorted to. The first treatment should be to attempt to wash the body out of the meatus by means of hot boracic lotion and an ear syringe, unless the body be a pea, bean, or grain of maize, because these would become swollen with the water. Under these circumstances, it is better to instil some glycerine mixed with a little rectified spirit and solution of cocaine, which causes them to contract, when a camel's-hair brush dipped in thick collodion may be carefully applied to the object. After waiting a little time for the collodion to set, traction can be made and the object removed. Failing these, attempts must be made to remove the body by Guye's fenestrated forceps, Politzer's gouge forceps, Tröltsch's aural hook, an aural curette, or, in the case of impacted steel bodies, the electro-magnet. If there is much swelling of the mucous membrane of the passage, it may be necessary to apply a solution of cocaine and adrenaline, after which extraction may be attempted. It is often advisable to administer an anæsthetic if a body is impacted in a child's ear. If all attempts fail, an operation is necessary, which is generally performed by detaching the auricle from behind and exposing the bone wall of the external auditory meatus, a portion of which is removed if necessary.

Animal Parasites.—Apart from foreign bodies, the following animals have been found parasitic in the external auditory meatus: *Cheyletidæ : C. heyletus, C. eruditus* Schrank, 1781. *Tyroglyphidæ : Rhizoglyphus parasiticus* Dalgetty, 1901. *Demodicidæ : Demodex folliculorum* Simon, 1842. Larvæ belonging to the Anthomyidæ, to *Sarcophaga carnaria* Linnæus, 1758, to *Wohlfartia magnifica* Schiner, 1862, and to *Chrysomyia macellaria* Fabricius, 1794.

Otomycosis.—Otitis externa parasitica, or otomycosis, is fairly common in the tropics, and is due to a number of fungi, among which may be mentioned: *Mucor pusillus* Lindt, 1886; *Lichtheimia corymbifera* Cohn. 1884; *Lichtheimia ramosa* Lindt, 1886 (these cause otomucormycosis); *Saccharomyces ellipsoides* Rhees, 1870; *Monilia rhoi* Castellani, 1909; *Aspergillus fumigatus* Fresenius, 1775; *Aspergillus niger* von Tieghem, 1867; *Aspergillus flavus* De Bary, 1870; *Aspergillus malignus* Lindt, 1889; *Aspergilius repens* De Bary, 1870 (these cause otomycosis aspergillina).

These fungi cause mild inflammations of the external auditory meatus, and are found not merely in natives, but also in Europeans

If they grow superficially, they cause no symptoms; but if they penetrate into the mucous membrane, they give rise to itching, and sometimes to pain. If they grow into the cerumen, they may give rise to blocking of the passage, and cause tinnitus aurium and deafness.

On inspecting the ear, it will be seen that the wall of the auditory meatus is covered with a white or black macerated mucosa. The diagnosis can be made by microscopical examination, and, if necessary, by cultivation. The treatment is to syringe with a watery solution of peroxide of hydrogen, or peroxide solution (2 parts) and alcohol (1 part) once or twice a day, followed by the insufflation of boracic powder, or, if there is eczema, some boracic ointment. Damond recommends injecting a few drops of a dilute solution of sodium iodide, followed by the injection of the same amount of 12 volumes hydrogen peroxide.

Hypersecretion.—Excessive secretion of the products of the ceruminous and sebaceous glands of the external auditory meatus is common in the tropics, and is probably induced by some hyperæmia, perhaps in part du[illegible]o irritating [illegible] and partly to the hot, damp air. As a rule both ears are affe[illegible] giving rise to a sensation of fulness and heavin[illegible] in head [illegible] ion in hearing, and tinnitus aurium, and more rarely to autophony while pain is rare, though neuralgia may occur, and reflex coughing. The diagnosis is easily made by seeing the brownish-red or black mass filling up the meatus.

If the plug is soft, it can easily be removed by warm syringing; if hard, it requires to be softened by a warm solution of bicarbonate of soda (20 grains to 1 ounce of water) or glycerine of borax, and then to be removed by syringing. If deafness persists after the cerumen has been removed, it is necessary to inflate the middle ear by a Politzer's bag, which must be used with care.

Otitis Externa Circumscripta. Boils due to the entrance of pyogenic germs into a sebaceous gland or hair-follicle are not rare. They usually cause much pain, which is aggravated by moving the jaw or touching the auricle, and may cause toothache, salivation, and vertigo.

The treatment should be to relieve pain by cocaine, and the meatus should be lightly packed with gauze soaked in weak carbolic lotion. Later an incision may be made into the boil with a Dundas Grant's furuncle knife, and the meatus dressed with carbolized, glycerine on gauze. To relieve the irritable condition of the meatus, which often persists after the boil has been relieved; a little cocaine or boracic ointment combined with lanoline may be applied, and a general tonic prescribed.

Otitis Externa Ossificans.—Müller has described a diffuse inflammation of the mucosa of the external auditory meatus in the tropics which often invades the periosteum and leads to ossification, and may cause exostosis.

Deaf and Dumb.

The number of deaf and dumb people is relatively high in certain parts of the tropics—*e.g.*, in Ceylon there are 9 deaf and dumb males and 7 females out of 10,000 persons of each sex. In India there are 6 males and 4 females out of 10,000 persons of each sex. There is a deaf and dumb school in Ceylon.

Ménière's Disease.

This disease, which is characterized by severe tinnitus, and vertigo is often met with in the tropics. It occurs especially in planters, who are exposed to the midday sun. The patients frequently recover on their return to the Temperate Zone. Large doses of bromides are useful.

EAR COMPLICATIONS OF TROPICAL DISEASES.

Leprosy.

The lobules of the ear are especially liable to be attacked in tubercular leprosy, and are usually left long and thickened when the disease has abated.

Quinine.

The prolonged or considerable use of quinine may cause simple hyperæmia of the labyrinth, and may be associated with middle-ear congestion, as described by Kirchner. The symptoms are usually tinnitus aurium and deafness. It is bilateral, and comes on gradually. The quinine should be stopped, and bromide of ammonium prescribed, and afterwards euquinine, associated with bromides, may be administered.

Arsenic.

A native treatment for ear disease in the Dutch East Indies is by the application of a powder, Warangangpulver, containing some 90 to 96 per cent. of arsenious acid. According to Benjamins, this may lead to destruction of the auricle and obliteration of the external auditory meatus, with sometimes necrosis of the bone, and even fatal hæmorrhage from the internal carotid artery.

Malaria.

Reports of suppurative otitis media being caused by malaria cannot be accepted as proven, but intermittent otalgia, intermittent attacks of deafness, and labyrinthine vertigo may be of malarial origin, especially if relieved by quinine.

DISEASES OF THE NOSE.

Disease of the nose is intimately connected with disease of the ear, and to a less degree with disease of the conjunctiva. The acute catarrhal rhinitis, or common cold, may be induced by prolonged exposure to the sun's rays, as well as to chills, and is in every case an infection, though it is difficult to determine the actual micro-organism causing the disease. The commonest organism is the *Micrococcus catarrhalis*. The tropical affections, are, however, described in Chapter LXXXI., p. 1875.

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DIVISION III.: SKIN DISEASES.

Pyogenic Infections.
Dermatomycoses.
Mycetoma and Paramycetoma.
Dermatitis Venenata.
Ulcerations.
Dermatozoiases.
Dysidroses and Dystrophies.
Miscellaneous Diseases.
Cosmopolitan Diseases.

CHAPTER XCI

PYOGENIC DERMAL INFECTIONS

Preliminary remarks—Pyogenic infections—The pyoses—The pyogenic folliculites—The pyogenic dermatites—References.

PRELIMINARY REMARKS.

In this chapter we begin a brief review of the more important skin diseases of the tropics. As this Manual is not a work on skin diseases, but is intended for the tropical practitioner, we have arranged these disorders from the standpoint of the practical physician, and have avoided a scientific classification. The chapters include pyogenic infections; fungal diseases, with the mycetomas considered separately; the dermatites due to plants; ulcers; the dermatites caused by animals; disorders of sweating and of nutrition; and miscellaneous and cosmopolitan diseases.

PYOGENIC INFECTIONS.

The skin diseases which we gather together under this heading are all caused by the pyogenic cocci, and may be distinguished as follows:—

A. Skin between the primary lesions not inflamed:—
  I. Non follicular—*The Pyoses.*
  II. Follicular—*The Folliculites.*
B. Skin primarily inflamed—*The Pyogenic Dermatites.*

THE PYOSES.

Definition.—A pyosis is a non-follicular dermal infection characterized by the appearance, on apparently healthy skin, of vesicles or bullæ, the contents of which rapidly become purulent. It is not associated with general symptoms, except slight fever in the early stages at times, and is due to the action of pyogenic micrococci.

Remarks.—The type of this variety of dermal affections is '*Pyosis mansoni,*' named in honour of Sir Patrick Manson, G.C.M.G.

Varieties.—A number of 'pyoses' are known to exist in the tropics, and these may be differentiated from one another as follows:—

A. *Primary lesions usually small* :—
  I. Situate typically in axillary and crural regions, without crusty lesions—*Pyosis mansoni.*
  II. Situate on arms and legs, with thick crusty lesions—*Pyosis tropica.*
  III. Situate on palms; rare; no crusty lesions—*Pyosis palmaris.*
B. *Primary lesions usually large* :—
  I. Typically bullæ without bright yellow crusts—*Pyosis corletti.*
  II. Typically large vesicles forming circular bright yellow crusts—*Pyosis discoides.*

Pyosis Mansoni.

Synonym.—Pemphigus contagiosus (Manson).

Definition.—Pyosis mansoni is a pyosis with primary lesions, usually small, but mixed with bullæ and affecting the axillary and scroto-crural regions. It is very common in the damp regions of the tropics.

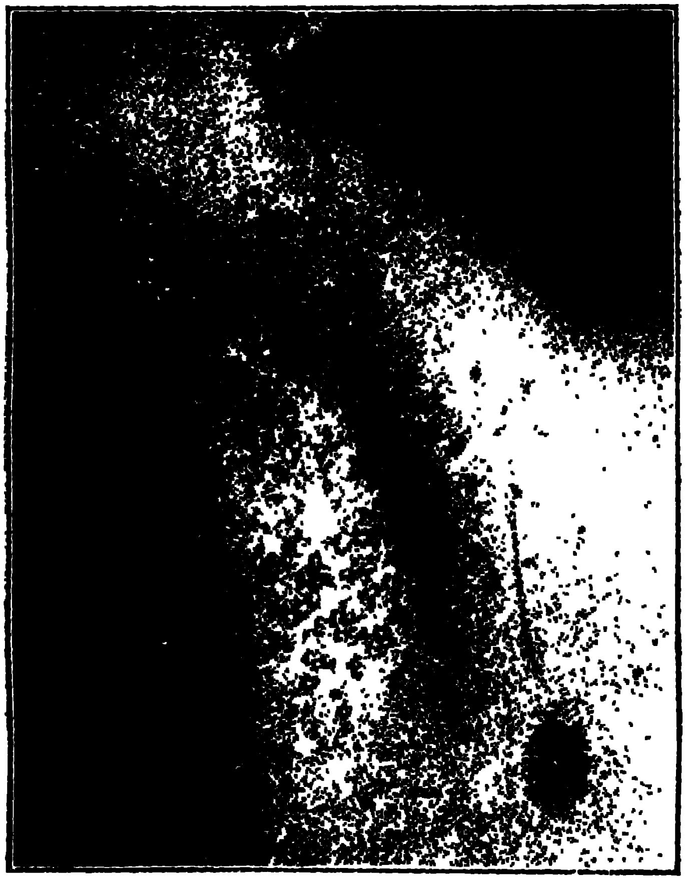

FIG. 794.—PYOSIS MANSONI.

Historical and Geographical.—This dermatosis was first described by Manson under the term pemphigus contagiosus. It is very common during the hot season in China, the Malay Peninsula, Ceylon, and Southern India, and probably in many other parts of the tropics. Castor has reported it from Burma. Very often epidemics occur among the crews of men-of-war stationed in the tropics, as observed by Clayton, or in offices, as observed by ourselves.

Ætiology.—Manson found a diplococcus; other observers have described Leishmania-like bodies; in Clayton's and our experience the examination of the contents of the vesicles shows the presence of cocci generally arranged in pairs, and having often a gonococcus-like shape. They are, however, Gram-positive, and in cultures present all the characters of the *Aurococcus aureus* and *albus*. The disease is probably spread by contact.

FIG. 794A.—PYOSIS MANSONI.
Same case as Fig. 794, but more magnified.

Symptomatology.—The affection has nothing to do with that group of diseases to which writers on dermatology apply the term 'pemphigus,' for it is much more closely related to impetigo, of which we consider it to be a variety. The eruption attacks generally the axilla, the inguinal and crural regions, from whence it often extends to the abdomen and back and limbs, rarely affecting the face. It is extremely contagious, and is generally more severe in individuals who perspire profusely and suffer from prickly heat. The eruption is made up of flattened, roundish vesicles, which quickly enlarge to the size of a small pea. Very large, flabby, pemphigoid bullae may occur, but not very frequently. The contents are at first transparent, but soon become turbid. The vesicles are often surrounded by a pinkish or reddish inflammatory halo. On being pricked, the vesicle collapses. The eruption does not usually affect the general health, but may be very persistent, and may be followed by crops of boils. As soon as the patient goes to the hills or to a cool climate it disappears spontaneously.

That the malady is merely a type of pyosis or impetigo due to the usual pyogenic cocci is shown by some cases presenting the typical bullae on the axillary regions, and soon after or though rarely at the same time boils on the arms and legs and impetiginoid lesions on the face.

Diagnosis. This is generally easy, the only difficulty being with chicken-pox. The absence of fever and the situation of the vesicles, which in pyosis mansoni usually appear in the crural or the axillary regions, however, should be sufficient to exclude this. The absence of crusty lesions differentiates the disease from the common type of impetigo contagiosa.

Prognosis. The eruption is very persistent, but does not affect the general health, except when complications such as boils develop.

Treatment. In severe cases treatment by an autogenous vaccine may be tried. Locally the affected regions should be disinfected regularly twice daily with a solution of perchloride of mercury (1 in 2,000), carbolic acid (2 per cent.), permanganate of potash (1 in 4,000), hydrogen peroxide (10 per cent.), cyllin (1 in 300), lysol or lysoform (2 to 5 per cent.). After this the vesicles are pricked, and the parts again washed with the disinfectant, an antiseptic powder being then thickly applied, such as:—

Acidi borici (finely

Europhen
Talci ven.

Dermatol
Talci ven

In some patients an ointment (europhen, 2 per cent.; protargol, 5 per cent.) answers better; the protargol ointment should never be used for the face in Europeans, as it discolours the skin after a time. It may be noted that in our experience the white precipitate ointment (1 per cent.), which is so efficacious in the usual impetigo of the Temperate Zones, has very little or no effect in pyosis mansoni. After the eruption has disappeared, it is advisable to use some Condy's fluid or other disinfectant in the bath to prevent relapses; and, if the skin is not too tender, a formalin soap may be regularly used. The underclothing should be regularly dusted with one of the above powders.

Pyosis Tropica.

Synonym.—Pyosis Castellanii, Kurunegala ulcers, Pyosis Caffra.

Definition.—Pyosis tropica is characterized by the presence of numerous crusty lesions on the legs and arms, caused by pyococci.

Historical.—Under the name 'pyosis tropica' Castellani described in 1909 a skin disease very common in Ceylon and Southern India. In Ceylon it is called by the natives Kurunegala sore, as it is especially common in that district. Pyosis tropica has been reported from other tropical countries. It has been observed, in 1912, in Tripoli by Gabbi and Sabella; in the Anglo-Egyptian Sudan by Chalmers and O'Farrell, in 1913; in South Africa by Ricono, in 1916; and by Pijper in 1918.

Ætiology. The disease is probably due to the usual pyogenic cocci, and is allied to the ordinary impetiginous and ecthymatous conditions, though much more severe. Chalmers and O'Farrell grew an organism from their case which, differing somewhat from the other species of aurococcus, was called by them *Aurococcus tropicus*. It was held to be causal because a vaccine made from it rapidly cured the case, but had no effect on a case of Nile boils; but in other cases other varieties of pyogenic cocci may be causal.

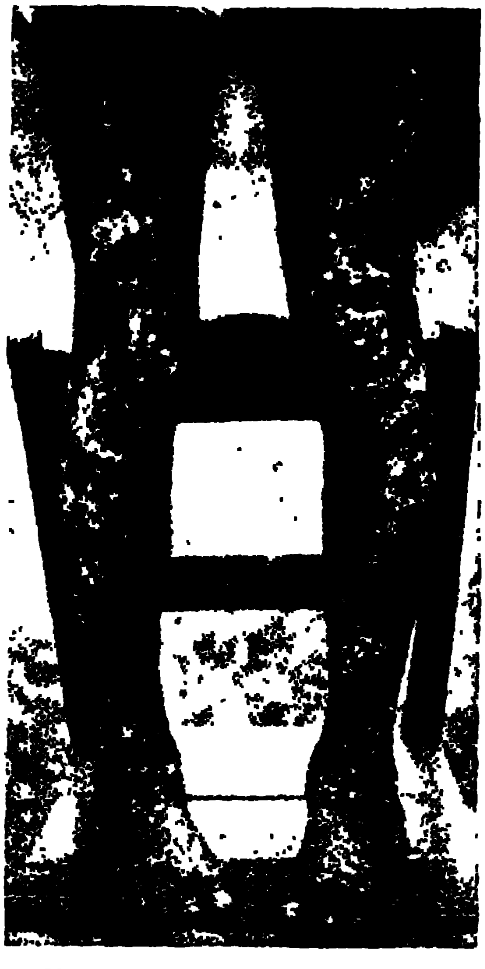

FIG. 795.—PYOSIS TROPICA.
The white patches are in reality thick yellow crusts.

Symptomatology.—The patient, generally a young boy or girl, though adults may also suffer from it, presents on the legs, arms, and occasionally all over the body, except the face, numerous crusty lesions, occasionally rupia-like, of a dirty blackish or yellowish colour. If the thick crust is removed, a shallow ulcer with an irregular margin and granulating fundus will be seen, or a small, flattened, or hemispheric nodule the size of a pea, with a pinkish, smooth surface. Besides these large lesions, small papulo-vesicles and minute pustules are often present. The larger lesions are frequently surrounded by a halo of hyperpigmentation. There is severe pruritus. On healing, also, the ulcers and nodules leave a zone of hyperpigmentation or, more rarely, depigmentation. In chronic cases plaques of hyperkeratosis may develop, especially on the exterior regions of the arms and the elbows.

Diagnosis.—On superficial examination, the disease might be easily mistaken for framboesia. In contrast to framboesia, the ulcers are superficial, and the nodules, when present, are generally smaller, have no moriform surface, and in scrapings from the lesions the *Treponema pertenue* Castellani is absent. From scabies it is distinguished by the absence of burrows and absence of the *Acarus*. From ecthyma, to which it is closely related, the condition differs by the fact that, on removing the crusts, besides the ulcerative lesions, rather large, smooth hemispheric nodules may be seen.

Prognosis.—The disease is very persistent, but the general health is not affected.

Treatment.—If the disease is not properly treated, it has a tendency to become chronic. In some cases the opsonic treatment gives satisfactory results. The vaccine should be prepared with staphylococci grown from the lesions. It has been used by Castellani with good results in Ceylon in 1910, by Chalmers and O'Farrell in 1913, and by Pijper in 1918. Chalmers and O'Farrell gave with success 250 millions of an autogenous vaccine to an adult, and repeated it in three days: Pijper treated children with 4 to 5 millions of an autogenous streptococcus obtained from a case, or by a mixture of streptococci and staphylococci. The local treatment consists in removing the crusts by soaking them with a salicylic oil made according to the following formula:—

Acidi salicylici	gr. xxx.
Olei ricini	q.s.
Olei olivæ	ad ℥iv.

or by compresses soaked in hot boric lotion.

All the lesions are then disinfected with a solution of perchloride of mercury (1 in 1,000), carbolic acid (2 per cent.), cyllin (1 in 300) or permanganate of potash (1 in 4,000). A slightly antiseptic ointment is then applied, such as europhen (2 per cent.), iodoform (2 per cent.), protargol (5 per cent.), calomel (5 to 10 per cent.). An ointment which in our experience is often efficacious is β-naphthol gr. ii.-v., acidi carbolici gr. v.-x., vaselini ad ℥i.

Pyosis Palmaris.

Definition.—Pyosis palmaris is characterized by the presence of numerous, discrete, conical, white pustules, which do not form crusts and which appear on the palms of the hands of native children.

Historical.—The disease was described some ten years ago by Castellani in native children in Ceylon, where it is rare.

Climatology.—So far it has only been recorded in Ceylon.

Ætiology.—Pyococci are present in the lesions, but may not be the true cause.

Symptomatology.—With little or no pruritus, discrete, conical, solitary pustules appear on the palms of the hands. These pustules do not coalesce or form crusts, and are not surrounded by a zone of hyperæmia.

Diagnosis.—It is distinguished from scabies by the absence of the acarus, from ringworm by the absence of a fungus, and from syphilis by the uselessness of the specific treatment.

Treatment.—Vaccines may be tried.

Pyosis Corletti.

Synonyms.—Impetigo bullosa, Impetigo contagiosa bullosa of Corlett.

Definition.—Pyosis corletti is an acute, contagious, bullous pyosis beginning on any region of the body, and characterized by the presence of medium-sized and large bullæ arising on seemingly healthy skin, and caused by *Aurococcus mollis* (Dyar, 1895).

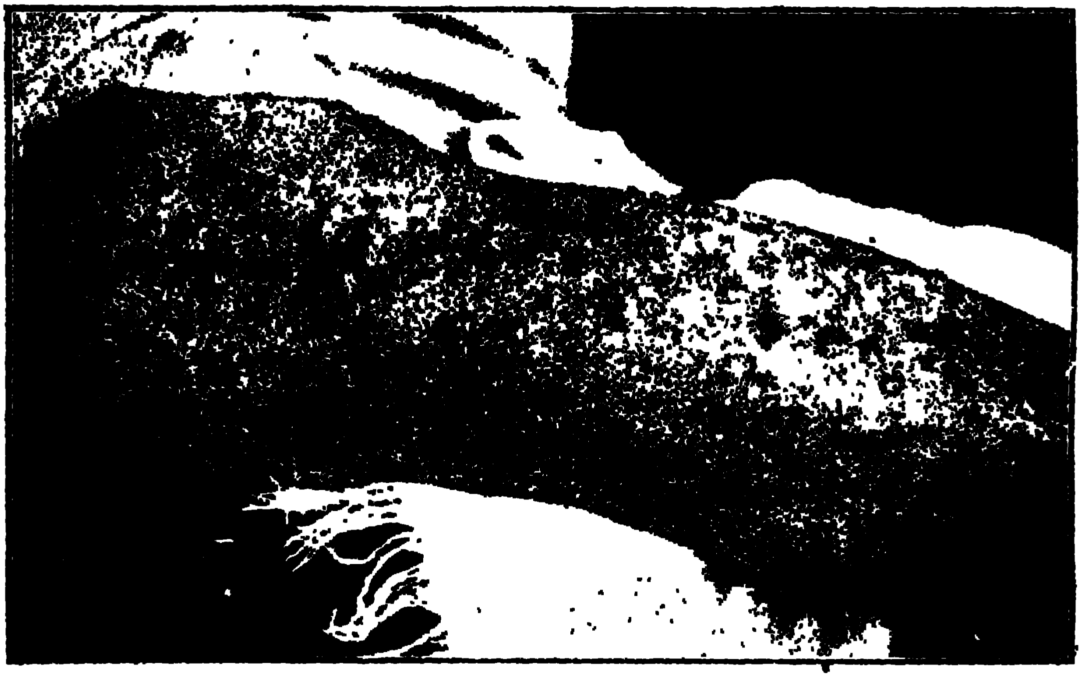

FIG. 796.—PYOSIS CORLETTI.

Historical.—In 1899 Corlett described a contagious bullous eruption as being endemic in Florida; later Singh in India invited attention to a similar disease. In 1912 Reguzis described an epidemic among Europeans in Cairo. In 1915 Chalmers and O'Connor gave a description of an epidemic of this disease as seen in the 1st Battalion of the Suffolk Regiment in Khartoum.

Ætiology.—The causal organism so far found is *Aurococcus mollis* (Dyar, 1895). It is causal because (1) it is the only organism present, and is found in the youngest vesicles: (2) it was obtainable from all the cases of the Khartoum epidemic, and a similar organism was found by Corlett, but not fully defined; (3) a vaccine prepared from it cured the patients quickly. It is, of course, possible that the same clinical correlation may be caused by various, as yet unknown, allied organisms.

The Khartoum epidemic was traceable to a case of 'Nile boils,' caused by the same organism.

Symptomatology.—The incubation period is unknown, but in some cases the initial lesion is a small papule on the head or chest, which is so quickly followed by an outbreak of bullæ that the eruption is well developed in two days.

The essential feature of the eruption is a bulla arising on apparently healthy skin, and measuring about 2 cm. in diameter, but associated with some much larger blebs measuring about twice this size, and also smaller bullæ which rapidly increase in diameter.

A bulla appears to start as a small vesicle situate in the epidermis, containing a clear, watery fluid. This vesicle rapidly increases in size until it forms a bulla, the walls of which are, first tense and the contents watery, but later they become flaccid and the contents purulent.

The bulla bursts, the contents escape, and the lesions dry up and disappear, usually without forming a scab, but in the case of the larger lesions it leaves behind it a certain amount of dark discoloration of the skin, indicating the affected area.

If a bulla is pricked it is found to have a glazed, parchment-like base. The edges of the bulla are also observed to be undermined, and it is apparent that the increase in size from a vesicle or small bulla to a larger one is by the spreading outwards of the edges. If scratched, excoriations and crusts are formed, but crusty lesions are rare and, when present, only slightly developed.

The bullæ are situate most abundantly on the thighs, back, and chest, and less abundantly on the neck, arms, and legs, and more rarely on the face and head. The axillary and scroto-crural regions are singularly free from the disease, only one case showing a slight amount of the eruption at the margins of the axillæ.

There are no constitutional symptoms, and only rarely do cases complain of a slight amount of itching, which is probably due not so much to the eruption itself as to the rubbing of the clothing producing slightly raw areas where bullæ have burst. When this takes place, small scabs are apt to form, especially if the patient scratches the area, but they are entirely secondary in nature and not part of the true eruption.

The differential leucocyte count based on 1,000 cells is:—

Polymorphonuclear leucocytes	86·7
Mononuclear leucocytes	3·8
Large lymphocytes	4·4
Small lymphocytes	3·2
Eosinophile leucocytes	1·9
Total	100·0

Diagnosis.—The important diagnostic characters of the eruption are the absence of constitutional disturbance, the absence of severe itching, the presence of relatively large bullæ arising from apparently sound skin and not surrounded by inflamed areolæ, the absence of marked incidence on the axillary and scroto-crural regions, the absence of crusts and of streptococci, the presence of *Aurococcus mollis*, and finally the ready reaction to treatment by a vaccine prepared from this organism.

Differential Diagnosis.– The differential diagnosis must be made from impetigo contagiosa, dermatitis bullosa plantaris, pemphigus acutus, and pyosis mansoni.

It can readily be differentiated from impetigo contagiosa by the absence of crusty lesions as a rule, and by the fact that even when the youngest vesicle is examined by Sabouraud's methods no streptococcus can be found and only *Aurococcus mollis* (Dyar).

From dermatitis bullosa plantaris it may be distinguished by not attacking the soles of the feet as far as has been recorded, by not extending between the toes, and by the absence of streptococci and *Epidermophyton cruris* Castellani.

From pemphigus acutus it can be recognized by the absence of the severe constitutional disturbance.

From pyosis mansoni it can be differentiated by the fact that it does not begin in the axillæ or scroto-crural regions, and that it but rarely, and then lightly, attacks those parts which are the primary seat of Manson's pyosis.

The principal feature of the eruption in Manson's disease is flattened, roundish vesicles which enlarge to the size of a small pea, while large, flabby, pemphigoid bullæ are rare; but in this eruption large pemphigoid bullæ are common. In Manson's pyosis the vesicles are often surrounded by a pinkish or reddish inflammatory halo, which is absent in the present eruption.

Complication. Eruptions of boils may occur.

Sequela.—When cases are not treated by vaccine therapy there appears to be a liability to boils as a sequela.

Prognosis.—The prognosis is excellent, as the disease is rapidly cured by a combination of vaccine and local therapy.

Treatment.—The best form of treatment is to prepare a vaccine which is to be administered in 200 and 450 million doses, with intervals of two to three days between each dose.

In order to expedite the cure local treatment is also useful, and this consists in pricking each blister and catching the exuding fluid on swabs dipped in 1 in 1,000 lotio hydrargyri perchloridi.

After pricking, each blister should be thoroughly disinfected with the same lotion, and be dusted with some antiseptic powder, the cheapest, but not the best, being boric acid, while the same with starch should be used for dusting the clothing in order to attempt to prevent the spread of the infection.

A vaccine prepared from a case of Pyosis corletti acts also generally on cases of Nile boils, and *vice versa*. This is easily understood, as the two conditions are due to the same organism—*Aurococcus mollis* (Dyar).

Prophylaxis.—The important points in the prophylaxis are to realize that the disease may originate from a case of boils, may cause no symptoms, and may be overlooked.

Pyosis Discoides.

Definition.—Pyosis discoides begins as a generalized vesicular eruption of fairly large roundish vesicles, which rapidly become purulent and then dry, forming circular, discoidal, bright yellow crusts surrounded by a slightly hyperæmic zone and associated with pyogenic cocci, and in the early stages often accompanied by slight fever.

Historical.- This eruption was found by Castellani in 1914, in a man in Ceylon, and again in the Balkans.

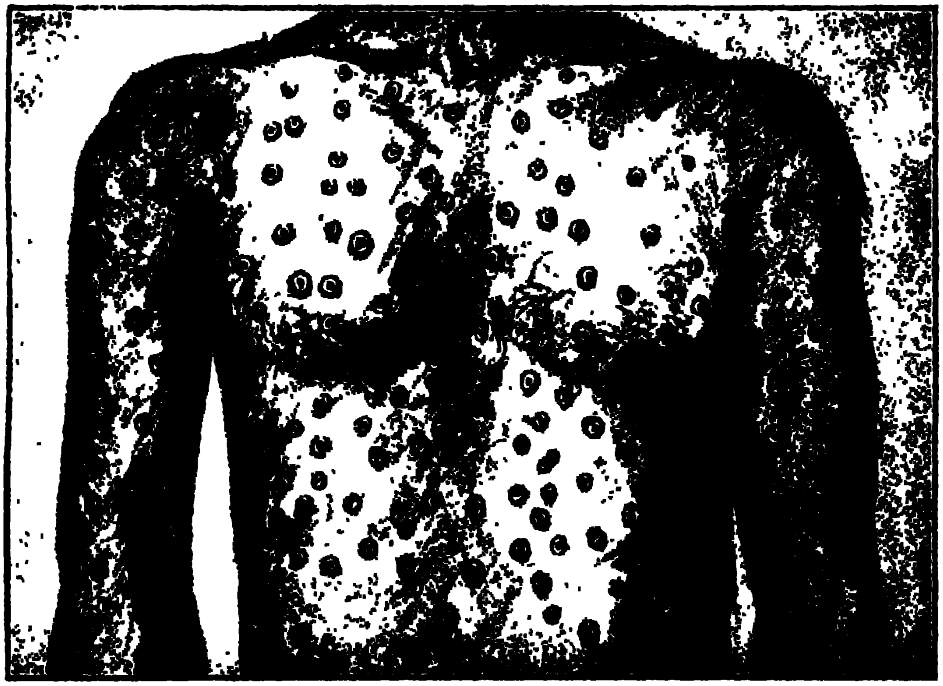

FIG 797.—PYOSIS DISCOIDES.
(From a rough sketch made by an Austrian prisoner in Macedonia.)

Ætiology.—Streptococci and staphylococci have been found in the lesions.

Symptomatology.—The symptoms may be discussed in two stages:—

Vesicular Stage.—There is a profuse generalized eruption of fairly large roundish vesicles, some of which are flaccid.

Stage of Discoidal Crusts.—The contents of the vesicles are at first clear, but soon become purulent, and then dry up, forming circular, discoidal, bright yellow crusts, firmly embedded in the deeper layers of the epidermis, and often surrounded by a hyperæmic halo. When these firmly fixed crusts are removed, shallow circular ulcers with sharply defined edges are produced.

General Symptoms.—Constitutional symptoms are of the slightest, but during the first few days of the eruption there may be slight fever.

Diagnosis.—The definition indicates the principal characters of the complaint. As regards the differential diagnosis, this must be made from chicken-pox, in which the bright yellow, discoidal, deeply attached crusts are absent.

Treatment.—The treatment advised is 1 per cent. white precipitate ointment.

THE PYOGENIC FOLLICULITES.

These are pyogenic affections of the hair follicles caused by cocci. The following varieties may be differentiated:—

A. Deep-seated in the hair follicle; occur anywhere—*Tropical boils.*

B. Superficially situate in the hair follicle; found on the legs and thighs—*Purulent folliculitis of the legs.*

Tropical Boils.

Synonyms.—Tropical furunculosis, Nile boils, Mango boils.

Definition.—A tropical boil is a deep-seated purulent inflammation of a hair follicle due to pyococci.

Remarks.—Furunculosis is very common in the tropics. It does not differ from what one sees in Europe except that it is often of much severer type, and has a great tendency to spread all over the body. The individual boils are frequently of very large dimensions and extremely painful. There may be fever. The condition is very common in people who perspire much and suffer from prickly heat.

Ætiology.—It is due to staphylococci. Carbuncle, especially of the neck and gluteal regions, with deep infiltration and multiple openings, is not rarely associated in our experience with ordinary boils. The so-called 'Nile boils' have been examined bacteriologically by Chalmers and Marshall and by Archibald, and have been shown to be generally caused by *Aurococcus mollis* (Dyar, 1895).

E. Black describes under the term 'furunculus contagiosus' a benign multiple furunculosis observed by him in Brazil.

Treatment.—The quickest and most reliable method of cure in cases of multiple boils is, in our experience, Wright's vaccine treatment, the vaccine being prepared from staphylococci isolated from the patient, or being prepared from organisms known to occur in a given district. When this treatment cannot be carried out, the administration of fresh yeast, half a wine-glassful twice daily, or of yeast preparations internally, will be found to be useful in some cases—*e.g.*, two or three ceridin pills twice daily. Ichthyol tablets (gr. v.), twice daily, may also be given, or calcium sulphide (gr. ¼) may be administered, but their beneficial effect is doubtful. Diluted sulphuric acid (♏ xx.-xxx.), well diluted, every four hours may be tried. Occasionally a small boil may be aborted by applying a droplet of pure carbolic acid by means of a pointed pencil of wood drilled into the centre of the papule, or four or five drops of 1 in 30 solution of carbolic acid may be injected beneath the boil, or Unna's carbolic and mercury plaster may be used, or spirit of camphor may be applied several times daily. For old indurated boils the continuous application of a carbolic lotion (2 to 5 per cent.) on lint occasionally causes them to become absorbed. Large boils in which suppuration has taken place should be opened, but it is a mistake to open them too soon. As a preventive, a salicylic-alcoholic lotion (1 to 2 per cent.), used after the daily bath, is advantageous, and it is also advisable to use a little Condy's fluid or cyllin in the bath.

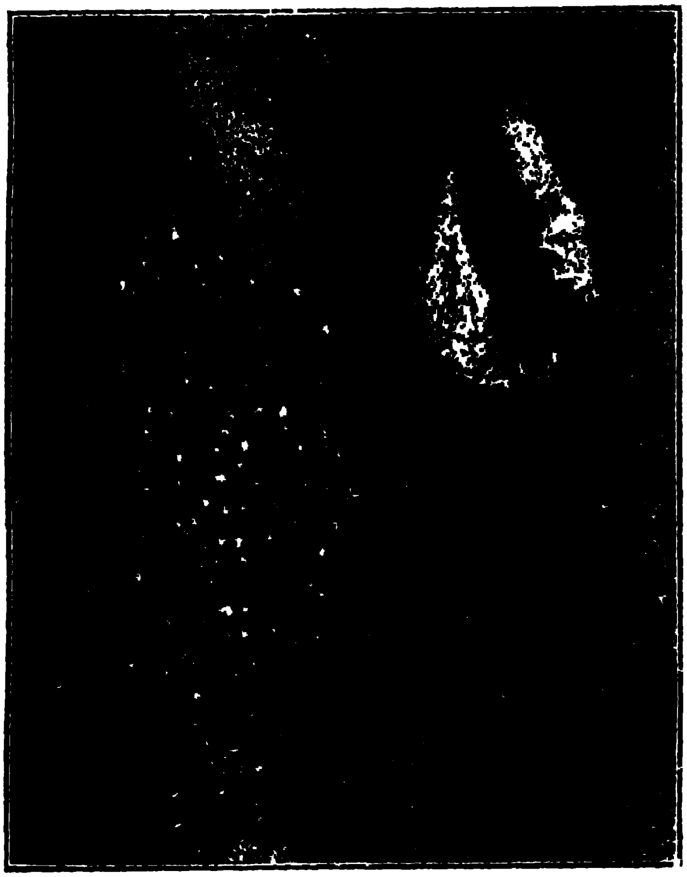

FIG. 798.—PURULENT FOLLICULITIS OF THE LEGS AND THIGHS.

Stanoxyl by the mouth only is not satisfactory, but is said to give good results when administered in baths.

Purulent Folliculitis of the Legs.

Definition.—A purulent inflammation attacking many hair follicles of the legs and thighs.

Historical and Geographical.—The condition is extremely common in Ceylon and Southern India, in the former especially among the moormen. It was investigated by Castellani some years ago. A very similar or identical condition has been noted by R. Cranston Low in Scotland in miners working in mines flooded with water.

Ætiology.—It is apparently due to the usual pyogenic cocci.

Symptomatology.—The patient presents on his legs—especially the extensor region—numerous whitish conical pustules. Each pustule is pierced by a hair. The pustules remain, as a rule, separate, do not increase in size to any extent, and do not coalesce nor form crusty lesions. After a time the skin of the legs may show a peculiar parchment-like appearance. The examination of the pus contained in the pustules shows the presence of the ordinary staphylococci.

Prognosis.—The disease, if left untreated, runs a very long course.

Treatment.—The treatment consists in depilation, application of antiseptic dressings, and, later, the application of an antiseptic ointment or paste. In obstinate cases the opsonic treatment, carried out with a vaccine prepared from the staphylococci grown from the lesions, gives good results. The following ichthyol application may be found useful: Ichthyol, 2 drachms; glycerine, 1 drachm; distilled water to 1 ounce.

THE PYOGENIC DERMATITES.

Definition.—The pyogenic dermatites are inflammations predominantly of the surface of the skin, which are caused by the pyococci.

Remarks.—The old term eczema was introduced by Ætius of Amida, in the sixth century A.D., for the breaking out of burning, itching, non-ulcerating vesicles, and was used by Willan for an eruption of minute vesicles, non contagious, closely crowded together, forming thin flakes and crusts when the fluid they contain is absorbed, and due to *irritation* whether *internally* or *externally* applied. The causes which Willan had in mind were mercury applied internally and the rays of the sun externally.

After years of confusion the modern tendency is to consider that the word 'eczema' is a cloak for ignorance.

In lieu of it the word 'dermatitis' may be employed, if by this is meant an inflammation predominantly of the surface of the skin. So defined, dermatitis may be classified into:—

1. Dermatitis due to chemical causes.
2. Dermatitis due to physical causes.
3. Dermatitis due to parasites.

The term eczema should only be used when the practitioner is unable to assign its proper cause to a dermatitis. The term is therefore a cloak for ignorance of the causation of the dermal condition.

In the present section we are considering a part of the third class of dermatites—viz., those due to parasites—and in particular that subclass which is brought about by the pyococci.

We, however, propose to further restrict our remarks to merely the streptococcal dermatites, and will consider them under two headings—viz.:—

Primary Streptococcal Dermatites.
Secondary Streptococcal Dermatites.

THE PRIMARY STREPTOCOCCAL DERMATITES.

Definition.—A primary streptococcal dermatitis is an inflammation predominantly of the surface of the skin, localized or generalized, and caused by streptococci.

Remarks.—Streptococci appear to have been first observed in cutaneous lesions by Crocker in 1881, and to have been later identified by Brockhart as *Streptococcus erysipelatosus* Fehleisen, 1883. Later they were carefully described by Whitfield, Colcott Fox, and many other observers, including ourselves. Colcott Fox classified streptococcal skin lesions with those which occur in the course of grave systemic affections, those which are lesions of the hypoderm, those which are primary, and those which are secondary cutaneous lesions.

With regard to the primary streptococcal dermatites, these are sufficiently numerous, but for our present purpose we will restrict our attention to those found in the tropics, which are *dermatitis veldis*, *dermatitis pratensis*, and *dermatitis cupoliformis*, which may be distinguished from one another as follows:—

A. *Nodules not produced*:—
  I. Begins as a large blister or bulla, and forms a superficial sore with ragged edges, and a fresh clean floor in recent, or a parchment-like floor in old cases—*Dermatitis veldis*.
  II. Begins as a small irritable papule or papulo-vesicle, which ulcerates, glazes over, spreads, and finally gives rise to an area defined by a raised margin, inside which are deep fissures and ulcerated areas, and often in later stages papillomatous outgrowths—*Dermatitis pratensis*.

B. *Nodules produced—Dermatitis cupoliformis.*

Dermatitis Veldis.

Synonyms.—Veld sore, Barcoo rot, Gift zeer, Brand zeer.

Definition.—A primary streptococcal dermatitis characterized by the formation of a bulla, followed by a superficial sore, which becomes very chronic, but does not lead to papillary acanthotic formations.

History.—For long the Bushmen of the region known as Barcoo River, North Queensland, have suffered from sores which they call Barcoo rot. In the Transvaal the inhabitants are afflicted with a sore which they call 'gift zeer' or poison sore, while in the Free State the residents are attacked by a similar sore which they call 'brand zeer' or burn sore.

In 1901 Ogston and in 1904 Harman reported upon these conditions under the name 'veld sore,' a term used by the English settlers in South Africa. Harman further proved that it was the same as Barcoo rot by the evidence of Australian Bushmen who had suffered from the one in Australia, and from the other in South Africa recognizing them as the same. In 1913 Black gave us his personal experiences of Barcoo rot. In 1917 Martin met with a similar condition in the Anzac Mounted Division operating in the desert east of the Suez Canal, and again it was recognized by the men who had seen or experienced Barcoo rot to be the same complaint.

Climatology.—The disease is known to occur in Tropical Australia, South Africa, Egypt, and Equatorial Africa.

Ætiology.—Harman obtained staphylococci and streptococci from his cases. He was inclined to consider his yellow staphylococcus as the causal organism, and called it *Micrococcus vesicans*, but it is more probable that the causal agent is the streptococcus which may be known provisionally as *Streptococcus vesicans*, and which may be only a synonym for some more fully worked out species such as *S. versatilis* Broadhurst, 1915. The disease can be reproduced in man by inoculating the fluid of the blisters on to a raw place in the skin.

Pathological Histology.—The fresh unopened blister has been studied by Harman, who found that it occurred in the layers of the epidermis. The stratum corneum is raised, forming the roof of the blister, which begins as a cleft in the stratum lucidum. The epidermis is never wholly absent from the floor, which is composed of swollen cells of the stratum lucidum and stratum granulosum. The dermis shows a moderate degree of leucocytic invasion beneath the floor of the ulcer. Cocci in the form of diplococci or short chains are found in spaces between the cells of the epidermis.

Symptomatology.—The dermatitis begins by the patient feeling a pricking or burning sensation in some part of the body. On examining this, he finds that on the site of some small abrasion there is a little blister surrounded by a hyperæmic zone. The blister quickly increases in size until it may attain that of a shilling, but more usually it grows slowly, and when the size of a sixpenny-piece is reached it usually bursts, setting free some sero-purulent fluid and forming a superficial ulcer with a red floor and roundish or somewhat festooned margins.

The floor of the ulcer remains dry like parchment. The ulcer may be painful, but, especially at the beginning, there is frequently more itching than pain. The proximal lymphatic glands may be enlarged. Several such sores may be present at the same time. The hands, forearms, feet, and legs are mostly affected. Harman has seen as many as twenty such sores on one man. The duration of the affection varies between one and three months, but occasionally may last as long as six months.

Treatment.—The correct treatment is by vaccines, either autogenous or from a locally prepared stock. The local treatment consists in keeping the sores dressed with antiseptic lotions, such as perchloride of mercury (1 in 4,000), or in washing the sores with a disinfecting lotion, and then applying an antiseptic powder, paste, or ointment, such as europhen (1 to 3 per cent.), iodoform (1 to 3 per cent.), protargol (5 to 10 per cent.), or calomel (5 to 10 per cent.).

Barcoo Rot.

For the reasons given above we consider Barcoo rot to be a condition identical with *dermatitis veldis*. It must, however, be admitted that the descriptions given by some authors may include other conditions. For example, Black described it as forming a crust which becomes larger, thicker, and harder until horny in consistence and difficult to remove. There is very little itching or pain.

Pain states that the term ' Barcoo rot ' is very loosely applied. According to him the original ' Barcoo rot ' was scurvy. Owing to the improved conditions of living scurvy disappeared, and the younger Bushmen applied the name to any superficial obstinate sore. Two conditions at least are now covered by the term: a seasonal staphylococcal infection, occurring generally in the autumn, and a deep-seated trichophytosis of the hands.

Dermatitis Pratensis.

Definition.—Dermatitis pratensis is a primary streptococcal dermatitis characterized by starting as a papule spreading by ulceration, and forming in late stages acanthotic papillary formations.

Historical. The disease has been studied by Castellani in Equatorial Africa and by Chalmers and Archibald in the Anglo-Egyptian Sudan. We give it the name *dermatitis pratensis* to bring it into line with the other *dermatites*.

Ætiology.—The causative organism is a streptococcus which can be found in the polymorphonuclear leucocytes, in the lesions, and can easily be grown in pure culture. In some cases in the Anglo-Egyptian Sudan the organism obtained was *Streptococcus versatilis* Broadhurst, 1915, which is a normal denizen of equine fæces, from which the infection probably comes. Its causal relationship depends upon not merely its presence in cases of the disease, but upon the fact that vaccines prepared from it will quickly cure not merely the person from whom the growth was obtained, but other patients also.

Pathological Histology.—When sections are made along a papillomatous projection of the acanthotic variety it will be seen that the outer covering is epidermal in nature, and that, superficially, it is covered by masses of scales, both on its free surface and on the surface looking towards another process.

This epidermis shows the defect of cornification called 'parakeratosis' by Auspitz, while with regard to the rete there is a certain degree of acanthosis.

The corium is full of dilated vessels, and is also slightly œdematous and fairly cellular.

The cells consist of forms with a large, well-stained nucleus and a fringe of cytoplasm, which are supposed to be derived from connective tissue cells. Plasma cells and mast cells may also be seen, as may an occasional polymorphonuclear leucocyte.

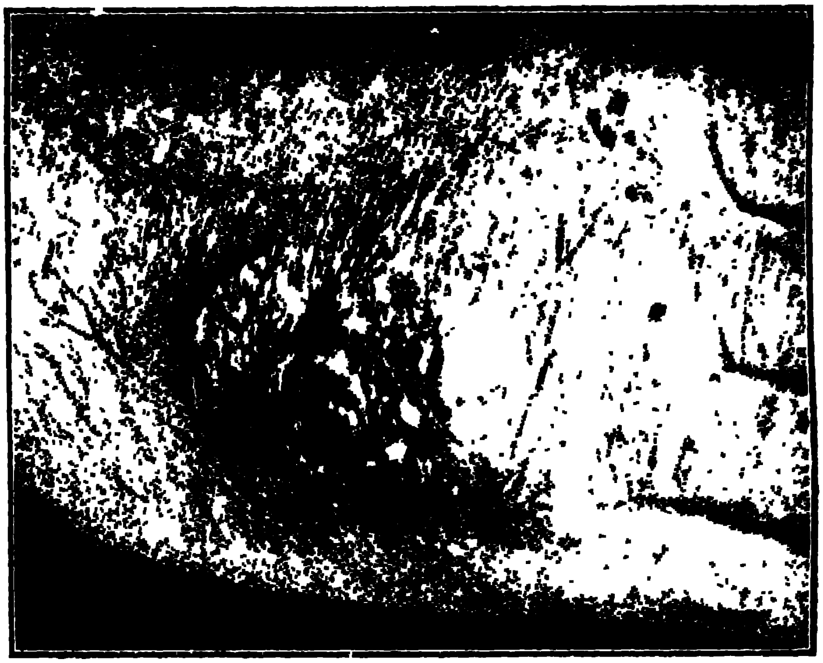

Fig. 700.—Dermatitis Pratensis.

Turning now to the non-papillomatous regions, there is a well-defined epidermis with parakeratosis and acanthosis, while the cellular infiltration of the corium is denser. It is somewhat œdematous.

Raw areas show parakeratoses, which are distinguished by the extraordinary development of the acanthosis.

In the region where the epidermis is missing all trace of a normal corium is lost superficially, and its place is taken by a fibrocellular exudate.

Embedded in this exudate can be seen the remains of the acanthotic prolongations of the epidermal cells.

In this fibrocellular mass lie numerous bloodvessels filled with corpuscles, while patches of serous exudation can also be observed.

The cells of the mass are largely composed of the same cells as in the corium of other pieces, but the amount of polymorphonuclear leucocytes in certain regions, and more especially superficially, is marked.

In the deeper part of the section isolated pieces of the ordinary connective tissue of the corium can be seen, while finally, in the depth of the section, well-defined connective tissue is seen containing here and there scattered collections of cells of the same nature, as already described for other portions of the tissue.

The sweat glands are much damaged, and surrounded by cells of the usual type found in these lesions.

Still deeper one meets with fatty tissue, between the cells of which lies an accumulation of the typical cells of the lesion.

Symptomatology.—The eruption begins as a small pruriginous papule or papulo-vesicle, which increases in size and ulcerates, scabs over, and extends at its margins. When fully developed it is surrounded by a raised margin, behind which small papillæ may be noted, which in older cases give rise to very distinct papillomatous outgrowths. The surface of the sore is composed of deep fissures and a few ulcerated areas, which exude a serous fluid, which is apt to form crusts. These ulcerated areas and fissures are separated by other areas coated by a thin epidermal covering, which gives rise to a false pealing appearance. The whole condition spreads slowly from the margin.

Diagnosis.—This is sufficiently effected by the table given on p. 2030.

Prognosis.—The prognosis is good provided that the patient is otherwise healthy.

Treatment.—The best treatment is, without doubt, an autogenous vaccine, but a polyvalent local (*i.e.*, made from local strains) vaccine acts quite well.

We generally give 10 millions to commence with, then 50, and, if necessary, 100 millions.

The affected part in chronic cases may be painted with iodine and a dry dressing applied.

Dermatitis Cupoliformis.

Synonym.—Tropical ecthyma (Castellani).

Definition.—Dermatitis cupoliformis is characterized by commencing as dusky red macules, which are follicular or perifollicular, which either disappear or slowly become cupoliform nodules, which after a time break down and ulcerate.

Historical.—This disease was first described by Castellani in 1914 as seen mostly in Europeans in Ceylon. Subsequently he met with the disease in the Balkans.

Climatology.—So far it is only reported from Ceylon and the Balkans.

Ætiology.—It is caused by a streptococcus belonging to the erysipelatous group (*vide* Chapter XXXVI., p. 929), which is named *S. tropicalis* Castellani, 1914.

Symptomatology.—The disease begins as superficial, dusky red, follicular, or perifollicular slightly itching macules on the feet and legs. Some of these spots disappear, while others become slowly larger, raised, hard, infiltrated, and cupoliform, reaching the size of a pea or a small cherry. After a time the centre of the nodule breaks down and forms an ulcer, with a reddish floor and undermined edges.

These ulcers are somewhat painful and very slow to heal, and when this does take place it produces patches of hyperpigmentation. The course of the disease is very long, lasting at times more than a year.

Diagnosis.—The characteristic features of the eruption are the presence of raised, hard, rather large cupoliform nodules, some of which show a central ulcer with undermined edges.

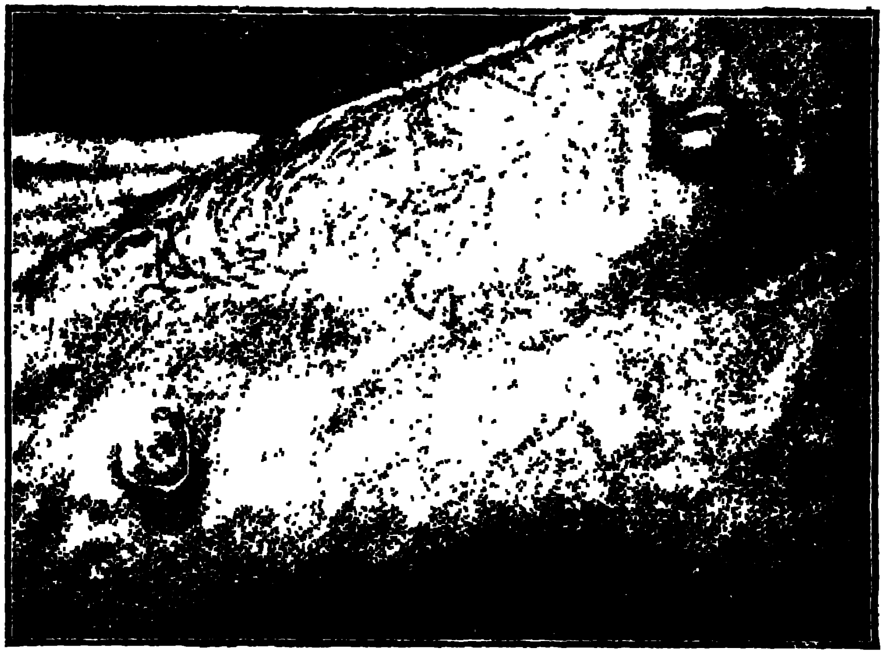

FIG. 800.—DERMATITIS CUPOLIFORMIS OF THE FOOT

The differential diagnosis has to be made from *Oriental sore* by the absence of Leishman-Donovan bodies.

From *ecthyma* it may be distinguished by the absence or rarity of the pustular lesions with a brownish crust. In ecthyma the initial lesions are always pustular, there being generally discrete flat pustules; when these rupture a brownish crust is formed beneath which suppuration goes on. In the condition known as 'ecthyma gangrenosum,' occasionally met with in cachectic children, especially during convalescence from varicella and other exanthemata, the initial lesions are vesicular or pustular, and no nodules are present.

In *pyosis tropica* the ulcers do not show undermined edges, and pustular lesions are present.

In *purulent folliculitis of the legs* there are no ulcers, only pustules pierced by hairs being present.

Prognosis.—The condition runs a very long course and is difficult to cure, unless treated by an autogenous vaccine.

Treatment.—An autogenous vaccine is the correct treatment, and generally produces a cure in two to three weeks. Local treatment by antiseptic lotions is also recommended.

THE SECONDARY STREPTOCOCCAL DERMATITES.

Only two forms of this affection concern us, and both are secondary to infections with *Epidermophyton cruris* Castellani. They are dermatitis interdigitalis and dermatitis bullosa plantaris.

They may be differing phases of the same affection, but they can be differentiated as follows:-

A. Situate primarily between the toes. Bullæ absent—*Dermatitis interdigitalis*.

B. Situate primarily on the soles. Bullæ present—*Dermatitis bullosa plantaris*.

Dermatitis Interdigitalis.

Synonyms. Dermatitis rimosa of the toes, Mango toe (Ceylon), Frieira (Brazil).

Definition.—Dermatitis interdigitalis is a streptococcal dermatitis secondary to an infection of the parts between the toes caused by *Epidermophyton cruris* Castellani.

Historical. This affection, which is popularly known in Ceylon as 'Mango toe,' was first brought into prominence by Sabouraud's observation that the primary cause was an infection by *Epidermophyton cruris* Castellani. In 1910 Castellani found that very often there was a secondary streptococcal infection.

A somewhat similar affection was described long ago by Martin Costa in Brazil, who stated that the condition was very common among natives, who called it 'frieira.' He believed it to be caused by the heavy perspiration, and accumulation of dust and dirt between the toes.

Geographical Distribution.—It is extremely common in Southern India, Burma, Ceylon, and many other tropical countries, being the cause of great discomfort to European residents, especially during the hot season.

Ætiology.—The condition seems to be a pyogenic infection, starting generally on slight lesions produced by a localization of *Epidermophyton cruris* Castellani to the toes. This localization of the fungus was first observed by Sabouraud. The fungus *per se* in this situation gives rise to very slight symptoms very often only some scaliness and pruritus.

Symptomatology.—The patient first complains of great itching between the toes, without there being present any papular or vesicular lesion. On scratching to relieve this itching, portions of the epidermis become removed, and small, superficial, red, irritable abrasions are seen. These become severer, and deep, extremely painful fissures appear between the toes in almost all the cases. This dermatitis is difficult to cure, but disappears rapidly on the patient going to the hills or to Europe. It may remain quiescent for long periods, and then reappear again. During the periods of quiescence some pruritus may occasionally be felt, and the skin between the toes may easily crack or be slightly scaly.

Treatment.—This consists in keeping the patient at rest for a few days, dressing the affected parts continuously with diluted carbolic lotion (½ per cent.), or resorcin lotion (½ to 1 per cent.), and later applying a zinc oxide paste, hazeline cream, or a bismuth boric ointment (bismuth subnitratis, gr. xxx.; acidi borici, gr. xv.; vaseline, lanoline, āā ʒiv.). The stockings should be white, and should be changed at least twice daily, and should be boiled before use. If a fungus is found in the lesions, an antimycotic treatment should be carried out when the acute stage is over, or during the quiescent periods, by means of silver nitrate (3 per cent.), or a strong solution of potassium permanganate (gr. xxx. to ℥i.), painted on once or twice daily; or tincture of iodine may be used if the lesions are dry and there are no excoriations.

Dermatitis Bullosa Plantaris.

Synonym.—Foot-tetter (Cantlie).

Definition.—Dermatitis bullosa plantaris is a streptococcal dermatitis, often secondary to an infection of the soles of the feet, caused by *Epidermophyton cruris* Castellani.

Historical and Geographical Distribution.—This affection was first described by Cantlie in China, but cases are met with in all tropical countries.

Ætiology.—The disease is probably a streptococcus infection, one of us having isolated a very virulent strain of the germ from the blebs of a number of cases. In several of our cases this streptococcus infection developed on some superficial lesions due to a localization of *Epidermophyton cruris* Castellani to the soles.

Symptomatology.—It commences with blebs on the sole of the foot. The blebs ultimately break, and by-and-by bare scaly flakes of skin form, and extend all over the sole and between the toes. There is intense itching. Occasionally the condition spreads to other parts of the body. It usually dies away in the cold season, but recommences in the hot season. According to Cantlie, patients who have returned to Europe see their affection reappearing regularly every summer for ten or twenty years after leaving the tropics.

Prognosis.—The condition is of difficult cure, and relapses occur.

Treatment.—In the acute stage the patient must stay at complete rest, and antiseptic dressings, such as mercury perchloride (1 in 4,000) or carbolic acid (½ per cent.), applied continuously. Later a lead lotion (liq. plumbi, ʒii., aq. destil. ad ℥x.), and still later some antiseptic powder (dermatol or zinc oxide) may be used. In our cases ointments were always badly borne. In mild cases we advise taking a foot-bath twice daily in warm boric (1 per cent.) or permanganate (1 in 4,000) solution, besides which the blebs should be pricked with a sterile needle and touched with a solution of permanganate (gr. xx.-xxx. to ℥i.), followed by dressing with zinc oxide, dermatol, or some similar powder.

If the eruption develops on lesions due to fungi, when the acute stage is passed off, an antimycotic treatment should be carried out by applying with care, and very little at a time, a silver nitrate solution (3 to 5 per cent.) if there are moist lesions, or tincture of iodine if the lesions are dry.

Cantlie recommends the application of pastes and plasters as palliatives. Manson advises the use of a daily foot-bath of a 2 per cent. solution of carbolic acid for half an hour.

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CHAPTER XCII

TROPICAL DERMATOMYCOSES

Tropical dermatomycoses—Tinea cruris—Tinea alba—Tinea albigena—Tinea sabouraudi tropicalis—Tinea nigro circinata—Tinea capitis tropicalis—Tinea barbæ tropicalis—Tinea ciliorum—Tinea unguium tropicalis—Tinea imbricata—Tinea intersecta—Tinea flava—Tinea nigra—Erythrasma—Blastomycosis—Sporotrichosis—Cryptococcosis epidermica—Intertrigo saccharomycetica—Aspergillosis—Penicilliosis—Acladiosis—Cryptococcosis epidermica—Pinta—Piedra—Trichomycosis—Rarer nodular and gummatous affections of hyphomycetal origin—References.

TROPICAL dermatomycoses—that is so say, tropical skin diseases caused by fungi higher than bacteria—may be classified as follows:—

TROPICAL DERMATOMYCOSES

Due to fungi of the genus *Epidermophyton* Lang, 1879, *Trichophyton* Malmsten, 1845, *Microsporum* Gruby, 1843

- *E. cruris* Castellani, 1905, common variety of Tinea cruris (dhobie itch).
- *E. p. perneti* Castellani, 1907, variety of Tinea cruris.
- *E. p. rubrum* Castellani, 1909, variety of Tinea cruris.
- *T. nodoformans* Castellani, 1911, variety of Tinea cruris.
- *T. macfadyeni* Castellani, 1905, variety of Tinea alba.
- *T. albiscicans* Nieuwenhuis, 1907, Tinea albigena.
- *T. blanchardi* Castellani, 1905, Tinea sabouraudi tropicalis.
- *T. ceylonense* Castellani, 1908, Tinea nigrocircinata.
- Varieties of Tinea capitis.
  - *T. soudanense* Joyeux, 1912
  - *T. violaceum* Bodin, 1902
  - *T. violaceum* Bodin, 1902, var. *decalvans* Castellani, 1911
  - *T. currii* Chalmers and Marshall, 1914
  - *T. discoides* Sabouraud, 1909
  - *T. violaceum* Bodin, 1902, var. *khartoumense* Chalmers and Macdonald, 1915
  - *T. polygonum* Uriburú, 1909
  - *T. exsiccatum* Uriburú, 1909
- *Microsporum flavescens* P. Horta, 1912, variety of Tinea capitis and corporis.

II. Due to fungi of the genus *Endodermophyton* Castellani, 1909

- *En. tropicale* Castellani, 1914. Tinea imbricata.
- *En. indicum* Castellani, 1911, Tinea imbricata.
- *En. castellanii* Perry, 1907, Tinea intersecta.

III. Due to fungi of the genus *Malassezia* Baillon, 1889	*M. tropica* Castellani, 1905, Tinea flava.	
IV. Due to fungi of the genus *Cladosporium* Link, 1809	*C. mansoni* Castellani, 1905, Tinea nigra. *C. madagascariense* Verdun, 1913, peculiar nodular affection.	
V. Due to fungi of the genera *Saccharomyces* Meyen, 1838, *Cryptococcus* Kützing, *Coccidioides* Rixford and Gilchrist, 1897, *Monilia* Persoon, 1797	Several species, some of which incompletely investigated	Varieties of blastomycosis.
VI. Due to fungi of the genus *Nocardia sensù lato*, Toni and Trevisan, 1880, and *Cohnistreptothrix* Pinoy 1911	*N. minutissima* Burchardt, 1859, erythrasma. *N. carougeaui* Brumpt, 1910, juxta articular nodules. *N. rieurei* Verdun, 1912, nodular affection. *C. tenuis* Castellani, 1912, trichomycosis axillarum. *C. thibiergei* Pinoy and Ravaut, 1909, nodular affection.	
VII. Due to fungi of the genera *Sporotrichum* Link, 1809, *Hemispora* Vuillemin, 1906, *Enantiothamnus* Pinoy, 1911, *Scopulariopsis* Bainier, 1907, *Cladosporium* Link, 1809, *Acremonium* Link, 1809, *Acladium* Link 1809	*Sporotrichum beurmanni* Matruchot and Ramond, 1905 *S. schencki* Hektoen and Perkins, 1900 *S. asteroides* Splendore, 1911 *S. indicum* Castellani, 1908	Varieties of sporotrichosis found in the tropics.
	Hemispora stellata Vuillemin, 1906 *Enantiothamnus braulti* Pinoy 1912 *Scopulariopsis blochi* Matruchot, 1911 *Cladosporium madagascariense* Verdun, 1913 *Acladium castellanii* Pinoy, 1916	Various types of gummatous affections.
VIII. Due to fungi of the genera *Aspergillus* Micheli, 1725, *Sterigmatocystis* Cramer, 1869, *Madurella* Brumpt, 1905, *Indiella* Brumpt, 1906, *Nocardia* Toni and Trevisan, 1889, *Cohnistreptothrix* Pinoy 1911, *Sporotrichum* Link, 1806, *Monosporium* Bonorden and Saccardo, 1898, *Glenospora* Berkeley and Curtis 1876	*Aspergillus bouffardi* Brumpt, 1906 *Sterigmatocystis nidulans* Eidam, 1883 *Madurella mycetomi* Laveran, 1902 *M. bovoi* Brumpt, 1910 *M. tozeuri* Nicolle and Pinoy, 1906 *Indiella mansoni* Brumpt, 1906 *I. reynieri* Brumpt, 1906 *I. somaliensis* Brumpt, 1906 *Nocardia maduræ* Vincent, 1894 *N. asteroides* Eppinger, 1890 *N. pelletieri* Laveran, 1906 *N. bovis* Harz, 1877 *C. israeli* Kruse, 1896 *Sporotrichum beurmanni* Matruchot and Ramond, 1905 *Monosporium apiospermum* Saccardo, 1911 *Glenospora khartoumensis* Chalmers and Archibald, 1916 *G. semoni* Chalmers and Archibald, 1917	Varieties of mycetoma.
IX. Due to fungi of the genera *Aspergillus* Micheli, 1727, *Penicillium* Link, 1809	*A. barbæ* Castellani, 1907, Aspergillosis of hairy parts. *P. barbæ* Castellani, 1907, Penicilliosis of hairy parts	

X. Due to fungi of the genera	*Aspergillus* Micheli, 1725 *Penicillium* Link, 1809 *Monilia* Persoon, 1791 *Montoyella* Castellani, 1907	Pinta.
XI. Due to fungi of the genus *Trichosporum* Behrend, 1890	*T. giganteum* Behrend, piedra.	
	Species as yet not well determined	Tropical varieties of nodular trichomycosis.
XII. Due to fungi of the genus *Pityrosporum* Sabouraud, 1903	*Pityrosporum cantliei* Castellani, 1907, variety of tropical seborrhœa.	

From the above table it will be seen that tropical dermatomycoses *sensû stricto*—viz., occurring only in the tropics—are comparatively few. Most of them are endemic also in temperate zones, though occurring there rarely, or at any rate less frequently than in the tropics. We may mention as examples tinea cruris and Madura foot. The same remark, however, applies to every other branch of tropical medicine.

The frequency of dermatomycoses in the tropics is probably due to the hot, damp climate being very favourable to the growth of vegetal parasites.

TINEA CRURIS (DHOBIE ITCH).

Synonyms.—Tinea tropicalis, Tinea inguinalis, Tinea axillaris, Eczema marginatum.

Definition.—The term 'tinea cruris' indicates a group of epidermophytoses and trichophytoses which are clinically characterized by their tendency to develop on the scroto-crural and inguinal regions.

Historical and Geographical.—Tinea cruris is extremely common all over the tropics: it is met with also in subtropical regions, and in temperate zones, being first described by Hebra in Europe under the name of eczema marginatum. In 1905, Castellani, as the result of the investigation of numerous cases, came to the conclusion that it should be separated from the ordinary forms of tinea corporis, and MacLeod suggested the name tinea cruris for the affection. For the fungus most frequently found in such cases, characterized by the yellowish cultures, Castellani used the name *Trichophyton cruris*. Pernet found and described a fungus for which Castellani suggested later the name *Trichophyton perneti*. In 1907 Sabouraud investigated in a complete manner the condition in France which he called tinea inguinalis. There can be no doubt that tinea inguinalis and dhobie itch, or tinea cruris, are the same entity, as Sabouraud and Pinoy, having compared cultures of *Epidermophyton cruris* isolated in Ceylon with those found in France, have found them identical.

Castellani's further researches have shown that other fungi besides *Ep. cruris* may give rise to tinea cruris, each species giving rise to a slightly different clinical variety of the eruption.

Ætiology.—According to Castellani's researches, at least three different species of *Epidermophytons* and one of *Trichophyton* may give rise to the eruption—*Epidermophyton cruris* Castellani, *Ep. perneti* Castellani, *Ep. rubrum* Castellani, and *Trichophyton nodoformans* Castellani—and there are probably several other not yet described species.

The description of these fungi is given in Chapter XXXVIII. (see p. 1014). Attempts at experimental reproduction of the disease made by Sabouraud and one of us in human beings and monkeys have failed.

Symptomatology.—The term 'dhobie itch' is used very loosely in the tropics by the lay public to denote practically any pruriginous skin affection. The term is, however, specially used to denote a form of severe pruriginous affection which mostly affects the inner surface of the thighs, occasionally the axillæ, and, in stout women, the regions under the breasts. It is in this stricter meaning that the term is used by medical men practising in the tropics.

The clinical features of the affection correspond to Hebra's 'eczema marginatum.' In a well-marked case the perineum, scrotum, and the inner surface of the thighs present large festooned patches, with an elevated abrupt margin; the whole of the patches are bright red, or, in a later period, the margin only is red, while the rest of the patch is of a fawnish colour, or even of normal colour. The pruritus is unbearable. Owing to scratching, a secondary pyogenic infection or an eczematous-like dermatitis may develop. The disease, if not properly treated, is extremely chronic; the condition improves during the cold season, but gets worse again during the hot months. Patients who suffer badly from dhobie itch may get almost well in a few days, without any treatment, on going to the hills; on returning to the plains the pruritus and all the other symptoms reappear. The affection has been known to last for many years. It is to be noted that after a time the eruption may spread to the other parts of the body—the abdomen, the trunk, legs, etc. In such situations it may develop in rings, or may form solid elevated dark red patches; while the disease may be clinically indistinguishable from ordinary tinea circinata. In some cases, though rarely, the eruption starts first on the chest and arms, and from there spreads later to the armpits and cruro-inguinal regions.

Clinical Varieties.—The above description mostly applies to the disease as produced by *Epidermophyton cruris*, which is the commonest fungus found, and by *Ep. perneti*. In the cases due to *Ep. rubrum* the affected parts often present from the very beginning an eczematoid appearance. The edge is perhaps not so raised as in other types of tinea cruris, but very abrupt, made up of numerous rather small, close-set papules, covered at times by minute bloody crusts due to scratching. The eruption may also be present in the shape of large complete or incomplete gyrations enclosing normal skin, or solid patches may be seen. The variety due to *Ep. rubrum* has great tendency to spread to other regions of the body.

In the cases caused by *Trichophyton nodoformans* the eruption has thick elevated margins, and along the edge deep-seated nodules resembling 'blind boils' are present, the fungus being capable of attacking the hair follicles and having pyogenic properties. The infection may spread from the inguinal regions to other parts of the body. We have seen a case presenting a nodular eruption due to this fungus in the groins, and at the same time presenting a typical kerion barbæ due to the same organism on the right cheek.

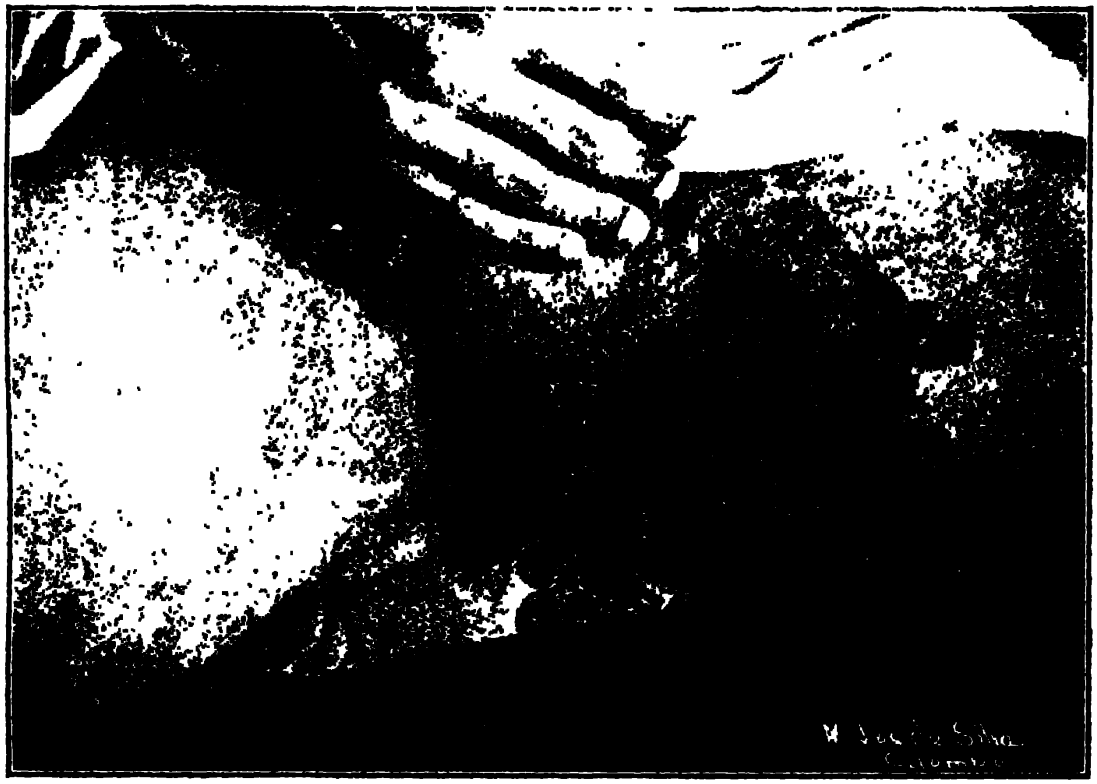


FIG. 801.—DHOBIE ITCH OF THE CRURO-INGUINAL REGIONS: TINEA CRURIS. From the same case (Tri [illegible] *yton cruri* Castellani) as [illegible] ed plate.

Regions of the Body affected.—The eruption, as already stated, is generally localized to the cruro-inguinal and axillary regions, hence the name 'tinea cruris seu inguinalis': but the same fungi may spread in many cases from those regions to any other part of the body, except the scalp. In some few cases the eruption may first appear on the arms or chest, etc., and then spread to the groins and armpits, or may never affect these regions. Hence the terms 'tinea cruris' and 'tinea inguinalis' are not altogether appropriate, and the term 'tinea tropicalis,' or the native term 'dhobie itch,' might be used as general terms to cover all the localizations.

A localization of great importance noted by Sabouraud, and later

PLATE VIII.

TINEA CRURIS

[illegible]

by Whitfield, is when the fungi invade the skin between the toes (tinea interdigitalis). In this situation the fungus—it is generally *Ep. cruris*—may remain for years, the fungus *per se* giving rise to practically no objective symptom, except perhaps a little scaliness, but generally induces very severe pruritus, especially in the hot weather. This localization of the fungus is often the starting-point of secondary bacterial affections causing a most distressing dermatitis, known to the planters by the name of 'mango toe,' and already described on p. 2036.

Communicability. Tinea cruris is known in the East as dhobie itch, from the popular belief that it is contracted from linen which has been contaminated while being washed by the dhobie (native laundryman). As to how far this belief is correct we are not in a position to say. We have never succeeded in finding the fungus in clothes newly received from the dhobie, either microscopically or by inoculating small portions of the linen in sugar media. We are, however, inclined to think that the popular belief may to a certain extent be correct. We have been told by old sufferers from dhobie itch, who used to be frequently reinfected, that on their ceasing to give their clothes to the dhobie, and having them washed in the house instead, the disease did not again affect them.* In Colombo dhobies are in the habit of washing the clothes in a lake,

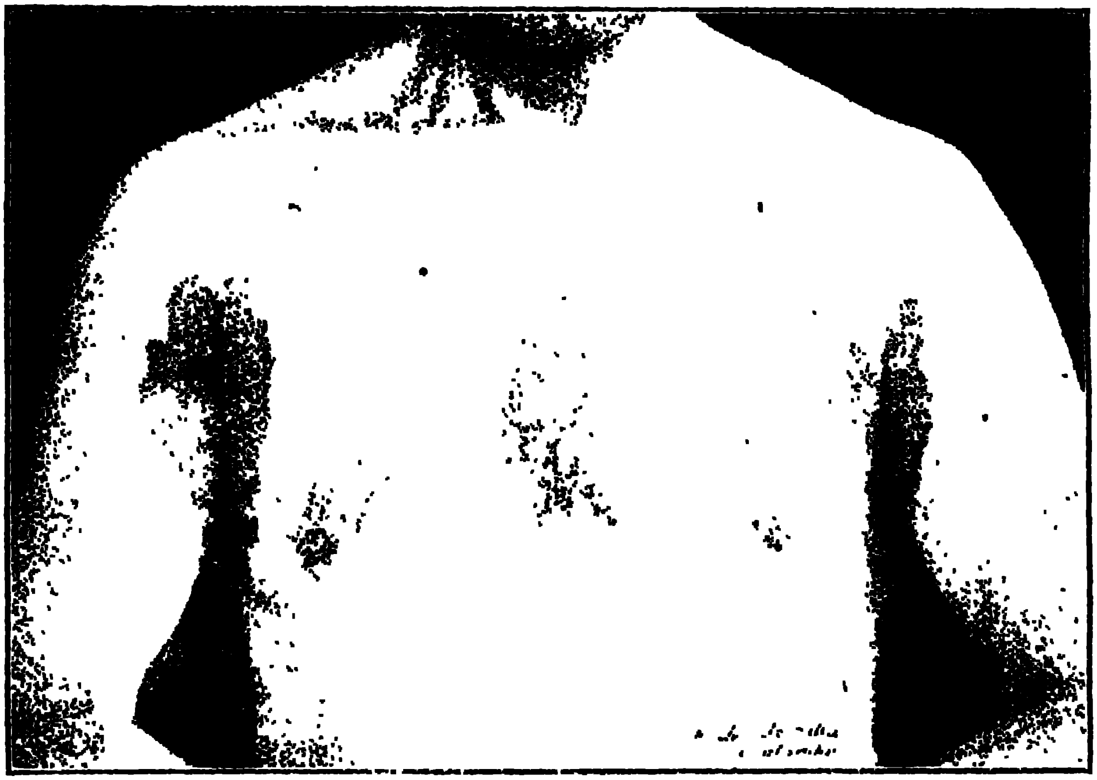


FIG. 802.—DHOBIE ITCH OF [illegible] AXILLARY REGIONS: TINEA AXILLARIS. Case due to *Epidermophyton cruris* Castellani.

or in small pools of water more or less stagnant. It is certain that clothes belonging to infected persons are washed together with other clothes. Dhobie itch is very contagious; true epidemics occur in schools and among soldiers in barracks.

Prognosis.—If the affection is not energetically treated, it has a tendency to become very chronic and last for years. Occasionally the eruption spreads to the whole body, forming rings or solid patches; at other times a distressing dermatitis develops on old dhobie-itch patches, due to scratching. Tinea cruris may disappear during the cold season, or when the patient goes to the hills, only to reappear as soon as the hot season commences. During the period of quiescence the skin of the affected regions often shows a brownish discoloration, furfuraceous, somewhat similar to erythrasma.

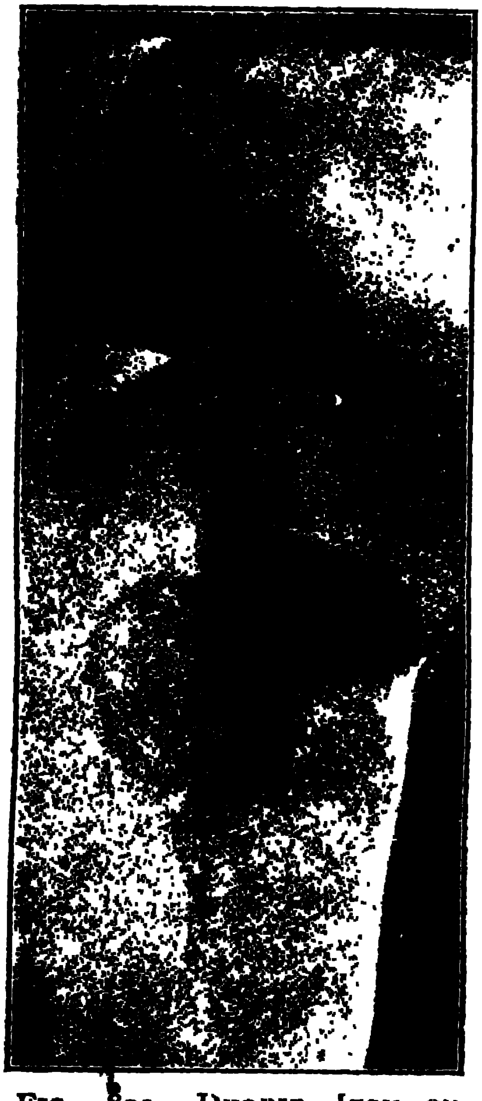


FIG 803.—DHOBIE ITCH OF THE AXILLARY REGIONS: TINEA AXILLARIS.

Case due to *Epidermophyton cruris* Castellani.

Diagnosis.—The diagnosis is easy in recent cases, the festooned appearance of the eruption, limited by a sharp, elevated, bright red edge, being quite typical. In old cases, especially when secondary lesions due to scratching are present, the diagnosis may be very difficult, the affection being often mistaken for eczema.

In doubtful cases the microscopical examination will be of great help. It must, however, be noted that in old cases the fungus may be extremely scarce, the mycelium being practically absent, and only a few spores being found; it is well to take the scrapings for microscopical examination from the edge of the eruption. The differential diagnosis must be made from erythrasma, intertrigo, and eczema.

In *erythrasma* the patches have a fawnish or dark reddish colour, and present often a fine pityriasic desquamation; the eruption is not limited by a raised red edge; the fungus *Nocardia minutissima* Burchardt is quite different from the fungi found in dhobie itch.

Intertrigo is very common in the tropics, especially in corpulent persons. The lesions are very superficial, have not a festooned contour, and the margin is not sensibly elevated; no *Epidermophyton*-

or *Trichophyton*-like fungi are found. Saccharomycetic intertrigo is rare; there is no elevated margin, and the fungus is found to be a Saccharomyces (*S. samboni*).

Primary eczema of the scrotum, and of the skin of the thighs in contact with it, is as frequent in the tropics as it is in temperate zones. The eczema is generally of the moist variety; the moist surface, the absence of the festooned elevated margin, distinguish it from tinea cruris. As already stated, however, an eczematous-like dermatitis due to scratching often develops after a time on old dhobie itch lesions.

Diagnosis of the Toes' Localization.—The complaining of severe itching between the toes, even if there are no objective symptoms whatever, should in the tropics always arouse the suspicion of a possible local fungus infection, especially if the patient suffers at the time, or has been suffering, from tinea cruris, and scrapings should be made and examined microscopically. It is important to make the diagnosis, as by treating the condition the development of that distressing dermatitis known as mango toe (see p. 2036) may often be prevented.

Treatment.—Our usual line of treatment is as follows:—

Mild Cases.—A resorcin salicylic ointment applied twice daily: Resorcin, ʒi.; salicylic acid, gr. x.; vaseline, lanoline, āā ʒiv. Tincture of iodine also is very efficacious, but induces a certain amount of smarting, and must be applied with care and in only very recent cases with no eczematoid lesions. In some cases we use Vleminckx' solution or lotio calcii sulphurati (slaked lime 4, sublimed sulphur 4, distilled water 35; boil together, evaporate, and filter to produce 20 of solution), pure or diluted. A sodium hyposulphite solution (sodium hyposulphite ʒii., aq. ℥i.) may also be used.

Severe Cases.—We use a chrysarobin ointment (2 to 5 per cent., a good formula being chrysarobin gr. x.-xxv., unguentum zinci ℥i.). The result is generally fairly successful. The patient should be informed that the medicine stains the linen, often irritates the skin, which may become œdematous and dusky red, and that occasionally unpleasant evidences of absorption may take place, with fever, diffuse erythema, and hæmaturia. Chrysarobin should never be used when there is some affection of the kidneys. The irritation induced by the chrysarobin ointment may be allayed by calamine lotion, lead lotion, or an ichthyol ointment 1 per cent.

Chrysarobin is obtained from araroba, which is known by the name of 'goa-powder' all over the East. The crude goa-powder, partly dissolved in vinegar, is often used, but frequently induces very severe inflammatory symptoms.

In obstinate cases we use local applications of turpentine-oil in the morning, and at night a resorcin salicylic ointment; if the parts are much inflamed, at night simply a boric ointment. This treatment gives good results. Turpentine is generally well borne, but patients often complain of a smarting and burning sensation a quarter of an hour after the application. Exceptionally one meets with patients who cannot stand turpentine.

Cases complicated with Eczematous Dermatitis and Fissures.—In such cases, in our experience, it is better to use at first a soothing treatment by lead lotion, or a solution of resorcin (½ to 1 per cent.), or glycerin. boracis in rose-water, with the object of first healing the eczematous lesions. Later, to the rhagades which so often develop in the inguinal regions, we apply a solution of nitrate of silver (arg. nitr., gr. v.-xv.; sp. æth. nitr., ʒi.). We touch with this solution the rhagades and the moist parts: this application is somewhat painful, but the pain soon disappears, and the fearful itching is relieved almost immediately: moreover, the nitrate of silver destroys the fungus. At night we apply a mild ichthyol ointment (1 per cent.) or hazeline cream all over the eruption: as soon as the parts have become less moist, we begin the chrysarobin treatment. A precaution, which must always be observed during and after the treatment, to prevent reinfection is to dust all the undergarments with antiseptic powder for instance, Manson's powder (ac. bor., zinc. ox., amyli, āā p. æq.): salicylic powder (ac. salicyl., gr. x.; talci venet., ʒi.); menthol powder (menthol, gr. v.: alcohol, q.s.; talci venet., ʒi.): dermatol powder (dermatol, gr. xx.: talci, ʒi.) It is advisable to wear small bathing-pants, which can be washed in the house.

Treatment of Generalized Dhobie Itch.- When the eruption is diffused all over the body, the simplest treatment is as a rule the application of tr. iodi or lin. iodi, treating only one portion at a time A chrysarobin ointment (2 to 5 per cent.) may also be used.

Treatment of Dhobie Itch localized to the Toes.- During the quiescent periods, or when there is only pruritus and a little scaliness, tincture of iodine may be used, or an alcoholic solution of salicylic acid (2 per cent.). When there are acute symptoms of dermatitis, the treatment must be at first a soothing one, as described on p. 2037.

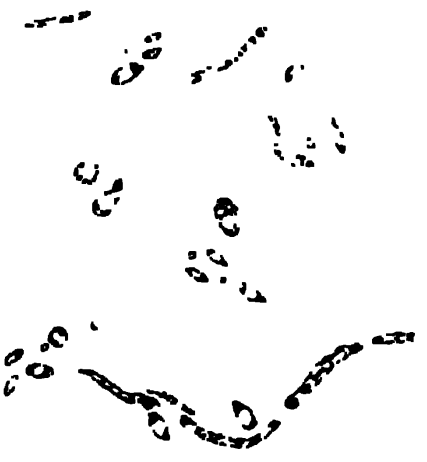


FIG. 804.—FUNGUS FOUND IN A VARIETY OF TINEA ALBA: *Atr. macfadyeni* CASTELLANI.

TINEA ALBA.

Remarks.—Tinea alba is in reality only a form of generalized dhobie itch; the term is applied to various diffuse trichophytic and epidermophytic conditions which give a white powdery appearance to the skin of the natives.

Historical.—This condition was first described by Castellani in 1905 in Ceylon. Cases have been recently reported by Pijper in South Africa.

Ætiology.—The commonest fungi found are *Epidermophyton rubrum* Castellani, 1909, and *Atrichophyton macfadyeni* Castellani, 1905 (*Trichophyton macfadyeni*), the description of which is given on pp. 1009 and 1016.

Symptomatology.—The arms, legs, chest, and occasionally the whole body, present a diffuse eruption of white powdery appearance, this being due to the very numerous small white pityriasic squamæ present. The margins of the eruption, when the causative fungus is *Ep. rubrum,* may be distinctly raised and dotted with minute, close-set papules.

Course and Prognosis.—The course is very chronic. Apparently the fungi have a disturbing action on the production of pigment in the skin, and after some years white leucodermic patches may develop, in which no fungus is found.

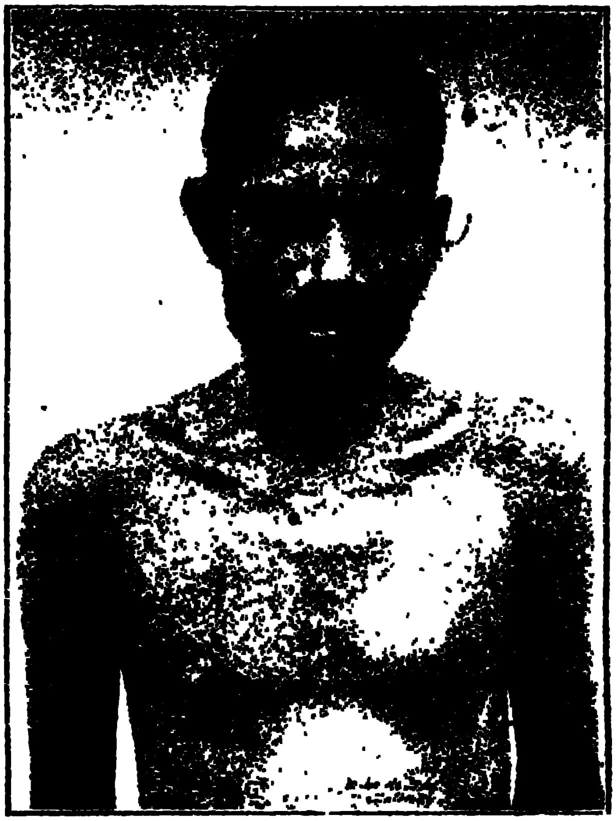


FIG ALBA DUE TO *ioum* CASTELLI

Diagnosis.—This is based on the diffuse eruption with the abundant fine pityriasic desquamation, and with well-marked limits—and the microscopical examination. It is quite easily distinguished from tinea imbricata by the squamæ being pityriasic, very small, easily detached. In leucoderma the surface is smooth, no squamæ being present and no fungus found. As already stated, however, if the eruption is left untreated for a long time, leucodermic patches may develop.

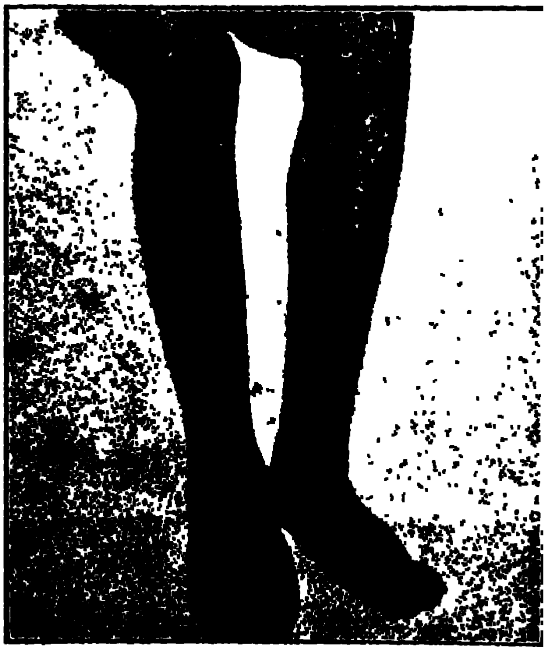


FIG. 806.—TINEA ALBA.

Treatment.—The best treatment is by a chrysarobin ointment (2 to 5 per cent.), applied with the precautions already mentioned. Tincture of iodine and liniment of iodine may also be used.

TINEA ALBIGENA.

This trichophytosis was first described by Nieuwenhuis in Java. Nieuwenhuis' researches have been confirmed and enlarged by Jeanselme in Indo-China and in Siam; in the latter country the disease is known as *khi*. The disease is fairly common in the Malay Archipelago, and is occasionally met with in Ceylon.

Ætiology.—The affection is due to a *Trichophyton* first described by Nieuwenhuis—*T. albiscicans* Nieuwenhuis, 1907.

The spores in fresh preparations from scrapings are almost always absent; the mycelium tubes are straight, occasionally showing a double contour; they are often dichotomous. Nieuwenhuis has grown the fungus, using Sabouraud's sugar media; the growth is very slow; the colonies are whitish, and show a powdery surface.

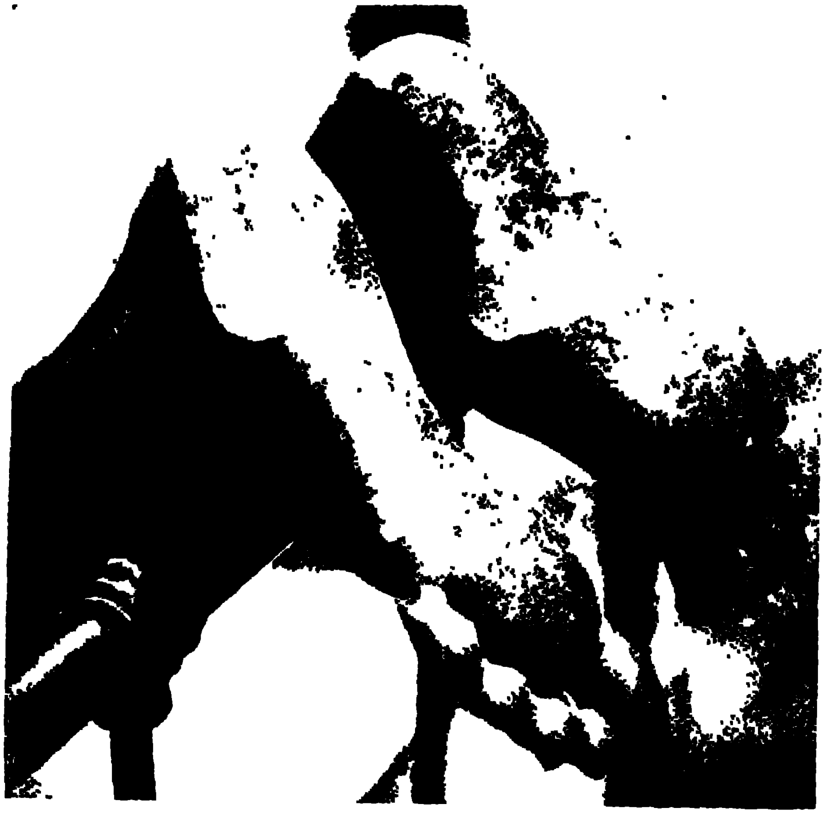


FIG. 807.—TINEA ALBIGENA.

Symptomatology.—The eruption generally affects the palms of the hands and the soles of the feet, but may extend to the forearms and legs, and may affect the nails. It begins with the appearance of small pruriginous spots on the palms and soles; the epidermis becomes raised, and bullæ develop, containing at first clear serum; the bullæ break, and the skin remains dry and peels off; the parts remain tender, and there is desquamation and pruritus. A process of diffuse keratosis develops, the palms and soles becoming double their usual thickness; deep fissures may be formed at the natural folds. Several horny semidetached discs can often be seen at the dilated orifices of the sweat glands. The affection is very chronic; it may begin in youth or in adult life. After some time a process of apigmentation of the skin sets in, white patches, leucoderma-like, developing, and extending often to the legs and arms.

Treatment.—Tincture of iodine and chrysarobin ointment (1 to 5 per cent.) answer fairly well, but the apigmented patches are not cured.

TINEA SABOURAUDI TROPICALIS.

This trichophytosis was first described by Sabouraud in patients returning from Indo-China, Japan, and Tonkin. We have seen a few cases in Ceylon.

Ætiology. The disease is caused by the fungus *Trichophyton blanchardi* Castellani, 1905 (synonym, *T. sabouraudi* Castellani, 1905). The term *T. sabouraudi* cannot be applied to this *Trichophyton*, as this name has already been used for another *Trichophyton* -*T. sabouraudi* R. Blanchard, 1905. This fungus cannot be grown on Sabouraud's media or any other media we have tried. Microscopically the mycelial tubes do not show a double contour, and are not very straight; they are often banana-shaped. The segments of the mycelium are all separated: the mycelial spores are roundish, and are shed without forming a filament by their union. They are of various sizes.

Symptomatology.- The eruption generally commences on the uncovered parts of the body, generally on the legs: the patients often state that they think the disease is due to prolonged immersion in stagnant water. The affection begins with erythematous patches, the surfaces of which are covered with minute pityriasic squamæ. After reaching the diameter of about 1 or 1½ inches, the patches become circinate. The circination, however, is incomplete; it is only segmentary. In dependent positions large polycylic patches may be seen, but only one-half or one-third of the circles are clearly seen, the rest being badly defined. The base of the patches at this stage is of a very dark bistre-brown colour. The border shows polymorphic lesions, fine pityriasic squamæ, minute vesicles and papules. The pruritus is very marked, and excoriations, due to scratching, are constantly present. In chronic cases a thickening of the skin, with lichenification, takes place, specially at the circinate borders.

Treatment.- - The disease is difficult of cure in the tropics, though it may disappear spontaneously on the patient proceeding to Europe. Chrysarobin ointment (1 to 4 per cent.) is the best treatment.

TINEA NIGRO-CIRCINATA.

This trichophytosis has been observed by one of us among Sinhalese natives.

Ætiology.—The eruption is due to a *Trichophyton*—*T. ceylonense* Castellani, 1908. The spores are very few in number, roundish, rather large (4 μ), and showing a double contour. The mycelial tubes are about 3½ μ in breadth, generally straight. The fungus does not grow on any of the ordinary or Sabouraud's media.

Symptomatology.—The eruption is found most frequently on the neck and scrotum, and consists of a few rings with thick, elevated margins, the encircled skin being black—much darker than the healthy skin—but not thickened nor presenting papules, vesicles, or pustules. The edge is thick, elevated, of a dark colour, with the upper portion pinkish or occasionally covered by a dark crust. The eruption often heals spontaneously, leaving dark roundish patches at the previous seat of the lesions.

Prognosis.—The eruption may disappear spontaneously, and the treatment is easy.

Diagnosis.—The only dermatomycosis to which it has a slight resemblance is *Tinea sabouraudi*. The latter, however, is very chronic, and invades large portions of the body; the rings are segmentary, not complete, and the edge is not so thick and elevated.

The condition may have also to be distinguished from a circinate frambœside or ringworm yaws, in which no fungus is found, while *Treponema pertenue* Castellani, is present.

Treatment.—Tincture of iodine, freely applied, answers well.

TINEA CAPITIS TROPICALIS.

Definition.—Tinea capitis tropicalis is ringworm of the head as seen in the tropics.

History.—Celsus in the second chapter of the sixth book of his 'De Medicina' gives an account of ringworm of the head under the name 'porrigo.' His words are: 'Porrigo autem est, ubi inter pilos quædam quasi squamulæ surgunt, eæque a cute resolvuntur; et interdum madent, multo sæpius siccæ sunt.'

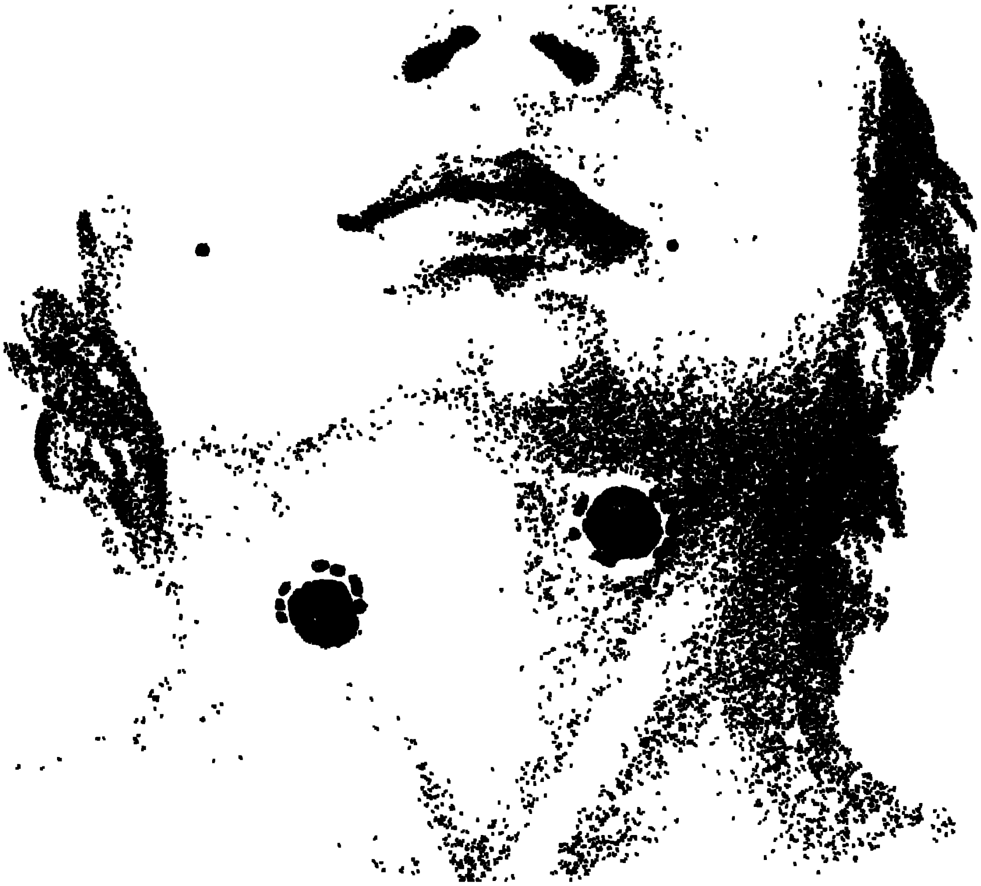
Bishop Fortunatus, who lived in the sixth century A.D., uses the name 'tinea' in the following passage: 'Lavans capita egenorum, defricans quicquid erat, crustam, scabiem, tineam nec purulentam fastidiens.'

In the tenth century Ali ben Abbas (often written Haly), who lived in Persia, described the complaint under the terms 'sahafati' and 'alvathim.'

The Anglo-Saxons applied the word 'teter' to any kind of skin disease which itched, and in this form it was used in middle English. In the fourteenth century Guy de Chauliac wrote a work on surgery in which he used the word 'teigne,' deriving it from 'tenir.'

With the advent of printing it was called 'tetters,' in England

PLATE IX.



TINEA NIGRO CIRCINATA.

Geo. Waterston & Sons, Ltd. Edin.

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(*vide* Langham's 'Garden of Health,' 1633), but in or before the sixteenth century the word 'ringworm' (*vide* Levins or Levens, 'Manipulus Vocabulorum,' London, 1570) had appeared for the disease tinea circinata. In 1695 Willis in his 'London Practice of Physick' devoted a chapter to the subject of the running scab, tetter, or ringworm.

With a history such as this it is not astonishing that the early English writers on tropical medicine refer to the same disease as seen in tropical countries.

Thus in 1746, in his work on the diseases of Barbados, Hillary says that it was noticed by the first voyagers to the West Indies, and that it probably is the same disease as that called by the natives 'cowrap.' He gives a good clinical description of tinea circinata as he saw it in Barbados, and he is supported by Wright ('Essays on the Malignant Fever of the West Indies'), who stated that it was common in Jamaica.

Winterbottom in 1803, under the term 'herpes,' describes the disease in Sierra Leone, calling it serpigo, ringworm, or tetters, and distinguishing it from kra-kra.

So far it would appear as though only the body ringworm or tinea circinata was meant by the terms 'tetters' and 'ringworm,' but in 1817 Bateman, the pupil of Willan, who completed his master's great work on skin diseases, published an atlas on the same subject, in which Plate XXXIX. induces Sabouraud to believe that he recognized the identity of the two conditions. In 1824 Plumbe showed that inoculation of ringworm of the scalp would cause ringworm of the body, and *vice versa*.

These publications appear to have stirred the practitioners of the tropics to study the disease, as it was described in India by Young, in 1826, and in the Malay Archipelago by Lesson, in 1829.

In 1832 Alibert published the first edition of his celebrated 'Monographie des Dermatoses,' which stimulated the continental medical mind of the day, as is reflected by Smith's description of the disease in Peru, in 1840, and Pruner's in Egypt, in 1847.

In 1839 Schönlein discovered the fungus causing favus.

In 1842 Gruby, who had already repeated Schoenlein's observations on the parasite of favus, discovered a new cryptogam in tinea barbæ, which was an ecto-endothrix.

In 1843 he found *Microsporum audouini*, and six months later, on April 1, 1844, he described an endothrix as the parasite of herpes tonsurans. It is, however, but just to state that, without Sabouraud's generous treatment, much of Gruby's work might have been permanently overlooked.

In 1845 Malmsten gave the name of *Trichophyton* to the parasite of tinea tonsurans.

It is asked that the reader will kindly observe the spelling of the names of these two genera. Gruby called the one *Microsporum*, not Microsporon, and Malmstén named the other *Trichophyton*, not Trichophytum.

These researches naturally aroused much interest, and in 1855 Heymann showed that the disease existed in the East Indies, but it is noticeable that he makes no mention of observing a parasite in the affection.

In 1874 Blanc described the occurrence of the disease in Abyssinia, where Merab states that it is very common, and where it is treated by the juice from the fruits and leaves of *Bryonia deoica* and by tobacco powder, as well as by sulphur ointment.

In 1872 the Army Sanitation Commission induced the British Government to instruct Tilbury Fox and Farquhar to obtain a better knowledge of the endemic skin diseases of India, and to bring about an agreement between the profession in India and England as to nomenclature, typical characters, varieties, and probable causes of these diseases. Thanks to the interest of Lord Granville, Lord Kimberley, and Sir Alexander Armstrong, this inquiry was extended to China, Japan, Egypt, Algeria, the West Indies, and Honolulu, and the finished report was published in 1876.

The net result of this inquiry as far as ringworm was concerned was unfortunate, as it led to the dogmatic assertion that the ringworm of the body in the tropics was the same as that of temperate climes.

In 1873 van Leent drew attention to the large number of cases of ringworm of the head in Chinese in the island of Banka, in Malaysia.

In 1878 Corre gave a description of the disease and its parasite as seen in Nossi-Bé.

From 1890 the possibility of plurality in the species of Trichophyton was raised, but it was not until Sabouraud in 1892 began those brilliant researches which he has carried on to the present day that this was definitely established. In this year he showed that ringworm of the scalp could be divided into two main groups—viz., those with small spores belonging to the genus *Microsporum* Gruby, 1843, and those with large spores belonging to the genus *Trichophyton* Malmsten, 1848. The large-spored fungi of the scalp he divided into five species, which were afterwards named *Trichophyton crateriforme* = *T. tonsurans*, *T. acuminatum* = *T. sabouraudi*, *T. gypseum*, *T. violaceum*, and *T. rosaceum*.

In 1893 he further divided the Trichophytons into two groups, which he named Endothrix and Ecto-Endothrix (Ectothrix), and which corresponded with Gruby's two divisions. His researches were speedily confirmed by many observers, among whom may be mentioned Adamson, Colcott Fox, Malcolm Morris, White, and Mibelli.

In 1900 Matruchot and Dassonville showed that the Trichophytons were closely allied to the Gymnoascaceæ, and that *Ctenomyces serrata* Eidam, 1880, when injected into animals produced a Trichophyton-like mycelium and eruption.

The further history may perhaps be better discussed according to the countries.

Brazil.—The history of ringworm in Brazil appears to date from the appearance of Silva Araujo's 'Atlas des Maladies de la Peau,' which contained an account of favus and of a Trichophyton causing sycosis, both supported by microscopical observations.

Later Fernando Terra grew *Achorion schoenleini* from an atypical case of favus, and some form of fungus from a case of tinea capitis tropicalis, which was traceable to infection from a cat, and was therefore probably *T. felineum*. The sixth Brazilian Congress of Medicine and Surgery, held in 1907, is remarkable for the appearance of papers on ringworm in which the parasitic fungi were studied according to Sabouraud's classical methods. It was at this meeting that Rabello announced that he had found *T. violaceum*, *M. audouini*, and *M. lanosum*.

In 1909 Lindenberg reported the presence of *T. sabouraudi*. Horta announced that *M. felineum* has been found in a considerable number of cases at São Paulo, and also isolated *T. album* Sabouraud, 1907.

In 1911 Horta discovered *M. flavescens*, and in 1914 he found a new Trichophyton, which was subsequently described and named *T. griseum* by Vasconcellos.

Argentina. In 1907 Uriburu discovered *M fulvum*, and in 1909 *T. exsiccatum* and *T. polygonum*.

Central America.—In 1913 Brumpt named a peculiar parasite, discovered by Darier in a dermatosis resembling pinta, *T. carateum*. This disease was found in Central America.

Africa.—In 1896 Cournont described two forms of tinea capitis tropicalis seen in Senegal

In 1902 Bodin found *T. violaceum* Bodin in North Africa.

In 1904 Jeanselme announced that Coumnont had found *M. audouini* among the negroes of Senegal, and that Sabouraud and himself had found a Trichophyton (subsequently named *T. circonvolutum* by Sabouraud in 1909) in white people returning from the Western Sudan.

In 1912 Joyeux discovered *T. soudanense* in the Western Sudan.

Ceylon.—In 1905 Castellani discovered *T. violaceum* var. *decalvans* in tinea capitis tropicalis, *T. macfadyeni* Castellani, in tinea corporis tropicalis, and *T. blanchardi* Castellani in tinea sabouraudi tropicalis a term also used for the disease caused by *T. circonvolutum* Sabouraud.

In 1908 he observed *T. ceylonense* Castellani, in cases of tinea nigro-circinata.

In 1912 he found *T. nodoformans* Castellani in tinea barbæ tropicalis and in tinea ciliorum.

Tropical Queensland.—In 1914 Priestley discovered *M. scorteum* Priestley in tinea corporis tropicalis.

In the Anglo-Egyptian Sudan Chalmers and Marshall found *Trichophyton currii* Chalmers and Marshall, 1914, to be the cause of an epidemic, and later *Trichophyton discoides* Sabouraud, 1909, in one case, while Chalmers and Macdonald have met with numbers of cases due to *T. violaceum* Bodin, 1902, var. *khartoumense*.

Geographical Distribution.—Tinea capitis is found in every part of the tropics, but its incidence varies from country to country, and is far less common than epidermophytoses and trichophytoses of the body.

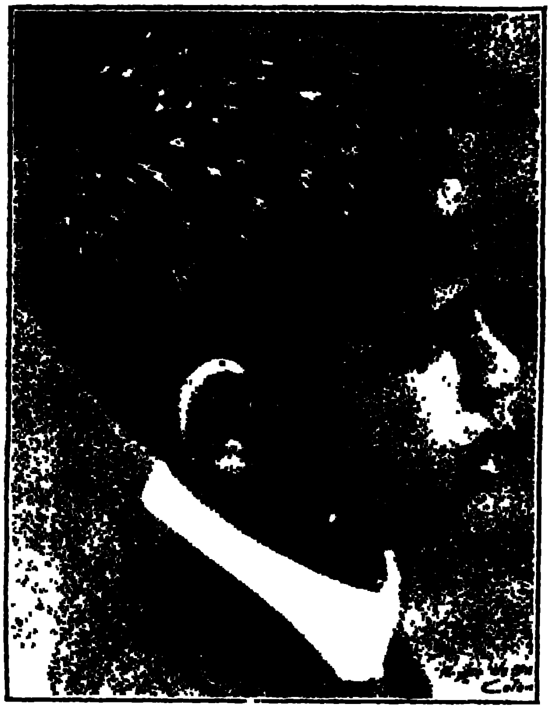


Fig. 808. Tinea Capitis due
Tr. violaceum Bodin var. *decalvan*

In our experience tinea capitis is less common in India, Ceylon, and tropical Africa than in Europe and America. On the other hand, it is extremely common in American negroes.

Ætiology. — The following fungi have been found in cases of tinea capitis tropicalis:—

Genus Microsporum Gruby, 1843.

1. *M. audouini* Gruby, 1843, in Brazil, Western Sudan, Northern Africa and Madagascar.
2. *M. fulvum* Uriburú, 1907, in the Argentine.
3. *M. scorteum* Priestley, 1914, in Tropical Queensland.

Genus Trichophyton Malmsten, 1848.

1. *T. circonvolutum* Sabouraud, 1909, in Senegal and Dahomey.
2. *T. exsiccatum* Uriburú, 1909, in the Argentine.
3. *T. polygonum* Uriburú, 1909, in the Argentine.
4. *T. sabouraudi* R. Blanchard, 1895, in Brazil.
5. *T. soudanense* Joyeux, 1912, in Western Sudan.
6. *T. violaceum* Bodin, 1902, in North Africa.
7. *T. violaceum* Bodin, 1902, var. *decalvans* Castellani, 1905, in Ceylon.
8. *T. violaceum* Bodin, 1902, var. *khartoumense* Chalmers and Macdonald, 1915, in the Sudan.
9. *T. currii* Chalmers and Marshall, 1914, in the Sudan.

Genus Ectotrichophyton Castellani and Chalmers, 1918.

E. discoides (Sabouraud, 1909) in the Anglo-Egyptian Sudan.

Genus Achorion Remak, 1845.

1. *A. schoenleini* Lebert, 1845, in the Anglo-Egyptian Sudan Egypt, Tunis, Tripoli, Algeria, China, causing favus.
2. *A. quinckeanum* Zopf, 1890; the cause of mouse-favus, rarely infects man.

3. *A. gypseum* Bodin, 1907; very rare.

The description of all these fungi is found in Chapter XXXVIII., p. 988.

Symptomatology.—It may be said in a general way that the principal clinical signs are the same in the tropical types of the affection as in the temperate zones, though the medical man who has studied the subject thoroughly will soon be able to detect small clinical differences, and will soon realize that as a general rule each species of fungus gives rise to a slightly different type of disease.

Tinea Capitis Microsporica (*Microsporosis*).—Tinea capitis due to fungi of the genus microsporum, usually known by the term microsporons in dermatological literature, is rare in tropical and subtropical countries. The affection attacks, usually, only children. The affected patches are studded with stumps of broken hair, which are loosened and brittle, have lost their natural gloss, and show a whitened appearance caused by the fungus producing a greyish sheath round the hair. The microscopical examination of the affected hair after treatment with liquor potassæ will show presence of so-called spores, roundish or ovoid, 2-4 μ in diameter, irregularly distributed, while those of the trichophytons are often larger (3-8 μ), square with rounded angles, or somewhat oblong, and arranged in definite regular chains.

Tinea Capitis Trichophytica (*Trichophytosis*).—This is common in the tropics and may be caused by a number of trichophytons which have been mentioned in the Ætiology. In Chapter XXVIII., p. 995, we have given a botanical classification of the genus Trichophyton, creating several subgenera. In most dermatological works, however, a simpler classification is followed. Two groups are differentiated: *endothrix* and *endo-ectothrix*, the latter corresponding to the original Sabouraud's ectothrix. The endo-ectothrix group is subdivided into two types: with large spores (megaspores), with small spores (microïdes). Those of the microïdes type produce a greyish sheath round the hairs, like the microsporons, but the so-called spores are arranged in regular chains, a feature never observed in the microsporons. The microïdes trichophytons are pyogenic, and often cause kerion.

As we have already stated, each species of trichophyton gives rise to a slightly different clinical type of the affection. Among the many types we may briefly notice "Black dot tinea tonsurans" and "Tinea decalvans tropicalis."

Black-dot Tinea Tonsurans.—This type is common in Europe, but is at times observed also in subtropical and tropical countries. It is caused by *Trichophyton sabouraudi* Blanchard, usually known in dermatological literature by the name of *Trichophyton acuminatum*. The scalp presents scurvy patches with minute dark dots, best seen with a lens. These dots are pigmented, coiled up stumps.

Tinea Decalvans Tropicalis.—This variety, described by Castellani, is common in Ceylon. It generally attacks children, especially of the moormen community. The scalp presents one or several white patches covered with an enormous number of heaped-up white pityriasic scales. The scales and the broken hairs, examined microscopically, show presence of an endo-ectothrix fungus, which, when cultivated, shows some characters of *T. violaceum* Bodin (*T. violaceum* Bodin var. *decalvans* Castellani). A very serious symptom is that the patches as a rule remain permanently bald.

Tinea Capitis Favica (*Favus*).—This affection, common in Southern and Eastern Europe, is found in some subtropical countries, such as certain parts of North Africa and China, but is rare in the tropics. The condition is recognized by the sulphur-coloured cup-shaped scabs, the peculiar mousy odour and presence of atrophic scarring. The hair is lustreless and discoloured, but does not break off as in ringworm.

Diagnosis.—This is based on the clinical characters mentioned, and on the microscopical examination of the hairs and squamæ in liquor potassæ. Cultural methods should also be used.

Prognosis. This is rather bad in the common variety found in Ceylon, due to *T. violaceum* var. *decalvans*, as the patches in most cases remain permanently bald, though fortunately they are, as a rule, of small dimensions. The treatment of every type of tinea capitis is long unless X rays are used.

Treatment. The Röntgen rays treatment, using Sabouraud's method, is by far the best and quickest. Details on the technique will be found in any up-to-date book on dermatology. In many tropical places this treatment is out of the question, and epilation and application of turpentine oil, tincture of iodine, or - with care - a chrysarobin ointment (2 to 5 per cent.) must be resorted to.

Garrett recommends the application of liquor ferri perchloridi fort. (B.P.) after thorough cleaning of the patches with benzene Sabouraud at one time recommended the internal administration of tallium acetate. Cicero uses a 5 per cent solution giving as many drops as is represented by twice the number of kilogrammes of the child's weight.

TINEA BARBÆ TROPICALIS.

The same remarks can be made on this subject as on tinea capitis. Cases are found in the tropics, though apparently less frequently than in temperate zones, and the fungi have so far been very little investigated. In Northern Africa a fungus commonly found is *Trichophyton violaceum* Bodin: in Ceylon *T. nodoformans* Castellani is often found.

Symptomatology.—The dry variety, with scaly, often gyrated lesions, and the pustular variety, with purulent folliculitis, can be distinguished.

We have seen a typical case of kerion barbæ due to *T. nodoformans* in a person who was suffering from tinea cruris due to the same fungus.

Diagnosis.—The diagnosis, in the pustular type, is based on the spreading folliculitis with brawny swelling and the microscopical examination of the hair: in the scaly type, on the frequent gyrate type of the eruption and the microscopical examination of the scales and hair.

Prognosis.—The disease takes a long time to get well, even under appropriate treatment.

Treatment.—This consists in epilation of the affected region, each day clearing a square inch or so, followed by the application of some antiseptic ointment such as Crocker's ointment of sulphur, ʒss.-ʒi.: ac. carbol., ʒss.; lanolin c̄ oleo, ℥i.: or oleate of copper, ʒss. to ℥i.

Tinea Ciliorum.

We have seen a case of this affection in a man suffering from generalized dhobie itch, due to *T. nodoformans*. The lid was swollen and red, many cilia were broken, and there was purulent inflammation of the hair follicles.

TINEA UNGUIUM TROPICALIS.

Synonym.- Onychomycosis tropicalis.

Cases of tinea unguium, or onychomycosis, occur in the tropics, and are generally due to the same fungi producing dhobie itch, both *Epidermophytons* and *Trichophytons*. The nails of the fingers as well as of the toes may be affected. Tinea unguium may be caused also by fungi of the genus *Endodermophyton*, the nails being often affected in tinea imbricata.

Symptomatology. The affected nails have often a peculiar yellowish opaque or blackish discoloration, and a rough surface; they become brittle, and splitting and chipping of the free border takes place.

The diagnosis is principally based on the microscopical examination of scrapings. A soaking in liq. potassæ (40 per cent.) for twenty-four hours is often necessary to disintegrate the nail substance and to find the fungi.

Treatment. This is most difficult. The affected nails must be softened by rubbing in liquor potassæ, and then wet dressings of hyposulphite of soda (25 per cent.), or a solution of potassium iodide grms. x., iodine grm. i., water 1,000 c.c., must be regularly applied. In the onychomycosis found in cases suffering, or having suffered, from tinea imbricata the daily application of resorcin in tincture of benzoin (ʒi. to ℥i.) is useful.

TINEA IMBRICATA (TOKELAU).

Definition.—The term 'tinea imbricata' is used to denote a tropical dermatomycosis, or, more correctly, a group of dermatomycoses, due to fungi of the genus *Endodermophyton* Castellani, and clinically characterized by the presence of extensive, flaky, scaly patches, the scales being large, tissue-paper-like, firmly adherent by their bases, and arranged in concentric rings or parallel lines.

Synonyms. As is the case with several other tropical diseases, such as framboesia and Oriental sore, there is a very large number of synonyms, which may be classified as follows:-

(*a*) From the name of the centres where the disease is rife: for instance, the term 'Tokelau,' generally used by French writers, is in reality the name of an island, Tokelau, where the malady is very common. Other synonyms are 'Tokelau ringworm,' used by Tilbury Fox, 'Bowditch ringworm,' the name Bowditch being used by some writers to indicate the island of Tokelau, 'South-west Gune,' the term 'gune' meaning skin.

(*b*) From the name of the patient who first introduced the disease in certain countries. In the island of Tokelau, for instance, the disease used to be known as 'Le Pita,' from 'Peter,' the name of the native of Tamana, one of the Gilbert Islands, who, according to Turner, in 1850 introduced the disease into Tokelau.

(*c*) From certain clinical appearances: 'Tropical ichthyosis,' a bad term, as in the tropics true ichthyosis is far from rare; 'Dermatomycosis chronica figurata exfoliativa' (Tamson); 'Herpes farinosus' (Ritter); 'Herpes desquamans' (Turner); 'Tinea imbricata,' a term introduced by Manson, and which is now the one most generally used.

(*d*) From the generic name given to the fungus: 'Aspergillosis' of Wehmer; 'Lepidophytosis' of Tribondeau; 'Endodermophytosis' of Castellani.

(*e*) From the name of the authors who have more completely studied the disease: 'Manson's herpes,' 'Turner's herpes,' etc., the term 'herpes' being used by Roux and others in the obsolete meaning of epiphytic skin disease.

(*f*) Terms apparently of unknown origin, such as 'Gugo,' a denomination much used in the Marshall Islands; 'Cascado,' a term used in the Molucca Islands; 'Buckwar,' etc.

History.—The first recognizable account of the condition is to be found in Dampier's 'Voyage Round the World,' published in 1789. Dampier saw the disease in the Philippine Islands in Mindanoa, in Guam, and in the Ladrone Islands. About the end of the same century Dentrescasteaux described cases of the same condition in Tonga. In 1811 Marsden observed it among the natives of Polo Mas, on the west coast of Sumatra. In Alibert's 'Atlas,' published in 1832, there is a reference to the disease. In 1841 the disease was recognized by the medical officers attached to the United States Exploratory Expedition led by Commodore Wilkes, and Fox in 1844 described it under the name of 'gune,' the term used by the Gilbert Island natives.

In the reports of the Samoa Medical Mission for the year 1869 there is a good description of the malady by Geo. Turner. In 1874 Tilbury Fox gave a description of the complaint under the term 'Tokelau ringworm,' and noted the presence of a fungus in the scales sent to him from the tropics. He considered it to be identical, or very similar to, the fungus of European ringworm. From the drawings given the fungus described by him seems, however, not to have been a trichophyton-like organism, but an aspergillus-like contamination. From that time discussion began, which went on for several years, on the subject whether the disease was a separate entity or merely European 'ringworm' modified by the different climatic conditions. Apparently the great majority of the European authorities, who, however, had no personal experience of the condition, were against considering the disease a separate one, while the medical men practising in the tropics generally believed it to be a different disease from ringworm. Valuable researches were carried out by McGregor in 1870 and Königer in 1878. Manson's researches on the malady—in China from 1879 to 1882—are by far the most important. He gave a complete clinical description of the malady, and introduced the very appropriate name of tinea imbricata; moreover, he very correctly described the microscopical appearances of its fungus, though, as might be expected, using the technique of that time, attempts at growing it did not succeed. More recently the condition has been studied by Tribondeau, Nieuwenhuis, Wehmer, and many others. Castellani has succeeded in growing the fungus artificially, and in reproducing the disease by inoculating pure cultures of it; he has shown also that there is more than one variety of the affection and more than one species of the fungus. He has

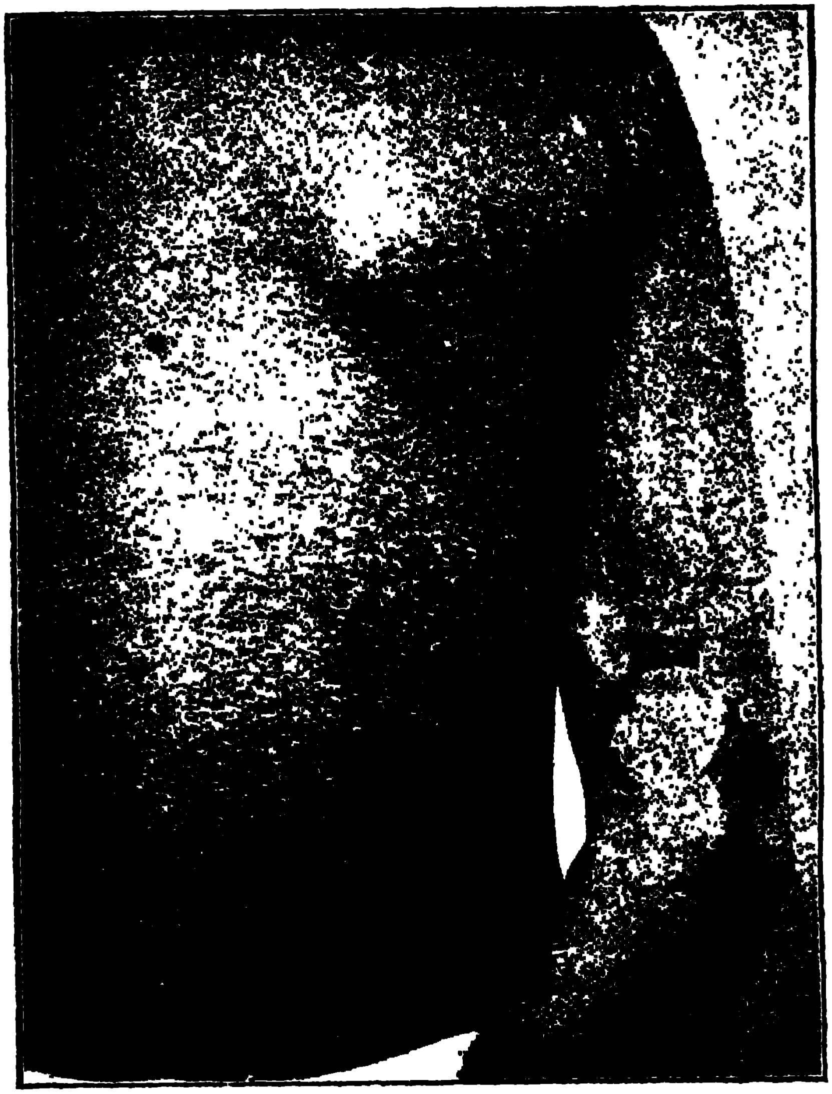


Fig. 809.—Tinea Imbricata.

demonstrated that the aspergillus-like fungi described by a number of authorities are merely saprophytes, and that the true ætiological agents are those fungi for which he has created the genus *Endodermophyton.*

Climatology.—The home of tinea imbricata seems to have been the Malay Peninsula, from whence it spread towards the south and the east to many islands of the South Pacific, northwards to some

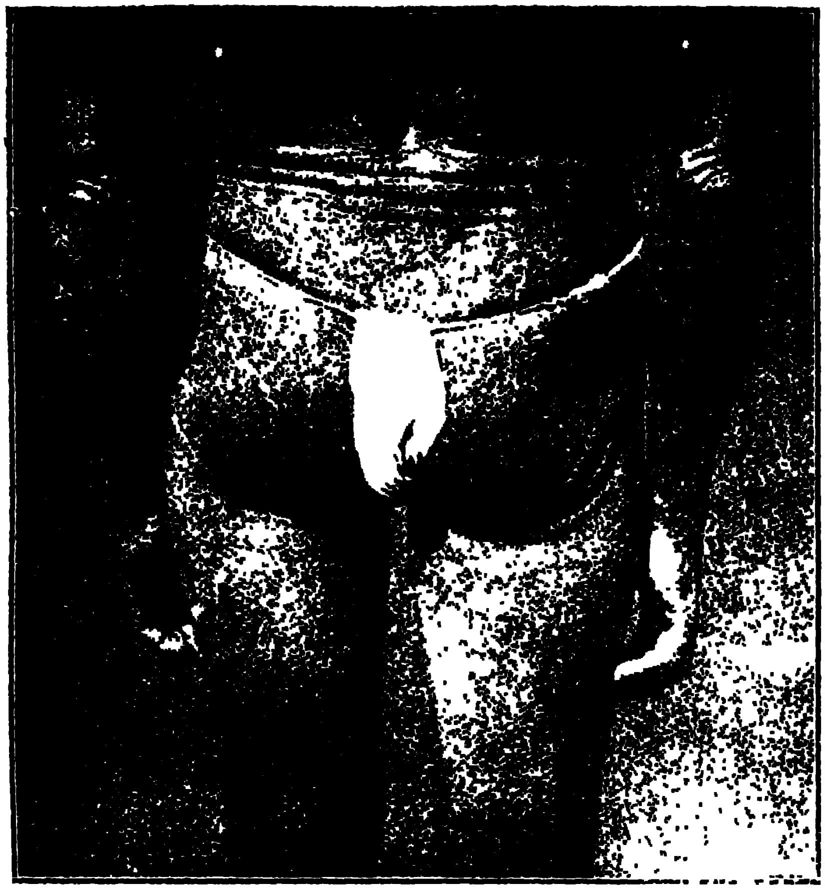


FIG. 810.—TINEA IMBRICATA.

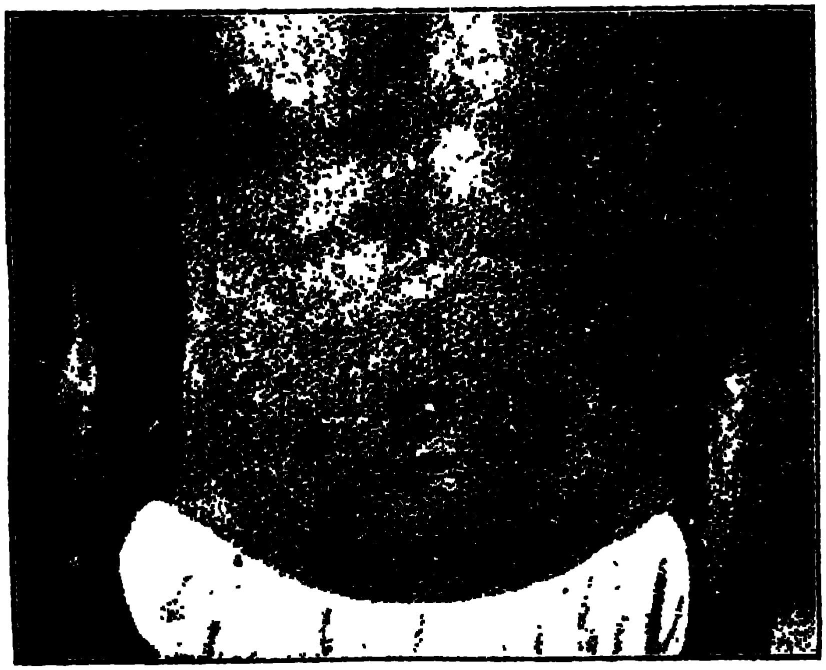


FIG. 811.—TINEA IMBRICATA.

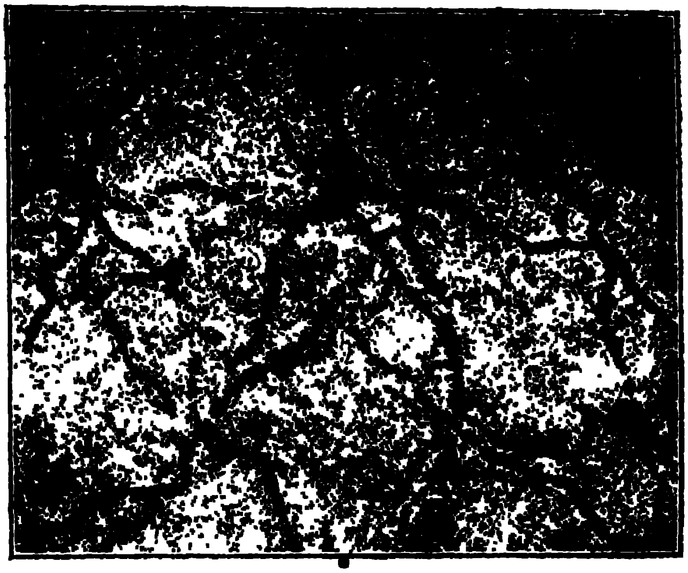


FIG. 812.—FUNGUS IN THE SCALES.
(From a stained preparation.)

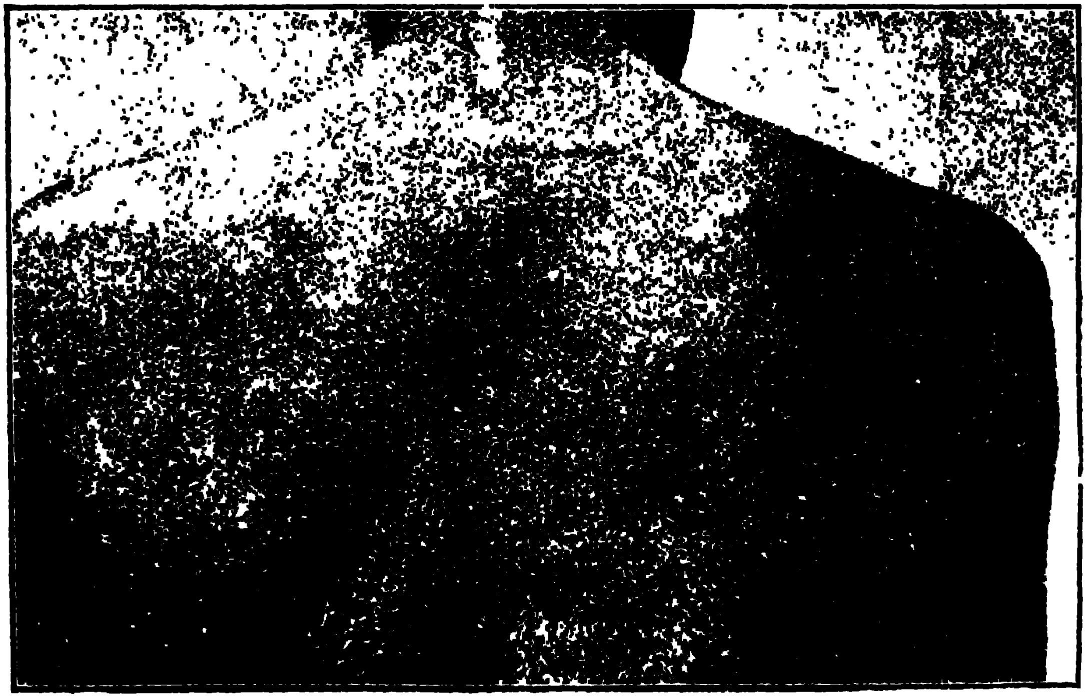


FIG. 813.—TINEA IMBRICATA.

parts of China, as far as Foochow and Formosa, and westwards to Burma and Ceylon. The Gilbert group of islands seems to have become heavily infected since the beginning of last century. In 1859 it is said that a native of Tamana, an island of the Gilbert group, affected with the malady, landed at Bowditch, an island called also Tokelau, in 1859. From that year onwards the disease spread rapidly all over the Bowditch or Tokelau Island. The Tamana man who brought the disease was called Peter, hence the disease became known in Bowditch or Tokelau as 'Le Pita' viz., 'The Peter.' From Tokelau the disease spread to Samoa, according to Turner and Königer, in 1869, and to many other islands, where it became known as Tokelau. At the present time the disease is extremely common in the Malay Peninsula, some parts of Indo-China and Southern

China, Borneo, Samoa, Java, the Solomon Islands, New Guinea, Sumatra, Fiji. According to Daniels, the disease was first introduced into Fiji by some Solomon Islanders in 1870, and within the following two years became extremely prevalent. In certain of the Pacific Islands one-third to one-half the population is affected. The disease is common in some districts of the Philippine Islands, the Ladrones, the Loyalty Islands, New Caledonia, and some districts of Burma. Until 1904 the disease was believed to be non-existent in Ceylon, but in that year Castellani recorded the first case. During the last few years the disease has greatly spread in this island, and it is now fairly common, though not so common as in the Malay Peninsula or Fiji. India is said to be so far immune, but two typical cases hailing from Southern India have been seen by Castellani. Cases have been reported from Brazil and other parts of tropical America, but some doubt has been expressed as to their being cases of true tinea imbricata. The cases so far reported from Africa are also doubtful.

FIG. 614—TINEA IMBRICATA.

The climatic conditions favourable to the rapid development and spread of the disease are represented by a warm, damp, equable climate, with a temperature of 80° to 90° F., the same climate, as Manson so truly remarks, that is favourable to the growth of cocoanuts; in fact, the geographical distribution of tinea imbricata corresponds almost exactly to the districts where cocoanuts thrive. In those countries which, though at certain times extremely hot, have a cold and cool season—such as many parts of India and China—the disease apparently does not spread.

Ætiology.—The ætiology of this dermatomycosis has been the subject of numerous controversies. Manson first, in 1872, described a trichophyton-like organism in the squamæ; with the laboratory technique of that time attempts at cultivation did not succeed. Blanchard considered it non-cultivable, and called it '*Trichophyton concentricum*'; on the other hand, Nieuwenhuis stated that it was quite easily cultivated direct on solid media from the squamæ, and was characterized by the colonies being crateriform. His results were not confirmed. In recent years the general opinion has been that aspergillus-like fungi were the real cause of the disease. Tribondeau described fructifications somewhat similar to those of an aspergillus, and created for the fungus the genus *Lepidophyton* (λέπις=scale; φυτόν=plant). Wehmer has described it as a true aspergillus—*Aspergillus tokelau*. The investigations carried out by Castellani have demonstrated that the aspergillus and aspergillus-like fungi have nothing to do with the disease. When they are present in the squamæ, they are merely saprophytes or contaminations. By using a special technique he has succeeded in growing the true fungi causing the disease, which must be placed in the genus *Endodermophyton*. Castellani recognized at first two species, and later four: *Endodermophyton indicum*, *Endodermophyton tropicale*, *Endodermophyton concentricum*, and *Endodermophyton mansoni*. It is probable that further investigation will reveal the existence of some more species. The description of these fungi will be found in Chapter XXXVIII., p. 1016.

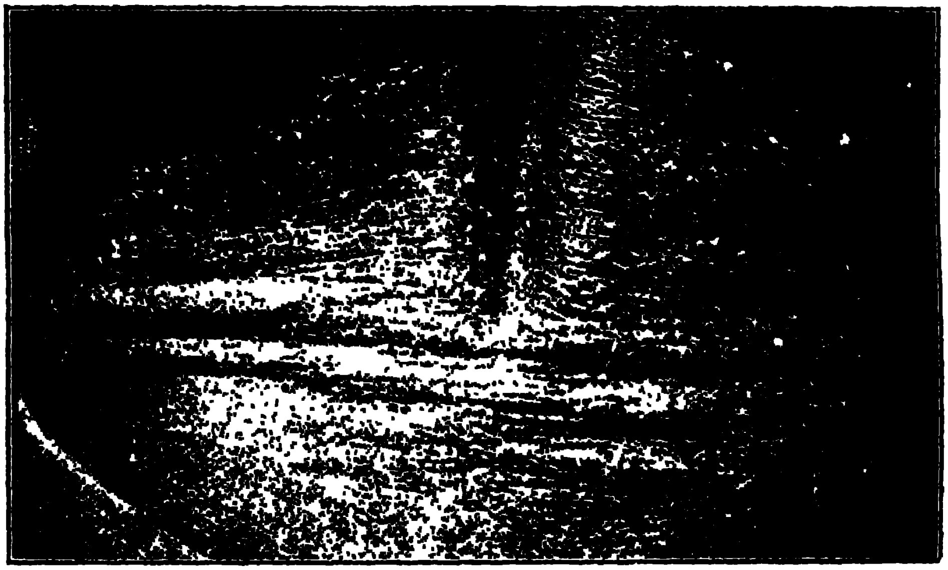


FIG. 815.—TINEA IMBRICATA.

Predisposing Causes.—As regards age, many authorities state that the disease is more common in children than in adults. In Ceylon, however, the condition is rare or absent in infants and children, while the persons affected are generally young adults, but it may be found also in very old persons. Women are attacked less frequently than men. Villagers and people living in the country are much more liable to contract the malady than people living in large towns. It is doubtful whether there is any racial disposition. In Fiji, however, it has been observed that while extremely common in the indigenous population, it is comparatively rare among the immigrant Indian coolies. The Tongans also are said to contract the disease rarely, and this relative immunity, according to them, is due to the habit they have of regularly anointing their bodies—a habit not shared by the Fijians. A hot, moist, equable climate seems to be the most suitable for the development of the fungus and the spreading of the disease. Manson has justly remarked that the climate which is suitable for the growth of cocoanuts is also the best for the fungus of tinea imbricata.

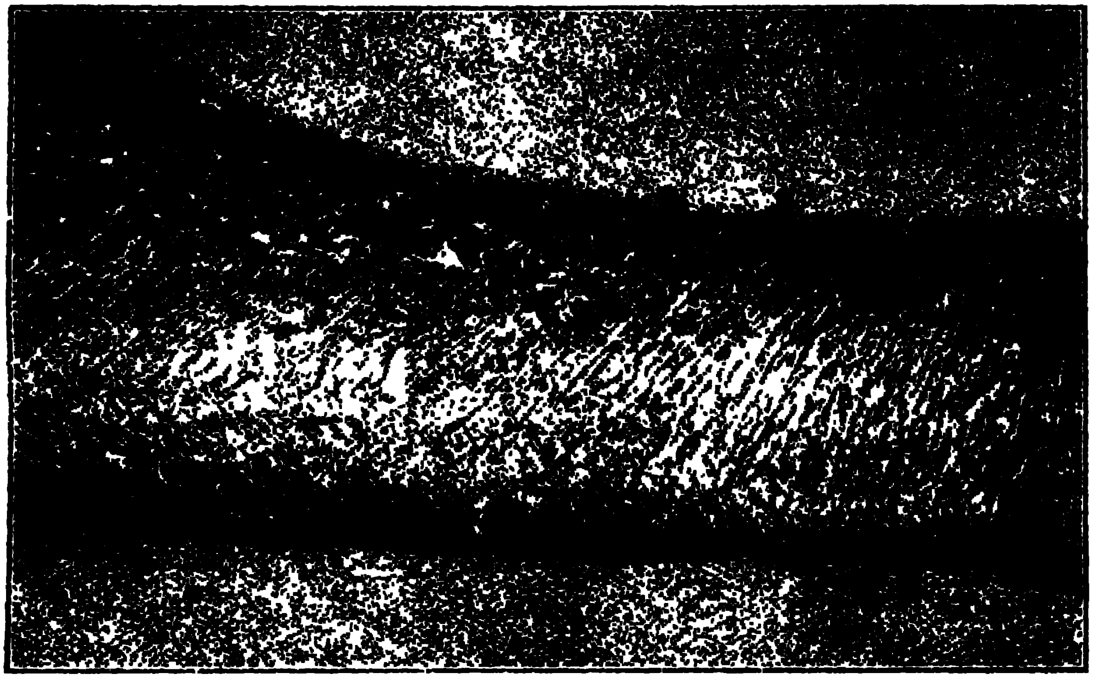
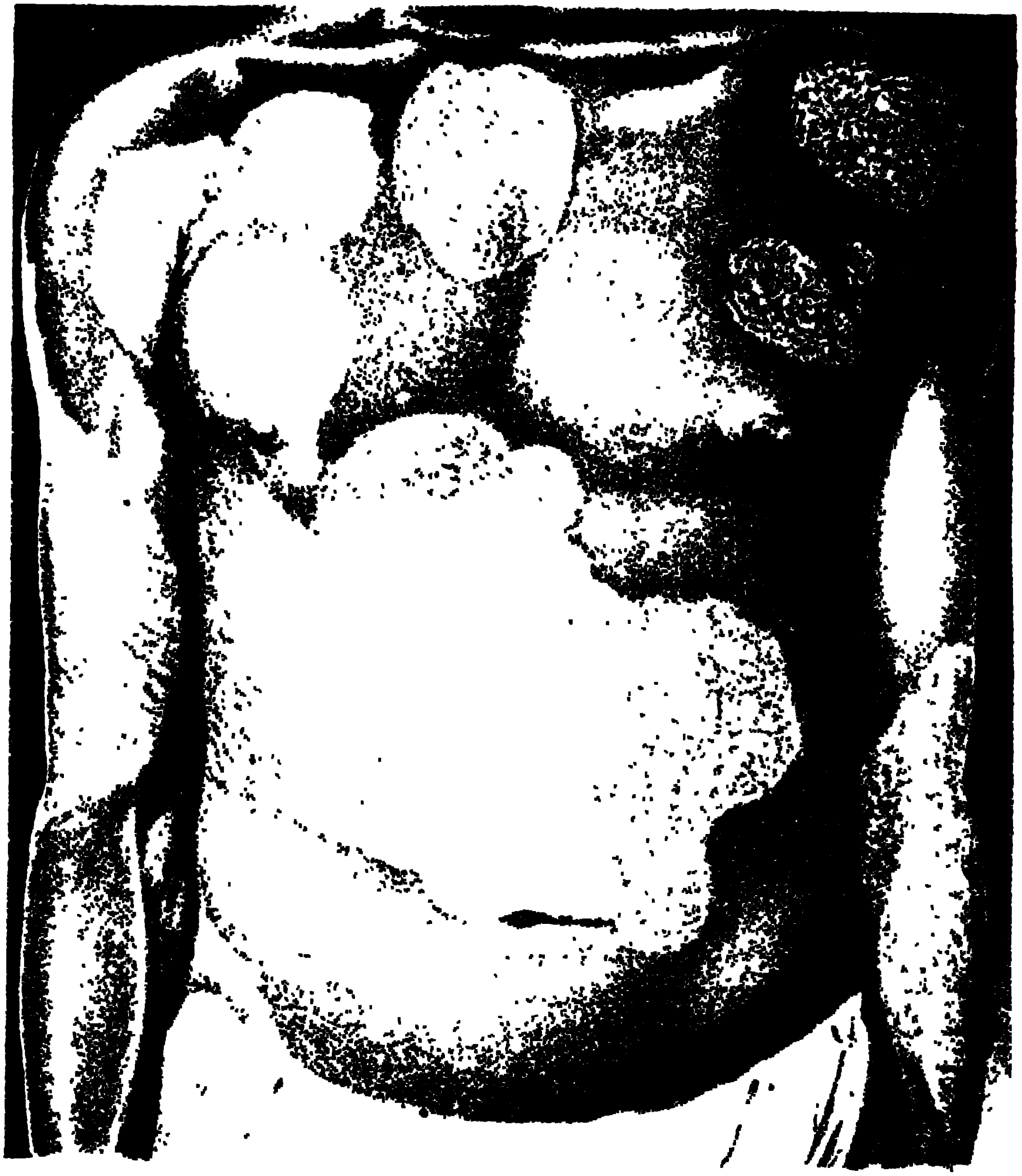


FIG. 816.—TINEA IMBRICATA OF THE FOREARM (OLD CASE).

Symptomatology.—The eruption begins with one or several small, roundish or oval, slightly raised, dark brownish patches, very itching. Soon the central portion of each patch splits, and a ring of flaky large scales attached at the periphery is formed. This scaly ring extends peripherally, and in the meantime another brownish patch appears in the centre at the site of the first brown spot: the new brownish patch breaks, and a second scaly ring is formed, which extends peripherically inside the first ring, and so on until a very large roundish patch is formed, containing several concentric scaly rings. Manson has aptly compared this formation of rings to concentric ripples

PLATE X.



TINEA IMBRICATA

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produced by a stone thrown into a pool of water, and when the eruption starts from many points, as is often the case owing to auto-infection, it is as if a shower of stones had fallen in the pond, and many systems of spreading rings are produced which intersect each other in various directions, and give rise to a more complex pattern. The patches extend at the rate of a quarter to half an inch a week. In a well-marked, advanced case of the disease the skin of practically the whole body is covered with round patches, each of which presents several concentric, not inflamed, scaly rings. The scales are flaky, resembling tissue paper, of large size—up to half an inch in length—dry, of a dirty greyish or brownish colour, and slightly curled. The largest scales are generally found on the back. Each scale has a free border, and is firmly attached by the opposite side; the free border of each scale is towards the centre of the circle, while the attached border is towards the periphery. If the scales are removed, rings of concentric circular dark lines remain visible, a quarter to half an inch apart. The number of rings forming the patch varies; as many as eight and ten may be present in the same patch. The eruption may spread to any part of the body except the scalp. Though several authors state that the eruption never affects the face or axilla, and rarely the palms and soles, it is often observed in such situations. The nails may be affected and become much thickened, with rough surface and deep cracks. Scrapings examined in liq. potassæ show the fungus. The fungus never invades the hair follicles. The general health is not much affected, but the patients complain of the disfigurement and of the unbearable pruritus. The pruritus greatly increases apparently if the patient is given certain diets—for instance, dry-fish diet. In the hot season the pruritus is

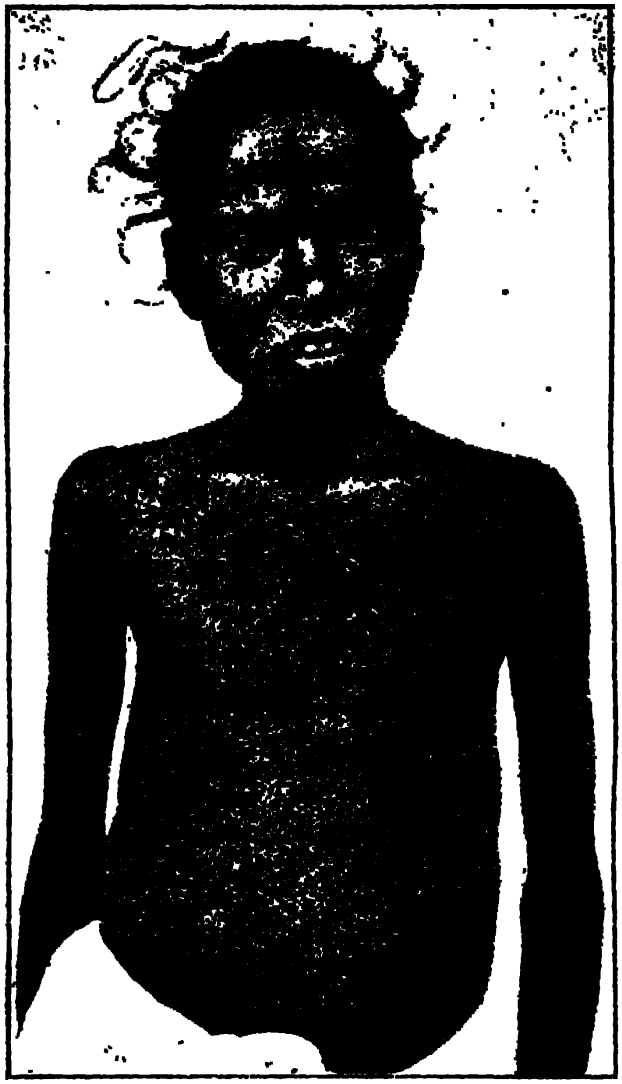


FIG. 817.—TINEA IMBRICATA.

much more marked. The disease is very chronic and very difficult to cure. In many cases the blood shows a certain degree of eosinophilia, the number of eosinophile leucocytes varying between 6 and 16 per cent. In some cases the eosinophilia is probably due to the presence of intestinal worms; the eosinophilia is, however, observed also in some cases in which the microscopical examination of the fæces does not show any ova of worms. In very old cases the eosinophilia is more marked than in recent ones, and signs of anæmia may be present.

Clinical Varieties.—The eruption may after a time or from the very beginning have a diffuse appearance instead of that of concentric rings. The scales, however, are typical and identical to those found in the concentric type—viz., they are large, tissue-paper-like, partially covering each other like tiles on a roof, and most of them firmly adherent by their bases. One variety* of the disease is characterized by the facility with which extensive pieces of epidermis can be stripped off—a condition almost comparable to moulting.

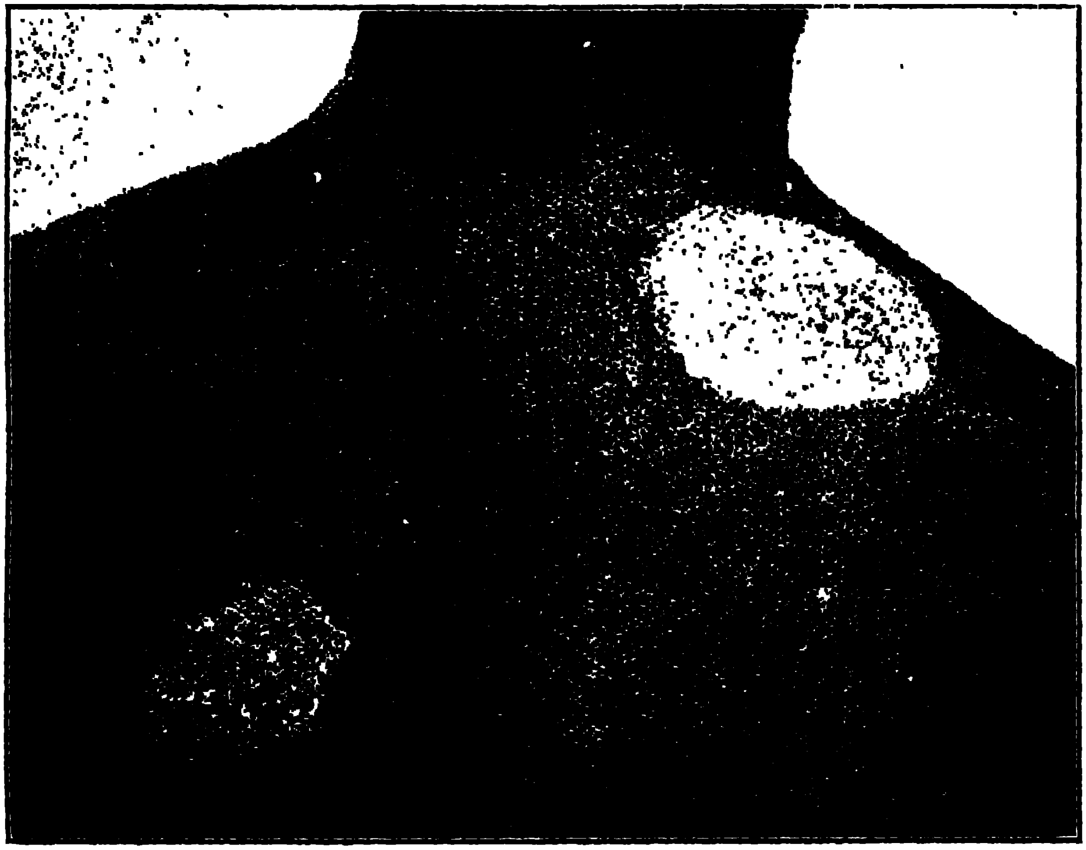


FIG. 818.—EXPERIMENTAL TINEA IMBRICATA OBTAINED BY INOCULATING CULTURES OF *Endodermophyton tropicale*.

The same fungus—viz., either *Endodermophyton tropicale* or *E. indicum*—may give rise at times to the concentric type, at other times to the diffuse type. In some cases the lesions caused by *E. indicum* seem to be slightly different from those given by *E. tropicale*, the lesions caused by the former being perhaps a little more superficial and the scales not situated so close together. Further researches will probably show that there are several other species of Endodermophytons, each of which will probably give rise to a slightly different type of the disease.

Experimental Reproduction of the Disease.—The disease is easily reproduced in human beings by inoculating scales, as was done by Manson, or pure cultures of the fungi, as done by Castellani. The incubation period by the first procedure is eight to ten days. By inoculating cultures of the fungi the incubation period is generally somewhat longer (twelve to twenty days), but the eruption develops typically. It is of interest to note that if very old cultures are used instead of young ones the inoculation may fail completely, or merely an evanescent, superficial, papuloid, trichophytic-like patch may be induced.

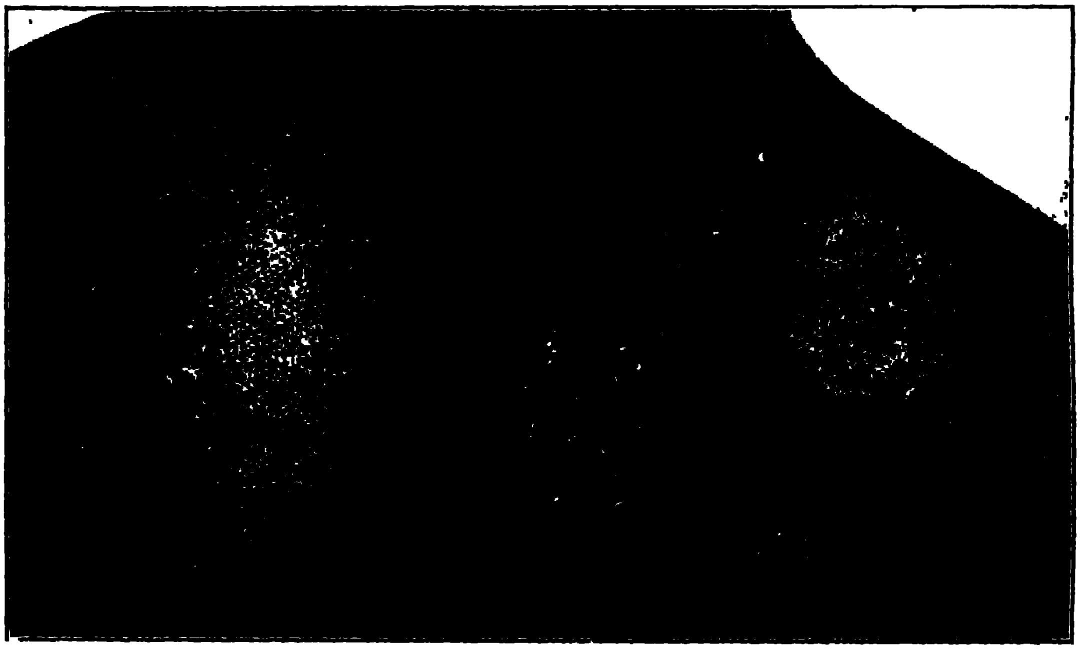


FIG. 819.—EXPERIMENTAL TINEA IMBRICATA OBTAINED BY INOCULATING CULTURES OF *Endodermophyton indicum*.

Compare with Fig. 818. Note the different clinical appearance from experimental tinea imbricata induced by *Endodermophyton tropicale*.

Diagnosis.—This is easy, the presence of concentric rings fringed with large tissue-paper-like scales being characteristic. Even when the concentric rings are not present and the eruption is diffuse the diagnosis is not difficult, being based on the characteristic large, dry, tissue-paper-like scales, overlapping each other like tiles on a roof, and containing under microscopical examination an enormous amount of interlacing mycelial tubes.

Differential Diagnosis—*Ringworm.*—Tinea imbricata has an absolutely different clinical aspect from any type of body ringworm; inflammatory signs are totally absent, and the scales are very large, flaky, firmly attached by their bases, and arranged in parallel lines or concentric circles. The scales contain an enormous amount of the fungus.

Ichthyosis.—The medical man newly arrived in the tropics often mistakes the disease—when of the diffuse type—for ichthyosis, so much so that it has also received the name of tropical ichthyosis. The microscopical examination of the scales will clear the diagnosis at once.

Pityriasis rubra.—In tinea imbricata there is not the intense hyperæmia of the skin, and the scales are firmly attached. The microscopical examination will clear the diagnosis in any doubtful case.

Tinea intersecta. Tinea intersecta begins in a manner somewhat similar to tinea imbricata, dark-brownish patches being present at first, and the fungus in both eruptions growing between the superficial and deep strata of the epidermis. In contrast to tinea imbricata, however, the eruption never develops in concentric rings, the scales are not firmly attached, and the cure is easy.

Prognosis.—The disease has no tendency to spontaneous cure, and the treatment is difficult. The general health is not much affected, but the patient complains of the disfigurement, which is very great, and of the pruritus, which in the hot season may be unbearable. Europeans complain also of pain, especially if the fungus attacks the hands. In very chronic cases signs of anæmia, general weakness, and emaciation may appear. Coolies affected with the malady in an advanced stage are unable to work owing to the extreme pruritus; hence the disease is of great economical importance, as it may greatly decrease the supply of labour on estates, etc.

Treatment.—Every medical man practising in the tropics well knows how difficult is the treatment of tinea imbricata. It is easy to obtain a temporary improvement, and even a disappearance of the eruption; but as soon as the treatment is discontinued the eruption, as a rule, starts afresh.

Strong iodine liniment, as recommended by Manson, or resorcin dissolved in tincture of benzoin (resorcin. ʒii.; tr. benz. co., ℥i.), as recommended by Castellani, or chrysarobin ointment (5 per cent.) give, on the whole, the best results.

In the Colombo Clinic of Tropical Medicine one of us made various experiments to test the efficacy of the various medicaments by applying simultaneously different liniments, ointments, etc., to symmetrical parts of the body, and comparing the result. According to his results:—

Sulphur has practically no effect whatever on the fungus.

Turpentine generally induces a slight improvement, some scales disappearing, and the skin becoming smoother; the improvement, however, is not permanent, and as soon as the turpentine application is discontinued the typical scales reappear.

Calomel and other ointments of mercurial preparations do not induce any improvement in the eruption.

Thymol and *Naphthol* ointments may cause a slight improvement.

Carbolic Acid and *Epicarin* ointments have no effect whatever.

Cyllin ointment (20 to 50 per cent.) may induce a temporary improvement.

Formalin is very effective for localized patches. The usual 40 per cent. solution is applied with care, treating each time a small portion of the eruption. Formalin often causes severe pain and a certain degree of inflammation, which is best relieved by applications of iced water. Soon after the application of formalin the patches become dark brownish, which colour lasts for a few days, when they clear. Care must be taken not to apply the formalin to too large portions of the skin, and not to repeat the application too often; otherwise a peculiar form of apigmentation, similar to leucodermic patches, may appear later on, to which disfigurement coloured patients strongly object.

Chrysarobin.—The repeated application of chrysarobin ointment (30 grains to 1 ounce of vaseline) may induce a strikingly rapid improvement in cases which are not of long standing. The eruption, however, recommences a few days or weeks after its apparent disappearance. Chrysarobin is a very toxic medicament; the patient must be watched and the urine regularly examined. In one of our cases symptoms of absorption appeared after a single application.

Salicylic Acid and *Methyl Salicylate* have very little, if any, action on the fungus.

Tinctura Iodi and Linimentum Iodi.—Tinctura iodi, freely applied, induces a very marked improvement, which, however, is not permanent. Strong iodine liniment, as recommended by Manson, is most effective; it cannot be used freely, however, on patients with a delicate skin, such as women and children.

Resorcin and Tincture of Benzoin.—Resorcin, alone or mixed with salicylic acid in alcoholic solution and in ointments, has very little efficacy. If, however, resorcin be dissolved in tinctura benzoini composita (60 to 120 grains of resorcin to 1 ounce of the tincture of benzoin), very good results are obtained; it is now the routine treatment for tinea imbricata in the Colombo Clinic. It is to be noted that tincture of benzoin without resorcin has very little action on the eruption. The resorcin, dissolved in tincture of benzoin, should be applied freely once or twice daily on the affected regions. If the whole body be affected, one day one half is painted, and the other days the other half, alternately. The treatment must be continued for several weeks. Once or twice a week the patient is given a very hot bath, and scrubbed all over with sand-soap. Symptoms of absorption are rare; it is always prudent, however, to proceed at first with care, as it is well known that individuals may be met with, though rarely, showing idiosyncrasy for resorcin.

Prophylaxis.—Some authorities recommend isolation: this is good wherever possible, but in regions where the disease is or has become endemic usually the great number of people suffering from the affection render the measure hardly practicable. In those tropical countries, however, where the disease has not yet appeared, the medical officers would do well to be on the look-out for it, and if a case is reported the patient should certainly be kept isolated and thoroughly treated before being allowed to mix with the general population, and all infected clothing should be boiled or burnt. We have seen an epidemic of tinea imbricata in a hospital in which a patient suffering from the disease was admitted and allowed to mix with the other patients. There is a general native belief that anointing the body with cocoanut oil or other oil will prevent infection; there may be some truth in the belief, but such a measure cannot be carried out in Europeans. Any itchy, scaly spot in the slightest way suspicious of incipient tinea imbricata should be immediately treated with lin. iodi, chrysarobin ointment, or resorcin dissolved in tr. benzoini. While the treatment of tinea imbricata in an advanced stage is extremely difficult, it is easy to stop the initial patches by these means.

TINEA INTERSECTA (*vide* Plate XI.).

This dermatomycosis and its fungus were first described by Castellani in 1907. It occurs in Ceylon and Southern India.

Ætiology.—If a portion of one of the brown patches or a scale be removed and treated with liquor potassæ, the fungus is easily detected. The fungus (*Endodermophyton castellanii* Perry, 1907) grows between the superficial and the deep strata of the epidermis. It is present on the inner surface of the scales, but not on the external surface. A very remarkable fact is the extreme rarity of free spores; in fact, in several cases one does not succeed in finding spores. The mycelium is fairly abundant, though far from being so abundant as in tinea imbricata. It is composed of long, straight articulated threads, which are sometimes dichotomous, the breadth being between 3 and 3½ μ. Each segment presents in fresh preparation two refractile bodies, one at each extremity. No aspergillar fructifications nor clusters of spores are seen. Attempts at growing the fungus have succeeded only in one case, the growth being somewhat similar to that of *Endodermophyton indicum* Castellani (p. 1020).

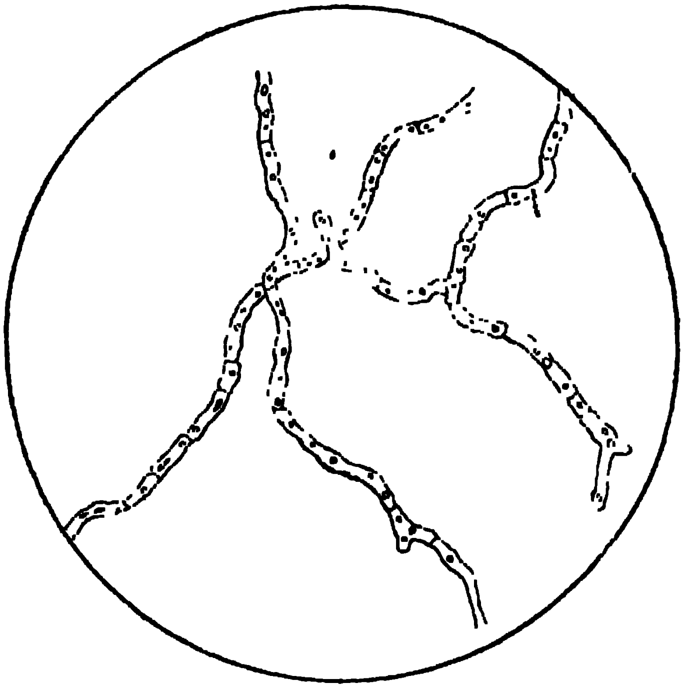
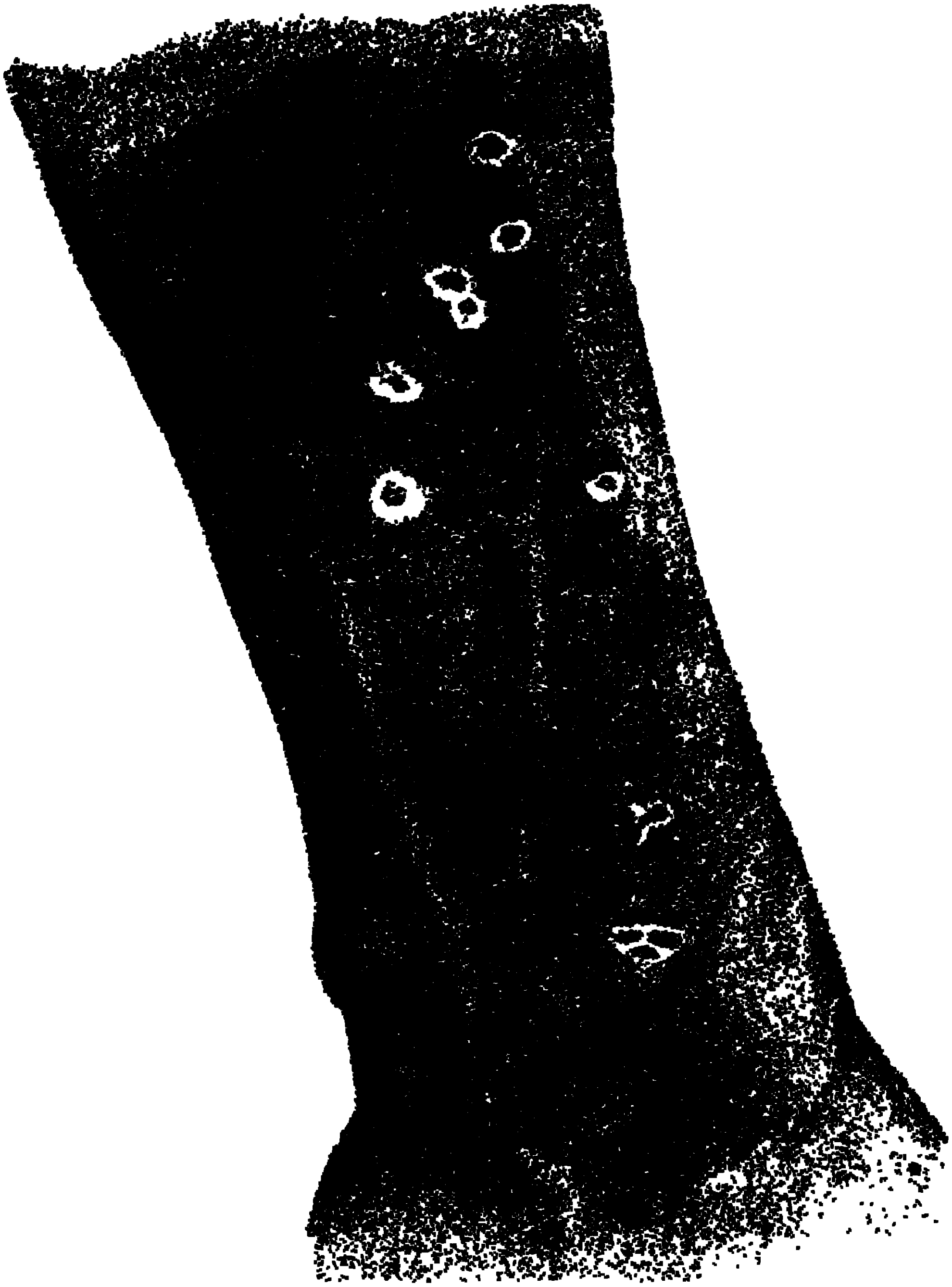


FIG 820.—FUNGUS OF TINEA INTERSECTA (From a scale in liq. potassæ.)

Symptomatology.—The eruption begins with small oval or roundish, very slightly elevated itching patches, generally situated on the arms, legs, chest, and back. The margins of these dark spots are at first slightly elevated, and dotted often with minute dark papules. The patches are dark brown in colour, much darker

PLATE XI.



LINEA INTERSECTA (KROMAYER)

[illegible]

than the surrounding skin, and presents a smooth, tense surface at first; they increase in size slowly, and some coalesce. After a certain time the surface of the patches is no longer tense; it becomes somewhat shrivelled and dry; superficial cracks appear in it, so that white lines are visible intersecting the brown surface. Later the cracks become deeper, the epidermis splits, and several flaky, curled-up scales, whitish inside and dark on the outer surface, are seen; the scales are often removed by friction, and whitish roundish patches only remain. The eruption never develops in concentric rings like tinea imbricata; the patches remain isolated or fuse together, forming irregular larger patches. Some patches may disappear spontaneously after a time. The general health of the patient does not seem to be affected. In some patients there is a slight degree of eosinophilia.

Diagnosis.—When the eruption is in the very first stage it might be mistaken for a form of pityriasis versicolor. In pityriasis versicolor, however, the epidermis does not split: moreover, in tinea intersecta the fungus is not found on the surface: it grows between the superficial and deep layers of the epidermis. Tinea imbricata begins in a manner somewhat similar to tinea intersecta, dark brownish patches being present, and the fungus in both eruptions growing between the superficial and deep layers of the epidermis. In contrast to tinea imbricata, however, the eruption of tinea intersecta never develops in concentric rings: is far less severe, as patches may heal spontaneously; and is cured without much difficulty.

Treatment.—Tincture of iodine and the usual antiseptic ointments, such as chrysarobin (2 to 5 per cent.), answer well.

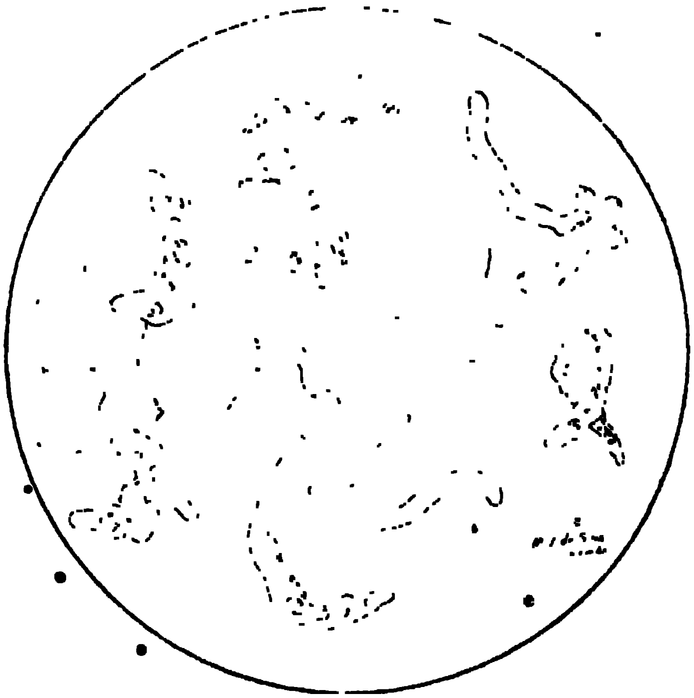


FIG. 821.—FUNGUS OF TINEA FLAVA (OLD CASE). (From a specimen stained by the Morris-Walker method.)

TINEA FLAVA

(*vide* Plate XII.).

Synonyms.—Tropical Pityriasis Versicolor of the old authors, Microsporosis Flava (Castellani), Achromie Parasitaire (Jeanselme), Pityriasis Versicolor Flava (Castellani), Achromia Squamosa (Crocker).

This dermatomycosis is extremely common in all tropical countries, and especially so in Southern India, Ceylon, Malaya, Java, Indo-China, and China. By many authors it has been, and is still, confused with the ordinary pityriasis vesicolor of temperate zones; the investigations of Castellani and Jeanselme, however, have clearly proved that it is a different affection.

Ætiology.—The affection is due to *Malassezia tropica* Castellani, 1905. The mycelial threads are generally thick, with numerous swellings, constrictions, and other irregularities in their shape. The spores are roundish or oval (3·50 to 4·50 μ), and have a double contour. In recent cases the fungus is abundant, with plenty of mycelium and spores which often run into clusters. In old chronic patches the fungus becomes very scanty; the spores are not numerous, and generally do not collect in clusters; the mycelium is very scanty, and is even more irregular in shape than it is in recent patches (degeneration forms of the fungus). For full description of the fungus see p. 1099.

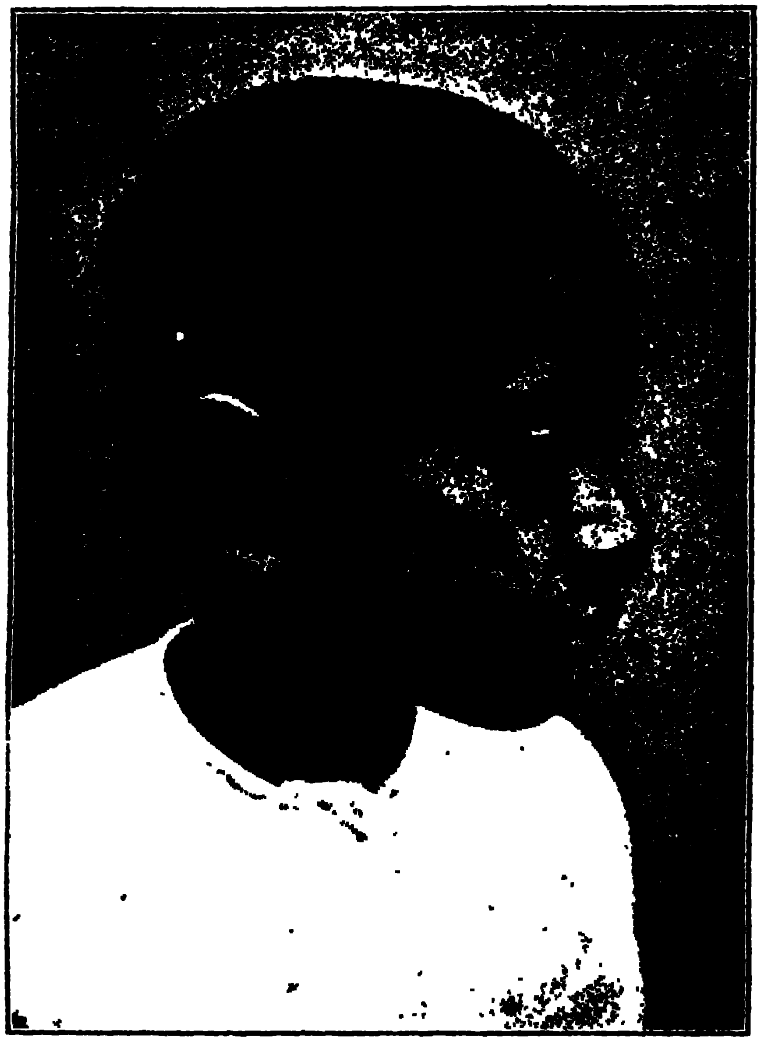


FIG. 822 – TINEA FLAVA ON THE FACE OF A SINHALESE.

Symptomatology.—The affected parts are yellowish, of much lighter colour than the surrounding healthy skin; the yellow colour may be of various tinges, from dark, deep orange-yellow in some cases to very light canary-yellow in others. The patches are of

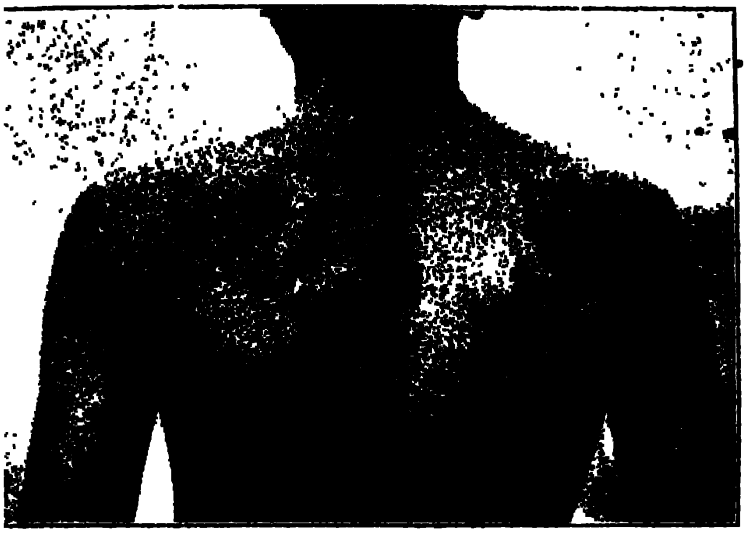


FIG. 823.—TINEA FLAVA ON THE BACK.

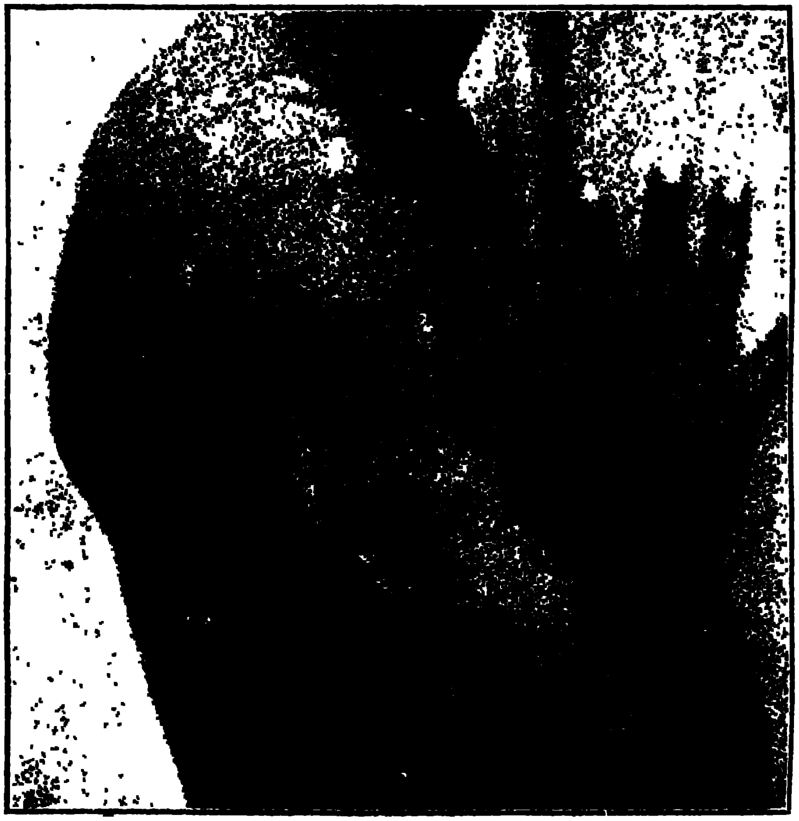


FIG. 824.—TINEA FLAVA OF THE ARM.

various sizes, generally roundish, smooth, sharply defined, with margins not elevated, or only slightly so. Sometimes the patches are irregularly festooned, and may encircle an area of healthy skin. Occasionally the encircled healthy skin appears to be intersected by many yellowish, ribbon-like lines originating from the surrounding yellow patch. The regions more frequently affected are, in order of frequency, the face, neck, chest, and abdomen. Large portions of the body may be involved. There is, as a rule, no pruritus. The patches are not desquamating, or only very slightly so. The course of tinea flava is very chronic. In the natives of the lower classes it appears in childhood in the shape of tiny spots on the face and chest, spreading slowly during years; they may coalesce, covering practically the whole of the face and chest.

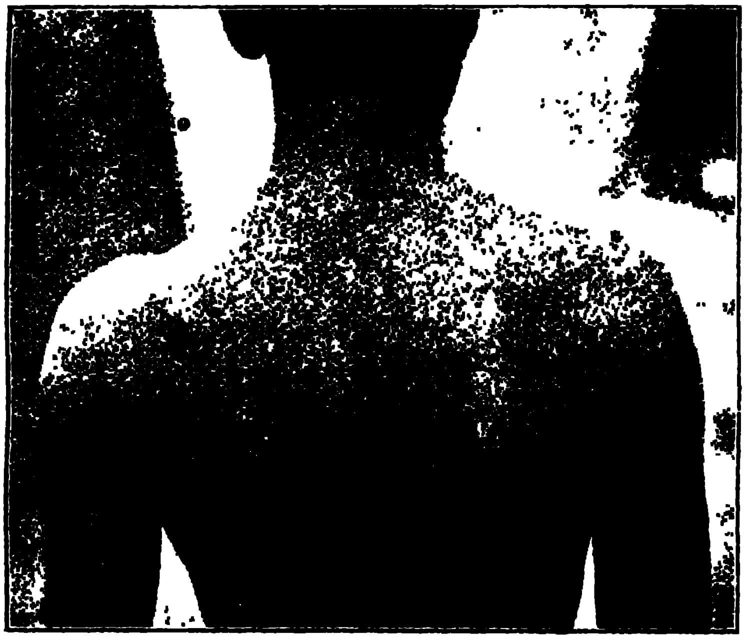


FIG. 825.—TINEA FLAVA: VARIETY GUTTATA.

One is occasionally surprised to see a native whose face and chest are quite light in colour; on closer examination, it may be found that this lighter appearance is due to a diffuse, very light-coloured form of tinea flava, covering the whole of the face, neck, and chest. In Ceylonese native women, when the patches of tinea flava are small, light, and situated on the face, they are considered to be beauty-spots, and are highly appreciated by the ladies and their admirers. Such patches are called in Sinhalese 'alu-hama,' which means ashy skin (*alu*, ash; *hama*, skin). There is also another word used by native poets for such condition—'gomera,' which means skin dotted with beauty-spots. The disease, which is extremely common, attacks mostly natives, but occasionally Europeans also. In Europeans the patches are yellowish-reddish or pinkish (tinea rosea), and may be due to different strains of *M. tropica*.

Prognosis.—The disease is very chronic and has no tendency whatever to spontaneous cure, but the general health is not affected.

Diagnosis.—*Pityriasis versicolor* of temperate zones is not of so light a tinge as tinea flava, never attacks the face, and is curable with the greatest facility; while tinea flava affects the face more frequently than any other part of the body, and is curable only with difficulty.

Tinea Alba.—Occasionally there may be some difficulty in distinguishing tinea flava of a light variety from tinea alba. In contrast to tinea flava, the patches of tinea alba are not smooth, and the fungi belong to the genera *Trichophyton* and *Epidermophyton*.

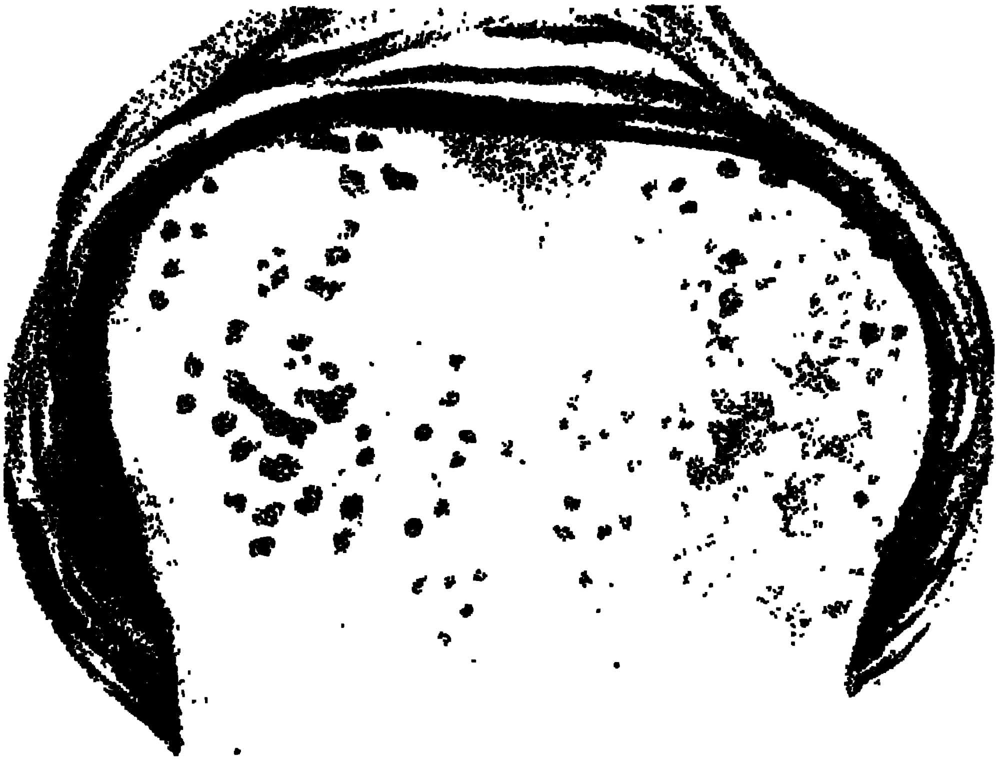


FIG. 826.—TINEA FLAVA ON THE BACK OF A EUROPEAN.

Tinea Flava and *Pinta* are easily distinguished by the characters of their respective fungi, the fungus found in pinta never having the characters of a *Malassezia*.

Leucoderma patches have a characteristic dead-white colour, are often surrounded by a hyperpigmented border, and no fungus is found.

In *Circumscribed Scleroderma* (Morphœa) the patches may present a peculiar yellowish tinge, which in coloured patients may resemble tinea flava. In tinea flava, however, there is no change in the texture of the skin, which is still pliable, and does not exhibit the peculiar parchment-like feeling of scleroderma. The microscopical examination will clear the diagnosis in any doubtful-case.

In Europeans, tinea flava, taking often a reddish colour (hence the term 'tinea rosea'), especially if the patient has been exerting himself and is perspiring, might, on superficial examination, be mistaken for a form of *Seborrhœa corporis.* The microscopical examination will clear the diagnosis, no *Malassezia* fungus being found in seborrhœa corporis.

Treatment.—Tinea flava shows no tendency to spontaneous cure unless the patient moves to a cold climate. Even then, very often the cure is only apparent, as the condition reappears during the hot weather. The treatment is difficult. Turpentine applied daily, followed by a naphthol or epicarin ointment (2 to 5 per cent.), or a salicylic-resorcin ointment (resorcin ʒi., acidi salicyli gr. x., vaselini ℥i.), is often successful, but the treatment must be continued for months. On covered parts of the body tincture of iodine may be used, or a chrysarobin ointment (2 per cent.).

It is to be noted that in several cases the fungus of tinea flava has apparently a deep permanent disturbing action on the pigmentation processes of the skin, as, even when the fungus has been destroyed, the patches may remain of a lighter colour than the surrounding skin for a long time, though ultimately they become again normally pigmented.

TINEA NIGRA.

Synonyms.—Pityriasis Nigra (Castellani), Microsporosis Nigra (Castellani).

This affection is fairly common in India, Ceylon, Java, Federated Malay States, and China. The first account of this, or a very similar, dermatomycosis was published by Manson in China in 1872. Manson's observations, however, were forgotten, as they were not quoted by him in his subsequent works. Castellani, in 1905, redescribed the disease in Ceylon, and succeeded in growing the fungus.

Ætiology.—The affection is caused by a fungus of the genus *Cladosporium*—*C. mansoni* Castellani, 1905. The fungus is found very abundantly in the lesions; the mycelial elements are rather short—18 to 20 μ in length, and 2½ to 3½ μ in breadth. Sometimes they may be irregular in outline, bent, banana-shaped. The spores are globular, and most of them very large—5 to 8 μ. They are frequently arranged in clusters.

The fungus is easily cultivated by inoculating scrapings of the affected patches on maltose agar. After two to four days roundish hemispheric colonies appear, which are black, but at first have usually a greenish tinge, and may present at the periphery some radiating, delicate, pale greenish hyphæ. These colonies may remain separate or more often gradually coalesce into a jet-black knobby mass, deeply rooted into the medium.

The fungus grows well, though less abundantly, on the other sugar agars, and also on ordinary agar. In *broth* and *peptone-water* the growth is very

PLATE XII.

TINEA FLAVA ON THE FACE AND
TINEA NIGRA ON THE NECK.

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To face page 23

slow, and takes place at the bottom of the tubes, with formation of a black or greenish-black sediment.

The *optimum temperature* for the growth of the fungus is betwen 30° and 32° C.; above 35° C. and under 25° C. the growth is much slower, and may be nil under 20° C. Further details on the fungus may be found on p. 1100.

Symptomatology.—The affected parts are of a black, dull, lustreless colour, much darker than the surrounding dark, healthy skin of the native. The patches may be small, roundish, and separated from one another, or may coalesce; the patches are often slightly elevated, and may present a slight desquamation. Little, if any, pruritus is present. The face is not usually affected, though the eruption may be found on practically any other region of the body. The neck and upper portion of the chest are apparently the regions most frequently affected. Tinea nigra usually attacks natives. We have, however, seen it also in one of our European patients, who went for a pleasure trip to Burma, where he remained about a month. On coming back to Ceylon, he noticed a small, roundish, very slightly elevated, non-desquamating, black patch on the palm of his left hand. There was no pruritus. The patch spread slowly for two months, reaching the size of a sixpenny-piece. It disappeared after a single application of formalin; three months later it reappeared in the same place as a tiny black dot, which slowly spread. Another application of formalin caused it to again disappear. From the patch a fungus was grown identical with the one found in native cases.

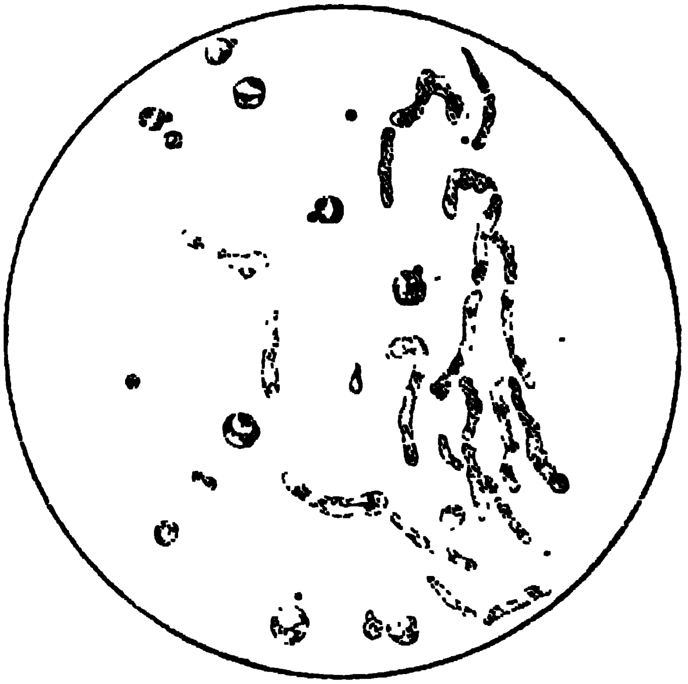

FIG. 827.—FUNGUS OF TINEA NIGRA.

Mixed Infections.—A mixed infection of tinea nigra and tinea flava is somewhat frequently met with. Several of our patients had on the neck a few round patches of tinea nigra, and on the face some smooth, yellow, roundish patches of tinea flava.

Diagnosis.—The characters of the fungus, and the fact that the disease is easily curable, readily distinguish tinea nigra from pinta. Pityriasis versicolor is generally of lighter colour than tinea nigra, and the fungus (*Malassezia versicolor*) is morphologically very different, and cannot be grown. In chloasma bronzinum no fungus is found.

Treatment.—The disease is easily curable, except when it attacks the palms of the hands, where the treatment must be more prolonged. A salicylic-alcoholic lotion (2 per cent.), followed by a resorcin ointment (resorcin, ʒi.; vaseline, ℥i.), answers well. When the patches are small, pure formalin may be used with care.

ERYTHRASMA.

This affection is frequently met with in the tropics, and is common on the continent of Europe, though apparently rare in America.

Ætiology.—It is caused by a fungus discovered by **Burchardt** in 1859—*Nocardia minutissima* Burchardt. This hyphomycete is very delicate and slender, less than 1 μ in breadth; is found in the superficial horny layer of the affected parts. Ducrey and Reale claim to have succeeded in cultivating it, but their results have not been confirmed. The description of the fungus is found on p. 1061.

Symptomatology.—The eruption generally affects the genito-crural and axillary regions, but may occasionally spread to other parts of the body. It is characterized by the presence of brownish-reddish patches, rounded or irregularly shaped, but with well-defined borders. The borders are not elevated; the surface of the patches appears slightly furfuraceous, and has often a somewhat greasy feeling. There are no subjective symptoms, except occasionally slight itching.

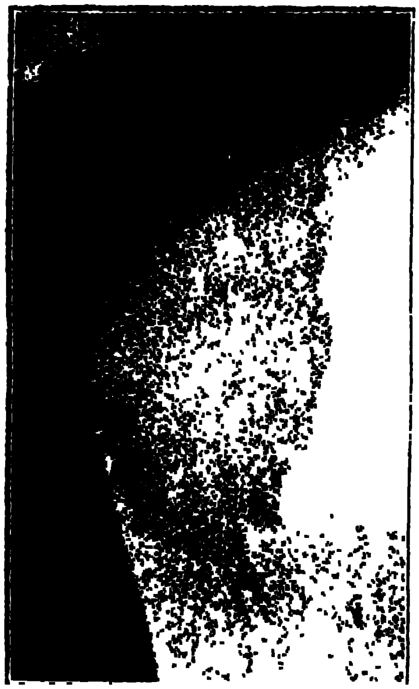
FIG. 828.—ERYTHRASMA.

Diagnosis. — Erythrasma is easily distinguished from tinea versicolor and tinea flava by the reddish tinge generally present; by the characteristic difference of its sites of development, and by the microscopical examination, which will reveal the presence of *Nocardia minutissima* Burchardt, a fungus morphologically very different from *Malassezia furfur* Robin or *M. tropica* Castellani. The differential diagnosis from tinea cruris has been discussed in this chapter under the heading Tinea Cruris (p. 2042).

As first noticed by Manson, after tinea cruris has been cured, the genito-crural region may in some cases present for years a peculiar brownish discoloration, and be slightly furfuraceous—a condition resembling erythrasma; in such cases neither *Epidermophyton cruris* Castellani nor *Nocardia minutissima* Burchardt will be found.

Treatment.—Washing the parts with ordinary soap and warm water, carbolic, tar, or sand-soap, and then regularly applying a resorcin-salicylic ointment (resorcin, gr. x. to xxx.; ac. salicyl., gr. x. to xx.; vaseline, ℥i.), will soon cause the eruption to disappear. Instead of the ointment, a hyposulphite of soda (1 drachm to 1 ounce) or sulphurous acid lotion may be used.

BLASTOMYCOSIS.

Synonyms.—Saccharomycosis Hominis, Oidiomycosis, Dermatitis Blastomycetica, Blastomycetic Dermatitis, Zymonematosis.

Definition.—The term blastomycosis covers a group of closely allied pathological conditions due to fungi of the genera *Saccharomyces*, *Cryptococcus*, *Coccidioides*, *Oidium*, and *Monilia*, generally characterized by the presence of warty patches and minute epidermal abscesses.

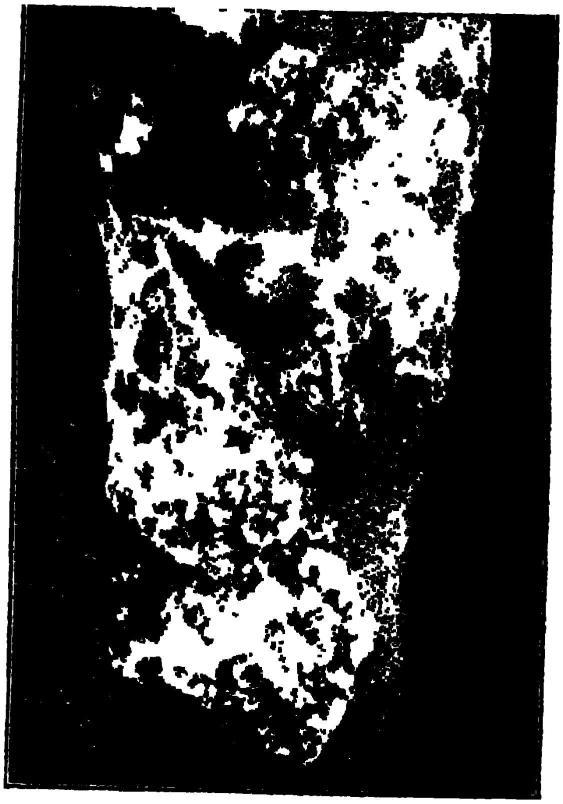

FIG. 829.—BLASTOMYCOSIS OF LEG.

Historical and Geographical.—Wernike, in 1890, described in Buenos Ayres two cases of papillomatous eruption in which he found peculiar bodies which were at first considered to be protozoa, hence the disease was called 'protozoic dermatitis.' Later Gilchrist and Ophüls showed them to be vegetal parasites. Gilchrist, in 1894, described yeast-like organisms in sections taken from a scrofuloderma-like eruption. In the same year, independently, Busse and Buschke published a case of a pyæmia-like condition due to a *Cryptococcus*. The disease has been investigated chiefly by American observers, among whom Ricketts, Ormsby, Hyde, Montgomery, and Pusey may be mentioned. The malady occurs in the tropics, and one of us has reported several cases from Ceylon, while Phalen and Nichols have described numerous cases from the Philippine Islands, Léger two cases in Tonkin, and Lutz, Splendore, and others, cases from South America.

Ætiology.—The fungi found belong to the genera *Saccharomyces*, *Cryptococcus*, *Coccidioides*, *Monilia*, including in the last-mentioned genus the following non-sufficiently defined genera: *Zymonema*, *Parasaccharomyces*, *Parendomyces*. The description of these fungi is found in Chapter XXXIX., p. 1035. There are also higher, not yet well-determined fungi, all of which are apparently capable of inducing identical clinical conditions. In the tissues all the organisms exist as yeast-like, oval, or roundish cells.

Among the organisms which cause the disease, Ricketts distinguished four types:—

1. Blastomycetoid or yeast-like type: reproduction by budding; in cultures only oval or roundish cells are seen, while mycelial tubes are as a rule absent.
2. Cryptococcus-like type: reproduction by endosporulation within the tissues.
3. Endomyces-like type: the cultures present abundant submerged mycelium, which breaks up into chains of endoconidia; proliferation by budding is rare.
4. Hyphomycetoid type: cultures present aerial hyphæ and submerged mycelium; proliferation by gemmation occasionally seen. There are many transition forms between these four groups.

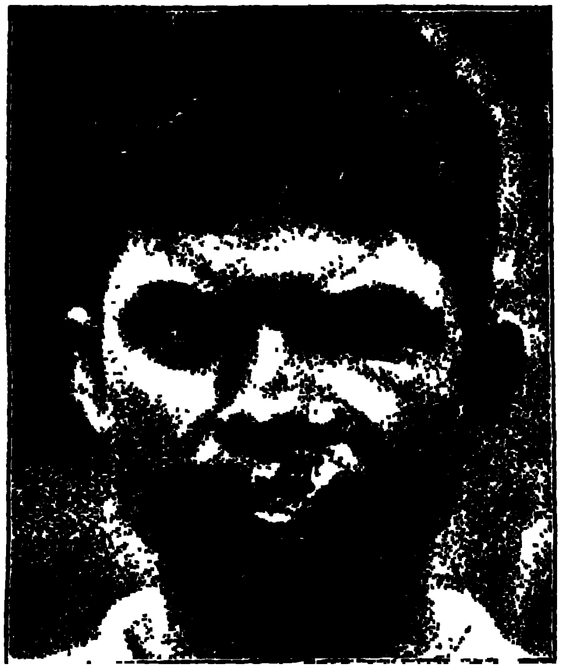

FIG. 830.—BLASTOMYCOSIS OF THE UPPER LIP: ULCERATIVE STAGE.

(From a case in the Colombo Clinic.)

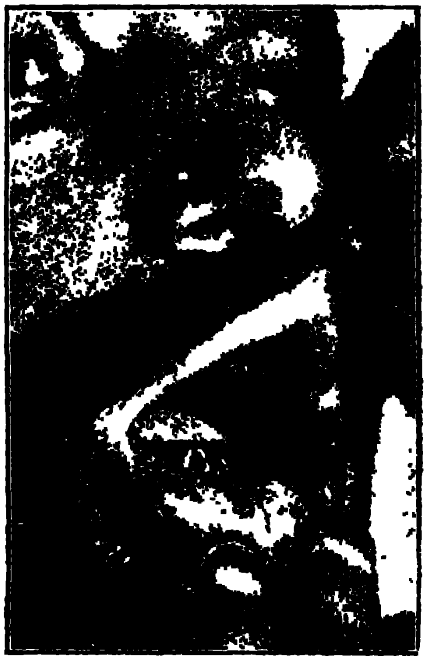

FIG. 831.—BLASTOMYCOSIS OF THE MOUTH.

(From a photograph by Splendore.)

Histopathology.—There is marked proliferation of the epithelial layers, with elongated, irregularly shaped down-growths into the corium, and epithelial globi are seen. The cells of the rete are swollen, and there is, between the cells, a polymorphonuclear leucocytic infiltration. Here and there minute miliary abscesses are present. In these, numerous polymorphonuclear and mononuclear leucocytes are found, also epithelioid cells and giant cells, some containing the parasite. It is in the miliary abscesses that the organism is mostly found. The corium presents a general cellular infiltration made up of polymorphonuclear leucocytes and young connective-tissue cells. The vessels are dilated and their walls thickened. Splendore has noted that when the lymphatic glands are affected, which is of rare occurrence, they may present histologically a tubercular appearance.

Symptomatology.—The disease, as seen by us in Ceylon, is characterized by the presence of elevated warty patches showing, especially at their margins, minute epidermal abscesses, and often small ulcers covered by yellowish crusts. The eruption may be gyrate. The lesions at a later stage may become more deeply ulcerated, the pr[illegible] ulceration generally beginning at their centre. There is very little or no pain, and very slight or no pruritus. The lesions may heal spontaneously, leaving, as a rule, soft, smooth scars. Occasionally the affection recommences after a time in the scar. The lymphatic glands are not often involved. In some cases subcutaneous abscesses and gumma-like swellings may be formed. All regions of the body may be affected. The course is very chronic, the disease lasting often for many years.

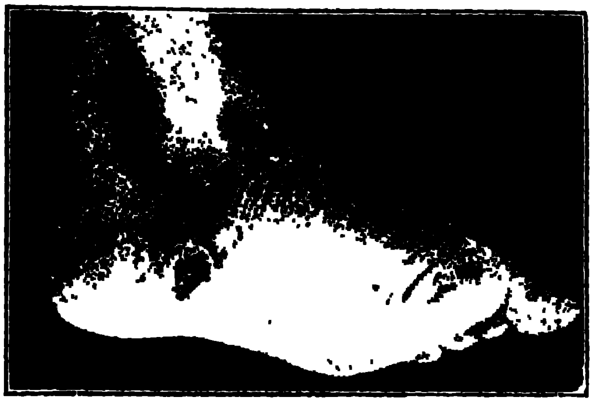

FIG. 832.—BLASTOMYCOTIC ULCER.
(From a photograph by Splendore.)

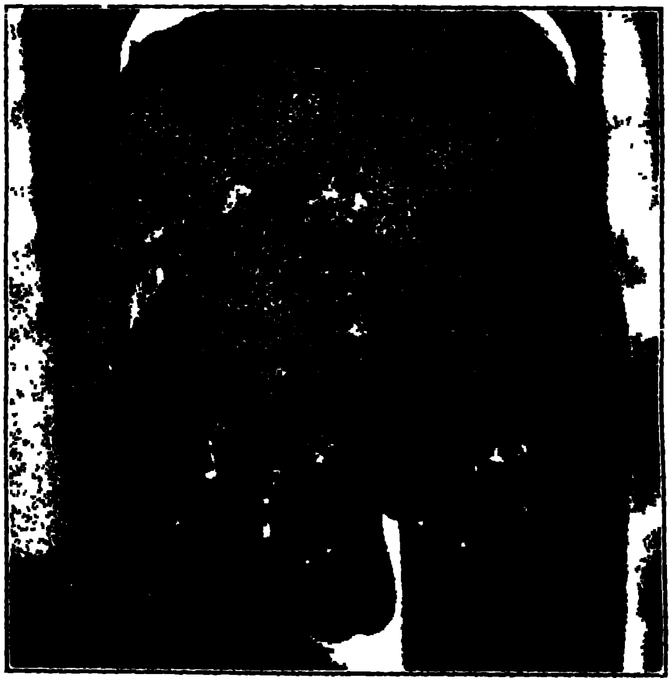

FIG. 833.—BLASTOMYCOSIS GLUTEALIS
(From a case in the Colombo Clinic.)

Clinical Varieties.—Several varieties can be distinguished:—[1]

1. The common cutaneous type, or North American and Asiatic type.
2. The oro-pharyngeal blastomycosis.
3. The Coccidioides blastomycosis.
4. The gluteal blastomycosis.

1. *Common Cutaneous Type.*—The description we have given of the disease refers to this type, which is quite common in Ceylon, Southern India, Philippine Islands, Indo-China, Tonkin, and probably in many other parts of the tropics. A very frequent localization in Ceylon is the upper lip (see Fig. 830), the disease extending later occasionally to the nasal mucosa, and very rarely to the oral mucosa. In several of our cases a monilia-like fungus was grown.

2. *Oral Blastomycosis.*- This variety has been investigated by Lutz and Splendore in South America. Splendore considers the fungus to be a *Zymonema*, and calls the disease zymonematosis. As most authorities do not accept the genus *Zymonema*, we place the fungus in the genus *Monilia* (see p. 1079). The skin lesions are identical with those found in the common type of the malady, but the infection spreads to the oral mucosa, lips, gums, soft and hard palate, giving rise to numerous small, verrucoid, papillomatous, or framboesiform patches, which later may undergo deep ulceration. The disease later invades the pharynx, nose, larynx, and bronchi, and often terminates fatally.

3. *Blastomycosis Coccidioides* (synonym, Protozoic disease) was described by Wernike of Buenos Ayres in 1890, and later by Posadas; it was further investigated by Ophüls, Moffit, and others. It was at first considered to be of protozoal origin. The lesions on the skin are somewhat similar to those found in the more usual type of blastomycosis—viz., verrucose patches with minute epidermal abscesses—but are generally of larger size, and visceral complications are the rule, the malady terminating almost always fatally. In the affected tissues peculiar large structures are seen, some of which may contain as many as 100 spore-like bodies (see p. 985).

4. *Gluteal Blastomycosis.*—This condition was described by Kartulis some years ago in Egypt. We have often observed it in Ceylon. The skin of the gluteal region—one nate or both nates—presents a diffuse induration, and is cribrated with the opening of sinuses, from which a thin pus exudes. The sinuses may be very deep and connected with each other, but in our cases did not communicate with the intestine. The pus does not contain grains, as is the case with actinomycosis. The patient may complain of pain and discomfort on sitting down. The disease is chronic.

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[1] **Maxwell has reported from Formosa cases of a fistulous disease of the buttocks, which may be of the same nature. He is inclined, however, to consider them to be of amoebic origin.**

Diagnosis.—This is based, in the usual type of the malady, on the presence of verrucose patches with micro-abscesses, in which the fungi are found. The disease has been often confused with tuberculosis verrucosa, with a syphilide, with an epitheliomatous lesion, and, in the tropics, with atypical framboesia and even ringworm. The microscopical examination and cultivation of scrapings, or, better, of the pus of the miliary abscesses present in the lesions, will be necessary to clear the diagnosis. A droplet of the pus, or a minute portion of teased tissue, is placed on a slide with a drop of a 30 per cent. solution of potassium hydrate, and a cover-glass is placed on the preparation; after about half an hour in a temperate climate, and generally a few minutes only in a tropical climate, the tissue and pus cells are disintegrated by the potash solution, while the organisms, being resistant, can be easily seen. Cultures should also be made from the pus. It is important to note that yeast-like organisms may be frequently found as saprophytes on the surface of various ulcerated skin lesions, which have nothing to do with true blastomycosis.

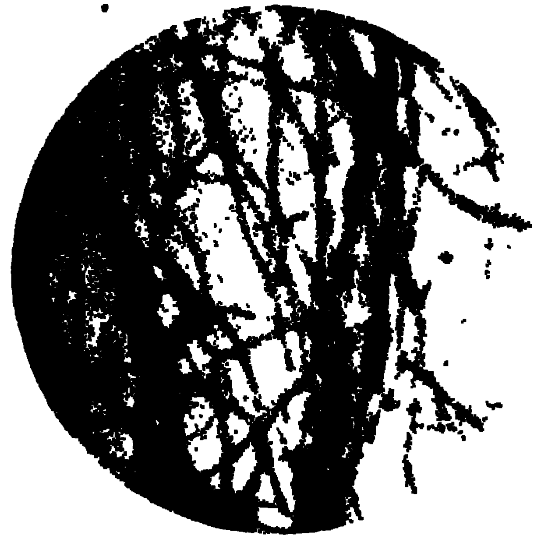
FIG. 834.—FUNGUS FOUND IN DERMATOSIS HYPHOMYCETICA INDICA. (BROTH CULTURE.)

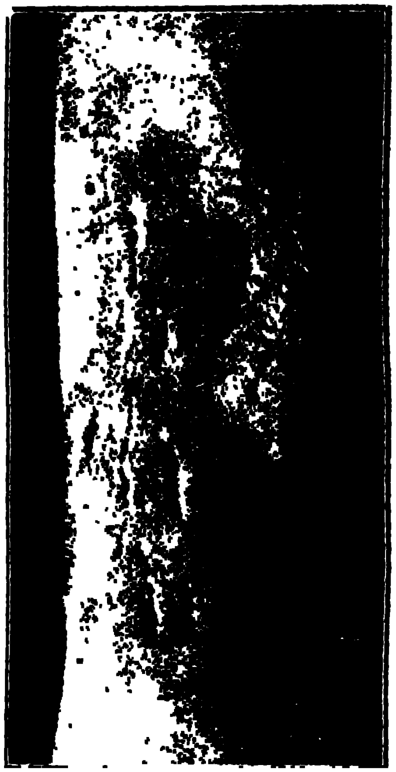
FIG. 835.—DERMATOSIS HYPHOMYCETICA INDICA (see p. 2086).

Oral blastomycosis may occasionally be confused with espundia, from which it is differentiated by the absence of Leishmania and presence of fungi. *Blastomycosis coccidioides* is easily diagnosed by the presence of bodies containing numerous—as many as 100—endospores. *Gluteal blastomycosis* is distinguished from actinomycotic and mycetomatous conditions by the absence of the grains and the characters of the fungi; from a syphilitic condition by the inefficacy of a mercurial treatment; from tubercular fistulous disease by the massive diffuse induration, and absence of tubercular cutireaction.

Prognosis.—The disease very rarely heals spontaneously. The general health in the common type of the malady is not much affected, but the patients complain of the disfigurement. Occasionally the organisms from the skin lesions enter the general circulation, and a condition similar to pyæmia develops. Cases of systemic blastomycosis terminating fatally, without any skin lesion, have also been described. The prognosis of blastomycosis coccidioides and oral blastomycosis is bad, while blastomycosis glutealis is most persistent, though the general health is not much affected.

Treatment.—Potassium iodide, given in large doses (gr. xv. to xx. three or four times daily), has a beneficial effect, though it is not so efficacious as in sporotrichosis. The application of Röntgen rays to the lesions is useful. In mild cases the local application of various disinfectants—*e.g.*, perchloride of mercury (1 in 1,000), diluted tincture of iodine, etc., may bring about a cure. The following ointment is useful, especially in the localization to the upper lip: Ichthyol, gr. xv; ung. belladonnæ, ʒii.; vaselini, ad ℥i. No treatment is apparently much use in blastomycosis coccidioides, in oropharyngeal blastomycosis, or in blastomycosis glutealis.

Dermatosis Hyphomycetica Indica.—This term has been used by Castellani to indicate a peculiar hyphomycetic condition he has once seen in Ceylon The patient had a number of gummatous swellings and indurated patches, but no warty lesions were present anywhere. A fungus was isolated which in various sugar broths and ordinary broth produced very long filaments, but owing to an accident could not be further studied

SPOROTRICHOSIS.

Schenk, in 1898, described a case of multiple chronic abscesses in the pus of which a *Sporotrichum* was found. Hektoen and Perkins reported two similar cases also in the United States in 1900. De Beurmann published in 1903 a case of similar nature in France. De Beurmann and Gougerot, from 1906 onwards, have published many cases, and have completely investigated the subject of human sporotrichosis bacteriologically and histologically, as well as clinically. Their researches have been confirmed by Gaucher and Monier-Vinard, Duval and Fago, Vaquez, Bonnot, Lambry, Adamson, Esmeni, and many others. Cases have been reported from the tropics by Lutz and Splendore in Brazil, and by us in Ceylon. Clair has observed the disease in Arab stokers on board some steamers of the Messageries Maritimes Company.

Ætiology.—The fungi causing the disease belong to the genus *Sporotrichum* Link, 1809, of which nine species have been so far described in man:—

Sporotrichum Link, 1809
S. ***schenki*** Hektoen and Perkins, 1901.
S. ***beurmanni*** Matruchot and Ramond, 1905.
S. ***dori*** de Beurmann and Gougerot, 1906.
S. ***gougeroti*** Matruchot, 1910.
S. ***jeanselmei*** Brumpt and Langeron, 1910.
S. ***indicum*** Castellani, 1908.
S. ***asteroides*** Splendore, 1909.
S. ***lesnei*** Vuillemin, 1910.
S. ***councilmani*** Wolbach, Sisson and Meier, 1917.

For the description of these organisms, see chapters on Fungi (p. 1117).

The species so far found in the tropics are—S. ***beurmanni*** Matruchot and Ramond in Brazil and Africa, S. ***asteroides*** Splendore, 1909, in Brazil, and S. ***indicum*** Castellani, 1908, in Ceylon. These fungi are morphologically very similar. In the human lesions the fungus appears morphologically as a yeast, and is very scarce. In cultures mycelial threads and numerous spores are seen. The spores are ovoid, 5 to 6 μ in length by 3 to 4 μ in breadth. The mycelial filaments are very slender (2 μ) in S. ***beurmanni*** and S. ***schenki***; somewhat broader ($2\frac{1}{2}$ to 3 μ) in S. ***indicum***. S. ***asteroides*** is characterized by the presence of peculiar radiate bodies in the affected tissues. These fungi grow easily on the ordinary culture media, best of all on Sabouraud's peptone-glucose agar. Colonies develop from the fourth to the tenth day as small white points, surrounded by a delicately rayed aureola of whitish colour. They gradually increase in size, coalesce, become convoluted, and take a dark greyish, brownish, and even black colour. These fungi, according to De Beurmann, may perhaps live saprophytic on vegetables (lettuce-leaves, and other kinds of vegetables used as salads) and on insects (flies, caterpillars, larvæ). According to De Beurmann, infection takes place by contact with unclean vegetables.

FIG. 836. SPOROTRICHIC LYMPHANGITIS.
(From a photograph by Splendore.)

The fungi may also, apparently, live saprophytically in the oral cavity and pharynx of certain individuals, who then become carriers.

The rat, mouse, monkey, cat, and very young guinea-pigs, are all more or less susceptible, and may be infected by subcutaneous or intraperitoneal inoculation. The rat is the most susceptible animal. In it Lutz and Splendore have described a spontaneous sporotrichosis due to a *Sporotrichum* apparently identical with *S. beurmanni*. Moore and Davis have described a case following the bite of a field-mouse. The patient's blood agglutinated equally well *S. schenki* and *S. beurmanni*. The affection has also been observed to occur spontaneously in the dog (Gougerot and Caravan) and in the mule (Fontoynont and Carougeau) in Madagascar.

Histopathology.—The histopathology of the cases due to *S. beurmanni* has been investigated by De Beurmann and Gougerot; that of the cases due to *S. asteroides* by Splendore; that of the cases due to *S. indicum* by ourselves. Whatever the causative species of *Sporotrichum*, the histological lesions are apparently the same, and correspond to the three principal types described by De Beurmann and Gougerot—viz., (1) An epithelioid type, with presence of giant cells—this corresponds to the tuberculoid type of De Beurmann and Gougerot; (2) a lympho-connective tissue or syphiloid reaction; (3) a polymorphonuclear or ecthymatiform type.

Symptomatology.—In a well-marked case, several gummatous-like swellings, situated in the subcutaneous tissue, are present on various parts of the body—the arms, legs, and trunk. The size varies from that of a small pea to that of an orange. On palpation, they are hard, resistant at first; later they soften, the skin becomes reddish or violaceous and after a time perforates. From the fistulous opening a yellowish homogeneous pus is slowly evacuated, or at times a thin serous discharge. In some cases the suppuration ceases, granulation sets in, and a coarse cheloid-like scar remains. In other cases the fistulous opening enlarges and a crateriform ulcer, with often a fungating fundus, develops. The lymphatic glands may occasionally become affected. The course of the disease is very chronic. In some cases deep gummata develop under the periosteum of various bones, and in the muscles. Large granulating ulcerations may form in the buccopharynx and larynx The general health, as a rule, is not much affected.

Clinical Varieties.—The commonest varieties met with are:—

1. The localized type, with sporotrichic chancre and ascending sporotrichic lymphangitis.
2. The disseminated gummatous type.
3. The disseminated ulcerative type, presenting often polymorphic lesions—viz., syphilitic-like, tubercular-like, ecthymatous, rupial, furuncular.
4. The extracutaneous type, with sporotrichic lesions of the mucous membranes, the muscles, the articulations, the bones, the organs of special sense, the internal organs—lungs, kidneys, etc.

De Beurmann has put on record a case of mycetoma of sporotrichic origin. Cases of systemic sporotrichosis have been described.

Diagnosis.—The principal clinical signs on which to base a *probable* diagnosis of sporotrichosis are the presence of gumma-like lesions while the patient is in a good general state of health; the mixture of lesions of different appearance: partial cup-shaped softening of the nodes, breaking down in the centre and ending in ulceration, with violaceous edges generally undermined; presence of viscous pus or of a serous lemon-yellow discharge; indolent evolution; absence in most cases of enlarged glands. The definite diagnosis can only be made by bacteriological methods. The simple microscopical examination of the pus of the abscesses, or scrapings of the ulcers, is not sufficient, as the fungus is extremely scarce. Cultivation must be resorted to. A few glucose-agar tubes are inoculated, and kept at room-temperature without capping. After four to ten days the first colonies of *Sporotrichum* will appear.

Treatment.—Potassium or sodium iodides in full doses (15 to 20 grains three to four times daily), well diluted in water or milk, induce a rapid disappearance of all the lesions. In persons who cannot take potassium iodide, saiodin in the same dose may be given in cachets. The ulcerated lesions may be dressed with a lotion of potass. iodide 10 parts, iodine 1 part, water 500 parts. Surgical measures should be avoided.

Pinoy has noted that the action of the iodides is increased by a salt-free diet.

Prophylaxis.—Any small wound should be disinfected with tr. iodi.

ACLADIOSIS.

Definition.—An ulcerative dermatomycosis caused by *Acladium castellanii* Pinoy.

Historical and Geographical Distribution.—The condition has been observed by Castellani since 1907 in Ceylon, but he did not fully describe it until 1916. Cases have been observed in Ceylon, the Federated Malay States, and Macedonia.

Ætiology.—The condition is caused by a fungus which Castellani isolated in Ceylon. Cultures were sent to Professor Pinoy, of the Pasteur Institute, who investigated it botanically and classified it, giving it the name of *Acladium castellanii* Pinoy, 1916. Professor Pinoy's description may be quoted:—

'The growth on artificial media (such as carrot, potato, glucose agar) consists of many small roundish masses, which later on may coalesce, covered by spiculated formations, giving them a prickly appearance, and consisting of erect, straight filaments, parallel to each other, or at times interlacing. These filaments are approximately 2 microns in diameter, and carry laterally pseudo-conidia of variable shape, cylindriform, pyriform, or spherical, attenuated in size at their points of insertion. Most of these pseudoconidia are 4 microns in length, with a breadth of 3 microns. This type of fructification recalls the type Acladium described by Bodin in certain species of the genus *Trichophyton* (Malmsten, 1848).

'These pseudoconidia become detached and then develop by sprouting, and mycelial filaments are formed. Certain filaments produce spherical chlamydospores arranged in small strings, as found in certain fungi of the genus Fusarium. These small chains of chlamydospores are very frequently terminal, the dimensions being variable—8-10 microns' (Fig. 595, p. 1113).

In cultures on carrot and potato the colonies are white, on glucose agar often amber colour. Very old cultures may show a certain amount of pigmentation (see p. 1112).

Histopathology.—The histopathological investigation of the condition is far from completed. From the preliminary investigation it would seem that the lesions are very similar to those one sees in sporotrichosis and that three types of lesions may be distinguished: (1) An epithelioid or tuberculoid type, with presence of giant cells; (2) a lympho-connective tissue type (syphiloid); (3) polymorphonuclear type (ecthymatous).

Clinical Symptoms.—In a well-marked case ulcerative lesions are present all over the body, though they are in smaller number or absent altogether on the face, scalp, palms, and soles. Most of the ulcers are sharply defined, roundish or oval, with red granulating fundus. Their appearance is well shown in the illustration, a photograph of a Ceylon case. In many cases there is abundant purulent secretion, which collects and dries up in thick yellow crusts, covering the ulcers. Gummata-like nodules and furuncle-like lesions may be observed. The superficial lymphatic glands may be enlarged. The lesions in most cases give very little pain, or none at all; itching is often completely absent, but occasionally the patient complains of slight pruritus. The general condition of the patient is not seriously affected for a long time, but he often complains of a certain degree of weakness and discomfort. Not infrequently there is serotine fever. The blood has been examined in two cases in the tropics; in one case in the Balcanic Zone: Wassermann reaction negative. In the first two cases red blood-corpuscles and hæmoglobin were slightly below the normal; in one there was eosinophilia (5 per cent.), which may have been due to a concomitant *Ascaris lumbricoides* infection. In the Macedonian case, the blood of which was examined, there was a distinct leucocytosis (16,000 leucocytes)

FIGS. 837 AND 838.—ACLADIUM CASTELLANII PINOY: HANGING-DROP CULTURE.

(*a*) After twenty-four hours', (*b*) after three days' growth.

of the polymorphonuclear type; in this patient there was abundant purulent secretion and serotine fever, which on some days reached 102° and 103° F.

Diagnosis.—A positive diagnosis can be made with certainty only by cultural methods. The microscopical examination alone is of very little use, hyphomycetic elements being as a rule absent microscopically in the scrapings from the ulcers and contents of nodules. The material should be inoculated in glucose agar tubes. Four to eight days after inoculation small, yellowish, amber-coloured colonies appear; they enlarge fairly rapidly, become hemispheric, and often coalesce in a knotty mass. At times the colonies may not fuse together; each colony then remains separate, reaches a large size, and occasionally presents peculiar radiating furrows as seen in certain species of trichophytons In many cases where the material has been collected from ulcerated lesions, the fungus grows in symbiosis with a coccus, and it may be difficult to separate the two organisms.

FIG. 839.—ACLADIOSIS OF THE ARM.

The malady is often taken for a syphilitic condition. The history, the negative examination of the lesions for spirochætes, the failure of mercury and salvarsan treatment, will exclude it. When the lesions are covered by raised, thick, bright, yellow crusts the condition must be differentiated from yaws: in acladiosis, on removing the crusts, ulcers are found, while in yaws, the typical frambœsiform nodules will be seen; in scrapings from yaws lesions the treponema will be found. Acladiosis can be differentiated from sporotrichosis and other affections of hyphomycetic origin by cultural methods.

Prognosis.—The course of the disease may be very long, and there is very little or no tendency to spontaneous cure; but if a proper treatment is carried out a cure can be obtained fairly rapidly in the majority of cases. A few cases respond to treatment extremely slowly.

Treatment.—Potassium iodide given in full doses (20 gr *ter diem*) acts satisfactorily. The drug appears to act at times more rapidly if given according to Professor Pinoy's method—viz., in conjunction with a salt-free diet. If potassium or sodium iodide is not well borne, sajodin and other similar preparations may be tried, but the result is not so satisfactory. Mercury and arsenic have no effect on the course of the malady. As regards local treatment, it is sufficient to keep the ulcers clean by using a weak mercury perchloride lotion.

CRYPTOCOCCOSIS EPIDERMICA.

Synonym.—Saccharomycosis epidermica (Castellani).

Historical and Geographical.—This condition was first described by Castellani in Ceylon. We have recently found cases in the Sudan and in the Balcanic Zone.

Ætiology.—The causal organism is *Cryptococcus epidermidis* Castellani, 1914.

Symptomatology.—The condition is fairly frequent in Europeans who have resided for some years in the tropics, but is also found in natives. It is characterized by the presence on the arms, and more rarely on the chest and neck, of small roundish patches of a dirty yellow or brownish colour, which can generally be removed by thorough scraping. These patches consist of large numbers of blastomyces-like elements of various size, rounded or oval, which so far have not been cultivated.

Treatment.—Thorough scraping with sand-soap and hot water is generally sufficient to remove the patches. In obstinate cases a salicylic sulphur ointment is useful.

INTERTRIGO SACCHAROMYCETICA.

Synonym.—Intertrigo Blastomycetica.

Remarks.—Cases of this affection have been observed by Castellani in Ceylon, and similar ones have later been reported by Whitfield and others in Europe. The affection is apparently rare. It generally attacks the scroto-crural and axillary regions. The affected skin is red, and there may be slight exudation. The borders of the eruption are fairly well marked, but never elevated. In most cases there is not much itching, and the affection may recover spontaneously.

Ætiology.—In scrapings a *Saccharomyces* (*S. samboni* Castellani, 1907), which is easily cultivated on sugar media, is found, or in other cases fungi of the genus *Monilia*.

Treatment.—The treatment consists in washing the affected parts with potassium permanganate lotion, 1 in 4,000, or resorcin, 1 in 100; followed by the application of powders of boric acid ʒi., talci ℥i.; or salicylic acid gr. x., talci ℥i.

ASPERGILLOSIS AND PENICILLIOSIS OF HAIRY PARTS.

The affected hairs—generally those of the beard and moustache, occasionally of the axilla—present dirty greyish or whitish punctiform formations, which on microscopical examination are seen to consist of penicillar or aspergillar fungi (*Penicillium barbæ*, *Asper-*

gillus barbæ). Occasionally both types of fungi are found on the same patient. The affection is very chronic. The diagnosis is easy, the characteristic aspergillus and penicillium fructifications distinguishing this condition from other parasitic nodular affections. The simplest method of treatment is by shaving, and afterwards using regularly a medicated soap, such as carbolic soap, tar soap, or sulphur soap. If the patient does not wish to shave his beard, turpentine may be tried.

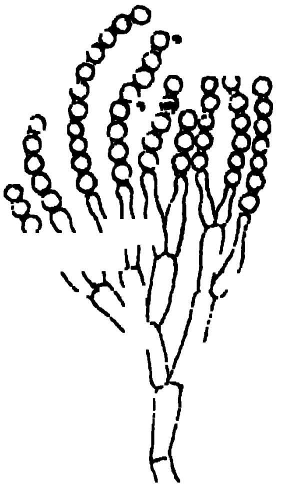

FIG. 840.—PENICILLIUM FRUCTIFICATION.

In natives who do not bathe frequently, such as old persons and beggars, the skin presents often large dark patches due to accumulated dirt, in which aspergillar and penicillar fungi are often present, living saprophytically. This condition has nothing to do with pinta, as a thorough scrubbing with soap will remove the dirt and the aspergillar and penicillar fungi which may be present.

PINTA.

Synonyms.—Mal de los Pintos, Mal del Pinto, Caraate, Tina, Quirica, Pannus Carateus (Alibert), Tache Endémique des Cordillières (Alibert), Lota, Cativi, Bulpiss (Lerch).

Definition.—The term ‘pinta’ does not indicate a single disease, but a group of closely allied dermatomycoses characterized by the presence of patches of various colour, due to different species of fungi of the genera *Aspergillus*, *Penicillium*, *Monilia*, and *Montoyella*.

History.—The disease first began to draw the attention of medical writers in the eighteenth century, though it was apparently well known to the inhabitants of the affected regions since remote times, as it is found to have formed the subject of prayers and supplications used by the Aztecs centuries before the Spanish Conquest.

A short description of the malady is found in the Encyclopædia of Polanko, of Mexico, in 1760; and in Juan de Velasco's ‘Historia,’ in 1789, in Columbia. Velasco believed the malady to have been imported by African slaves. A fairly complete description is given by Alibert, in 1829, under the name of ‘tache endémique des Cordillières,’ or ‘pannus carateus.’ Among the modern authors, the clinical and pathological investigation of Gomez, Uribe, Vribechyel, Iryz, Ruiz y Sandoval, Gastambido, may be mentioned.

More recently the investigation into the ætiology of pinta by Montoya has been of the greatest importance.

Climatology.—Pinta is practically limited to tropical America, where it is found in Venezuela, Peru, Chili, Central American States, Mexico. Cases have been reported from Brazil. It is extremely common in Columbia, where, according to Montoya, 4 per cent. of the total population is affected. There the patient affected with the disease is called ‘caratejo.’ The disease is not equally distributed; in each country there are localities where the disease is common, while other districts are almost unaffected. In Columbia it is the northern province of Santander which is more particularly affected; in Mexico the disease is most frequently found in the provinces of Tabaxo, Chiaspas, Valladolid, Michoacan.

A few cases of pinta have been reported from Egypt by Madden, Goodman, and Sandwith, and previously Legrain described somewhat similar cases from Tripoli and the Sahara. Legrain, however, did not find any fungus. A few isolated cases have also been reported from the Gold Coast, and others from the Philippine Islands by P. G. Woolley. In Ceylon and India only imported cases are seen.

Ætiology.—Previously to Ruiz y Sandoval and Montoya's investigations the disease used to be ascribed to many different causes. Some authors believed it to be due to the mineral salts (sulphates) contained in the waters of the mines and other localities where the malady is endemic; others considered it to be due simply to insanitary conditions, insufficient food, and a hot and damp climate; others, again, believed the affection to be induced by the action on the skin of volcanic cinders: while, according to some authorities, the malady was an hereditary complaint.

Ruiz y Sandoval, in Mexico, first detected the parasitic nature of pinta. He believed there was only one species of fungus to be found in the affection, and that the different colours of the patches were due to the different depths at which the fungus was growing in the various strata of the epidermis. Montoya's classical researches in 1898 clearly showed the plurality of species and genera of the fungi found in the disease, and demonstrated that each variety of pinta is due to a different fungus. More than twenty different species were found by him.

In the present state of our knowledge of pinta it is impossible to give a satisfactory classification of these fungi. The principal ones may be collected into the following groups:—

I. Fungi of genus *Aspergillus*: *Aspergillus pictor* Blanchard, 1895, and several other species. *A. pictor* is found in the pure violet variety of pinta; the other species are observed in the pure blue and bluish and violet-black varieties, as well as in a form of the red variety. Several of these species are not in reality true *Aspergilli*, as they possess organs of fructification intermediate between those of the genus *Aspergillus* and those of the genus *Penicillium*.

II. Fungi of genus *Penicillium*: *Penicillium montoyai* Castellani, 1907, and several other species. They are found in some greyish-violet varieties of pinta.

III. Fungi of genus *Monilia*: *Monilia montoyai* Castellani, 1907. Found in some cases of white pinta.

IV. Fungi of genus *Montoyella*: *Montoyella nigra* Castellani, 1907. Found in one variety of black pinta. *M. boxini* Castellani, 1907. Found in a red variety of pinta.

The term *Aspergillus* (*Trichophyton*) *pictor*, introduced by Blanchard in 1895, when the plurality of species of the fungi found in pinta had not yet been demonstrated, is now used in a restricted sense to indicate the *Aspergillus* found in the pure variety of the disease.

Montoya believes that the fungi found in Columbian pinta, or caraate, are different species from those found in Mexican pinta.

Appearance of the Fungi in Fresh Preparations.—Scrapings from the patches examined in liquor potassæ show in most cases between the epithelial cells long dichotomous mycelial threads, from which shorter and thicker branches take origin at various points. These thicker branches terminate in comparatively large fructifications. The morphological characters of these fructifications vary according to the species and genus of the fungus present. They may be typical aspergillar or penicillium-like fructifications, or they may show intermediate characters between those of *Aspergillus* and *Penicillium*. In many cases the fructification organ is represented by a pear-shaped or triangular formation, surmounted by five to six rods (sterigmata), each of which supports a string of five to six spores. The number of these spores, however, may vary. They are globular, have a smooth surface, show a double-contour, and their diameter is much larger than that of the mycelial tubes.

In the cases where the fungus present is a *Monilia* or a *Montoyella*, such or similar fructifications are absent, and only mycelial tubes and some scattered spores are seen.

Cultures.—The various fungi found in pinta are easily cultivated, the best medium being Sabouraud's maltose agar. The *optimum* temperature is between 30° and 40° C.

The composition of Sabouraud's medium

Maltose	4 grammes.
Peptone (Chassaing) ..	1 gramme.
Agar	1·5 grammes
Distilled water	100 c.c.

Culturally, the fungi may be divided in five groups

1. Those showing in cultures aspergillar fructifications.
2. Those showing penicillium fructifications.
3. Those showing intermediate fructifications between the *Aspergillus* and the *Penicillium*.
4. Those showing simpler fructifications characteristic of the genus *Monilia*—viz., a mycelial thread terminating in a single string or small bunch of roundish spores.
5. Those in which higher organs of reproduction are absent, and reproduction takes place somewhat similarly to what is observed in the genera *Microsporum* and *Trichophyton*—by conidia and terminal segmented and unsegmented 'spindles.' The fungi of this group, found by Montoya in a variety of black pinta, by Bodin, and later by Castellani, in a variety of red pinta, constitute the genus *Montoyella*.

Inoculation Experiments.—Montoya has tried to infect rabbits, using various cultures of the fungi found in the disease. On several occasions a desquamation of skin and loss of hair was observed, and some chromatic patches appeared. Uribe succeeded in inoculating several mulattoes.

According to Montoya, the fungi of pinta live saprophytically in certain waters, especially in those of mines and localities where the temperature is constantly high. He states that he obtained pure cultures of the pinta fungi direct from such waters. He has also found the same fungi as ectoparasites on the bodies of mosquitoes of the genus *Culex*, on sandflies (*Simulium*), and on the body of some bugs (*Clinocoris*), which are very common in the mines. He believes, therefore, that mosquitoes and other insects play a rôle in the transmission of the disease.

In some old chronic cases of pinta an *Acarus*—somewhat resembling *Acarus scabiei*, though larger—has been found to live in the epidermal squamæ, and some writers believe that this *Acarus* also plays a part in the transmission of the malady.

Predisposing Causes.—What the older authors believed to be the true causes of pinta—viz., a hot, damp, climate; insanitary surroundings and poor feeding; the mineral salts contained in the waters—are only predisposing causes, some of which, however, are of great importance. The hot, damp climate favours the growth of the fungi: the water of the mines, which contains a large amount of mineral salts (especially sulphates), produces after a time in those who use it for washing, etc., a dermatitis with fissures and other eczematous-like lesions which greatly facilitate the infection.

All races are liable to be attacked by the disease, but mulattoes seem to be particularly prone to become infected. Albinos are said to be immune. Both sexes are equally liable to become infected, though males, on account of their occupations, are more frequently affected. The malady generally appears between the age of fifteen and twenty-five, but it may appear at any age, and has been seen in children three or four years old.

It has been observed that individuals of the negro race are more liable to contract the black variety than any other kind of the disease, while whites are especially liable to contract the red variety. Miners and agricultural labourers are affected in most cases by the violet variety.

Symptomatology.—The disease begins very gradually. After an incubation period varying, according to different authors, between a few weeks and some months, one or several small slightly pruriginous spots appear on uncovered parts of the body. The spots increase very slowly in size, and some may fuse together. They are roundish, or may have an irregular outline. At first they are hardly raised above the normal skin. The surface of the patches is generally dry and rough, and is covered with fine pityriasic squamæ in recent cases, with larger and thicker scales in older ones. Occasionally, in chronic cases, the surface of the patches, instead of being dry, may be moist or somewhat greasy or glutinous.

The hairs of the affected regions become atrophied, and later on fall out. The shedding of hair is not due to the fungi invading directly the hair; it is due to a peculiar fibrosis of the hair follicle, at the place of the hair a hard formation remaining, like a grain of sand (fibroid folliculitis of Montoya).

Pruritus is generally well marked, especially at night-time. There are often patches of hyperkeratosis on the palms and soles, and the normal lines and sulci appear much deeper.

Old chronic cases occasionally exhale a peculiar musty odour, which has been compared to the smell of cat's urine, or to the bad smell of dirty linen kept in a warm, damp place.

The affection may spread to the whole body, except the palms of the hands and the soles of the feet. The nails are never attacked. The scalp is not usually affected.

The disease has no tendency to spontaneous cure. Its course is very chronic, and may last the whole of the patient's life.

Some of the older authors state that the patients during the incubation period suffer from fever, vomiting, and diarrhœa. Montoya says that pinta patients have not got an odour *sui generis*, as stated by most observers. In cleanly patients no smell whatever is noticeable, apart from the peculiar odour of the negro race.

Clinical Varieties.—Clinically, six different varieties may be distinguished, each of which shows several subvarieties:—

1. The Black Variety.
he Blue Variety.
he Violet Variety.
he Red Variety.
he Yellow Variety.
he White Variety.

Black Variety.—The patches are of a black colour, and are very often found on the face, though they may be present on any other part of the body except the palms and soles, similarly to all the other varieties. The patches are hardly raised, and their surface is slightly desquamating. Pruritus is generally complained of, but is not, as a rule, so unbearable as in the other varieties. Black pinta is found in negroes more frequently than in individuals of Caucasian race. The course is very chronic. The treatment is difficult, though not so difficult as in the other varieties.

Black pinta shows two subvarieties—one is characterized by the presence of patches of a black-violet colour: the other by patches of jet-black, indian-ink black colour. The fungus found in the first is an *Aspergillus* (species undetermined): in the second a ***Montoyella*** (***M. nigra***).

Blue Variety.—This is much less frequent than black pinta. The patches are of a blue colour. They generally begin to appear first on the dorsum of the hands, and then tend to spread over the whole body—uncovered as well as covered parts. There generally is intense pruritus.

The fungus usually found in blue pinta is ***Aspergillus.***

Violet Variety.—Apart from the colour of the patches, which is violet, the clinical symptoms and course of this variety are identical with those of blue pinta. It is extremely common among rural labourers and miners.

There are numerous subvarieties of violet pinta. In some cases the patches are of a pure violet colour; in other cases the colour may be violet-greyish, violet-brownish, violet-purplish. There are cases in which the patches are at first of a greenish colour, to become violet-bluish later on. The fungus found in the pure violet pinta is an *Aspergillus* (*A. pictor* Blanchard, 1895); the fungus found in the violet-greyish cases is a *Penicillium*—*P. montoyai* Castellani, 1907; the fungi found in the other varieties are *Aspergilli* or fungi presenting transition characters between the *Aspergillus* and the *Penicillium*.

Red Variety.—This is the commonest variety found in white patients. The patches first develop, as a rule, on the dorsum of the hands and feet, and spread to large portions of the body. The patches are red—often brick-red—and usually show a rather abundant desquamation. Pruritus is very distressing, especially at night-time. Secondary lesions due to scratchings and inoculation of pyogenic micro-organisms are not rare. Ulcerative lesions have been reported by several observers as occasionally occurring.

In some cases of red pinta an *Aspergillus* (species not determined) is found; in others a fungus of the genus *Montoyella*—*M. bodini* Castellani, 1907, found by Bodin in 1903 in a patient who was under the treatment of Darier.

Castellani, in 1907, found the same or a very similar *Montoyella* in a case of red pinta observed in a European sailor who had long been in tropical America. In this case the disease had not yet spread much. Besides the red patches, there was on the right forearm a small greyish-violet spot, in which a fungus was found, which gave *Penicillium* fructifications in cultures (*P. montoyai*).

Red pinta is more serious than any other variety, as it affects not only the superficial strata of the epidermis, but the rete Malpighii as well as the corium.

Yellow Variety.—Very common among half-castes. It generally begins on the chest or arms. The patches are yellow, and at first are not pruriginous and not desquamating. In old cases, however, there is pruritus. This variety is very frequently mixed with patches of white pinta, and is difficult to cure. The fungi found belong to the genera *Monilia* and *Aspergillus*.

White Variety.—The patches are of a dull white colour, and are generally very large. The surface is usually rough and desquamating, but at times it may be smooth. In some cases a fungus of the genus *Monilia* is present, but, according to Montoya, in other cases no fungus whatever is to be found. Montoya considers the white variety of pinta to represent in many cases the ultimate retrogressive stage of all the other varieties except the red. The patches of white pinta would be in such cases in reality unpigmented leucoderma-like areas due to the disturbing action of the various fungi on the pigmentation processes of the skin.

Montoya's belief on the nature of white pinta in some cases is supported by Castellani's observations on tinea flava and tinea alba. In both these dermatomycoses white, pseudo-leucodermic patches may occasionally be seen long after the fungus has died out, and these patches may remain unpigmented for months and years.

Mixed Variety.—Not infrequently the same patient may be affected with several varieties of pinta, presenting a grotesque tattooed or piebald appearance.

It is especially white pinta which is found associated with one or more of the other varieties.

Diagnosis.—This does not present any difficulty in the countries where the disease is endemic. In any doubtful case the microscopical examination, supplemented when necessary by the use of cultural methods, will clear the diagnosis.

Differential Diagnosis—*Tinea nigra.* In contrast to the black variety of pinta, tinea nigra is very superficial, does not extend to large portions of the body, may attack the palms of the hands, is not pruriginous, is easily cured except when affecting the palms. The microscopical examination of scrapings from patches of tinea nigra will show mycelial tubes of irregular shape and large globular spores collected in bunches. The spores are grouped together in a somewhat similar manner to what one sees in pityriasis versicolor.

Tinea Flava.—In contrast to yellow pinta, the fungus of tinea flava is a *Malassezia*, has the same morphological characters of the fungus found in pityriasis versicolor, and cannot be grown artificially.

Tinea Albigena and Tinea Alba.—These are generalized trichophytic and epidermophytic affections, and are easily distinguished by the characters of the fungi.

Leprosy can be distinguished from white pinta lesions by the sensibility not being impaired in pinta.

Only white pinta patches with no fungus might be mistaken for *leucoderma* on superficial examination. White pinta is very often associated with other varieties of pinta, which are easily diagnosed. Leucodermic patches are smooth, non-pruriginous, and the skin surrounding them is often hyperpigmented.

Prognosis.—Pinta, though not a fatal disease, must be considered a serious affection, as its course is chronic and the treatment very difficult. In most cases the general health remains satisfactory, but the disfigurement is very distressing to the patients, who often become nervous and irritable. The pruritus, which is generally more marked at night, is also a cause of great distress and sleeplessness.

Treatment.—The popular treatment in Columbia is citrine ointment (mercury nitrate ointment). Other parasiticides have been tried, with a varying degree of success. When the eruption is at the very beginning, tincture of iodine may suffice. The best results have been obtained by using chrysarobin (chrysarobin, gr. x. to xxx.; ung. zinci ox., ℥i.). This must be applied cautiously. When the malady affects large tracts of the body, only a portion should be treated at a time, to prevent as far as possible symptoms of absorption. The urine should be regularly analyzed during the treatment. The chrysarobin ointment must not be applied to the face, lest a severe conjunctivitis should develop. For the face a resorcin, or resorcin-sulphur, or resorcin-salicylic, or salicylic acid ointment (resorcini, gr. xxx. to ʒi.; ac. salicylici, gr. xv.; vaseline, ℥i.), is advisable, or citrine ointment may be used.

Montoya recommends chrysarobin dissolved in chloroform (chrysarobin 10 parts, chloroform 90 parts). Apply with a fine brush. When dry, apply gutta-percha dissolved in chloroform (gutta percha 10 parts, chloroform 90 parts).

Chrysarobin may conveniently be applied in the form of a vernisol varnish cent.).

PIEDRA.

Synonym.—Trichosporosis Tropica.

Definition.—Piedra is a mycotic disease of some parts of South America causing very hard, small nodosities on the hair.

Historical and Geographical. The condition has been known locally in Columbia since remote times, but the first scientific descriptions are due to Desenne (1878), Morris (1879), Osario, and Megalhães. More recently the condition has been studied by Juhel Renoy, Pernet, J. M. H. MacLeod, Horta, and others. This disease of the hair is common in some districts of Columbia, especially the valley of Canca; but closely allied conditions are observed in several parts of the tropics, and occasionally in temperate zones (*piedra nostras*).

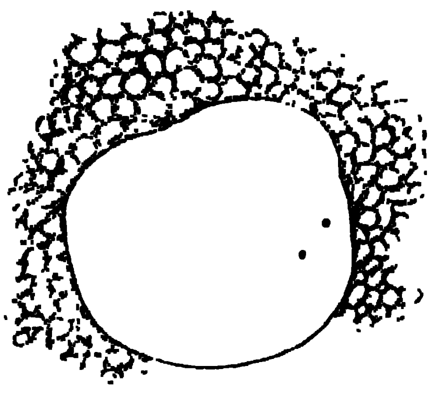

Fig. 841.—Transverse Section through a Piedra Nodule

Fig. 842.—Piedra.

Ætiology.—If an affected hair is washed in ether, and then treated with liquor potassae, and examined microscopically, the nodules will be seen to consist of large polyhedric refringent bodies, held together by an amorphous substance acting as cement. These bodies are the spores of the fungus causing the disease (*Trichosporum giganteum* Behrend, 1890). The description of the fungus is given on p. 1101. In Columbia it is generally believed that the infection takes place by washing the hair with a mucilaginous oil, much used by the women of the country. In British

Guiana natives consider it to be due to bathing in certain white or milky waters, while it does not occur if they bathe in the brown peat bush waters.

Symptomatology.—The hair of the head of women, and less frequently the hair of the head and beard of men, is affected. The affected hairs present strings of pin-head-sized nodosities, which are better felt than seen. The nodosities may be very numerous, and are found on the surface of the hair-shaft, either on one side or surrounding it like a sheath. They are black and hard, though not so hard as the name piedra (stone) would imply, and a kind of crepitation is produced when the hair is combed. There is often matting and knotting of the hair. The disease is chronic, and the nodosities do not disappear spontaneously.

Horta has described a variety of piedra in Brazil, characterized by the nodules containing large cyst-like structures, which Pinoy considers to be probably asci (see p. 1102).

Diagnosis.—The microscopical examination of the nodosities renders the diagnosis easy.

Prognosis.—The affection is of long duration, and has no tendency to spontaneous cure.

Treatment.—This is difficult. It has been recommended to apply a 5 per cent. salicylic alcoholic solution or benzene and turpentine to the hair, and to wash the head regularly with a perchloride lotion (1 in 2,000). In obstinate cases it is necessary to shave the head.

Trichosporosis Indica.

In India and Ceylon a condition similar to piedra is occasionally observed. It is, however, much less severe, a few minute nodules only being present on the hairs of the beard and moustache, and the hair of the scalp being rarely affected. The fungus seems to be different from that of the Columbian piedra.

Trichosporosis of Temperate Zones.

Cases of trichosporosis of temperate zones or piedra nostras (tinea nodosa) have been described by Biegel (1869), Caro, Behrend, Unna, Pick, Vuillemin. The nodosities in such cases have been found on the hairs of the moustache and beard, not on the hairs of the head. The fungi are slightly different from *Trichosporum giganteum*. Several species have been described—*Trichosporum beigeli* Rabenhorst, 1867, *T. ovoides* Behrend, 1890 *T. ovale* Unna 1896.

TRICHOMYCOSIS FLAVA, RUBRA, NIGRA.

Synonyms.—Trichomycosis axillaris, Trichonocardiasis, Tropical lepothrix, Castellani's Trichomycosis, Trichomycosis chromatica, Chromotrichomycosis.

Definition.—A nodular affection of the hair, usually of the axillary regions, caused by *Cohnistreptothrix tenuis* Castellani (*Nocardia tenuis* Castellani), either alone or in symbiosis with chromogenic cocci.

Historical.—Nodular affections of the hair have been described by European observers under various names, such as Lepothrix (E. Wilson), Trichomycosis nodosa (Patterson), Trichomycosis palmellina (Pick), but a great deal of confusion has existed until recently on the subject, very different clinical descriptions having been given and the condition being ascribed to widely different germs.

Paxton, Wilson, Pick, and later Payne, Patterson, Crocker, Pusey, etc., described the hairs as presenting irregularly lobed masses of hard consistency in which were often embedded some of the fibres of the cortex.

According to Crocker, the fibres of the whole shaft may be split up and the hair may break off with a brush like termination. The researches on the ætiology by various authorities gave the most widely different results, various bacilli being described by Payne and Patterson, a diplococcus by Eisner and later Sonnenberg, and a micrococcus by Colombini, etc. Babès, Pick, Balzer, and Barthemly considered that the *Bacillus prodigiosus* played a rôle in the causation of the affection

In 1911 Castellani carried out an investigation in the tropics, describing the condition as seen there and differentiating three varieties- the yellow variety, the black variety, the red variety. He demonstrated that the yellow variety was caused by a nocardia (*Nocardia* or *Cohnistreptothrix tenuis* Castellani); the black variety by the same nocardia plus a black pigment producing coccus (*Nigrococcus nigrescens* Castellani) living in symbiosis with it; the red variety by the same nocardia plus a red pigment producing coccus living in symbiosis with it, and which was later on called *Rhodococcus castellanii* by Chalmers and O'Farrell. Castellani's work was confirmed and amplified in the Sudan by Chalmers and O'Farrell, who suggested for the affection the term 'trichonocardiasis', in West Africa by Macfie, who described a variety of the red type: *fusca*; and by various observers in several other countries. In 1915-1918 Castellani observed in the Balcanic-Adriatic Zone the three varieties he had described in the tropics, and found the same organisms.

Ætiology.—The researches of Castellani have demonstrated that the yellow variety is due to a very thin, bacillary-like fungus, for which he proposed the name *Nocardia tenuis*, later changed into *Cohnistreptothrix tenuis*. The black and red varieties are due to a symbiosis of this fungus with chromogenic cocci, a coccus producing black pigment in the black variety, a coccus producing a red pigment in the red type.

Nocardia tenuis Castellani, 1912 (*Cohnistreptothrix tenuis* Castellani, 1912) — The microscopic examination of the nodules reveals the presence of enormous numbers of bacillary like bodies, which are Gram positive, but not acid-fast. If the nodules are kept in alcohol or formalin for several months, the fungus apparently loses partially or totally its property of being stainable by Gram's method. They vary in length, 4 to 10 μ and more; the average breadth is approximately 0·3 to 0·6 μ, they may be straight or variously bent, occasionally branching; they are fairly closely packed together, and are embedded in an amorphous cementing substance In regard to cultivation, Chalmers and O'Farrell observed some slight growth in hanging drops of equal parts of human serum and normal saline. Macfie in one case succeeded in cultivating the fungus on ascitic agar, the colonies being very small and translucent.

Characters of the Coccus-like Organism found in the Black Variety (*Micrococcus* or *Nigrococcus nigrescens* Castellani, 1911).—It is a Gram-positive, rather large, non-motile coccus, which in certain media may take the appearance of a cocco-bacillus. Sugar media are more suitable for the growth of the organism than the ordinary agar.

Sabouraud Agar.—Colonies appear twenty-four to forty-eight hours after inoculation. They are roundish, at first white, but after a couple of days the centre of each colony turns black, and this pigmentation slowly spreads excentrically. After a time the colonies coalesce into a jet-black mass.

Glucose.—Growth similar to Sabouraud, but slightly less abundant. The black pigmentation develops from the centre of the colonies and slowly spreads towards the periphery

Ordinary Laboratory Agar.—Growth much less abundant than on most sugar agars, and black pigmentation less marked.

Levulose Agar.—Identical to glucose.

Saccharine Agar.—The pigmentation is less pronounced, and does not spread to the whole of the growth.

Raffinose Agar.—Same as saccharine.

Lactose Agar.—Scanty pigmentation.

Alkaline Maltose Agar.—Black pigmentation well marked, though in many cases it does not extend to the whole of the growth.

Acid Maltose Agar.—Growth less abundant than on acid maltose. Black pigmentation well marked.

Mannite Agar.—As alkaline maltose.

Inulin Agar.—As alkaline maltose, but pigmentation less pronounced.

Saccharose.—As inulin.

Glycerine Agar.—Abundant growth, the whole of which after a time becomes of jet-black colour.

Galactose.—As inulin.

Adonite.—Like acid maltose.

Serum.—Growth fairly abundant, but there is only a trace of pigmentation. The medium is not liquefied.

Gelatine.—No liquefaction. The growth on the surface shows after a time some dark pigmentation, but the colonies along the stab are white.

Milk.—No change.

Broth.—General turbidity. A thin pellicle is often present. The microscopical examination shows cocci arranged in pairs or irregularly. They are not capsulated.

Peptone Water.—Some growth at the bottom, while the rest of the tube is clear.

Sugar Broths.—No formation of acid or gas

Indol.—Most strains produce a trace of indol.

Characters of the Coccus-like Organism found in the Red Variety of the Affection.—The coccus found in the red variety is more difficult to isolate and grow than the coccus observed in the black type of the affection. As a rule it grows better and shows more pigment on ordinary agar than on sugar media. It is non-motile and Gram-positive.

Agar.—The growth is at first white, then a red or red-yellowish or yellow spot appears in the centre. The pigmentation very slowly progresses towards the periphery, but seldom, if ever, spreads to the whole of the growth. On maltose and glucose agar the same pigmentation is present, but on most of the other sugar media no pigment is produced. Gelatine and serum are not liquefied. This coccus, as already stated, is Gram-positive and non-motile. The coccus has been recently further investigated by Chalmers and O'Farrell, who have observed that the best medium for showing the pigment is the potato They have called the coccus *Rhodococcus castellanii*.

Symptomatology.—The affected hairs of the axilla present nodular formations, plainly visible to the naked eye, of rather soft consistency. They are easily removed by scraping with a triangular needle or any similar instrument. The formations are either yellow or black, or, less frequently, red. They may be very abundant, and form a yellow, or black, or red sheath round the hair (Figs. 843 and 844), which may at times become lustreless and depigmented. The same patient may have two varieties: The hairs of one armpit may show the yellow variety, while the hairs of the other armpit may present the black type. Sometimes the same individual hair may present some of the nodules yellow and others black, or, rarely, red. We have not yet observed all the three varieties present at the same time on the same patient.

The microscopical examination with a low power shows that the affected hair is covered at several places by roundish formations, partially or totally encircling the shaft. Using a higher power, these formations will be seen to consist, in the yellow variety, of enormous numbers of bacillary-like bodies embedded into an amorphous cementing substance. In the red and black varieties in addition to these masses of bacillary bodies which are the mycelial segments of the *Nocardia* (*Cohnistreptothrix*), large groups of cocci-like bodies are observed. The affection in our cases was never associated with chromidrosis. It may attack the pubic hair.

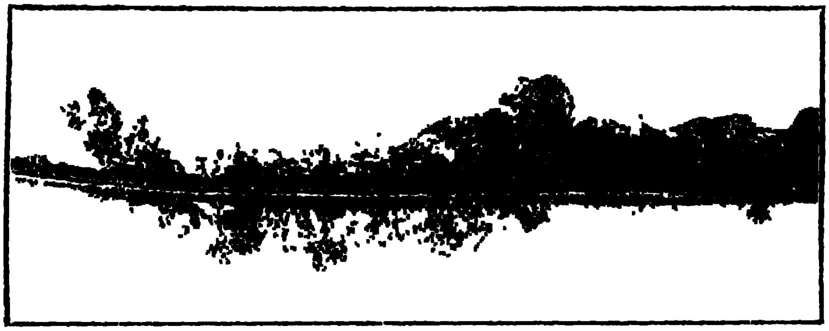

FIG. 843.—TRICHOMYCOSIS AXILLARIS FLAVA.

FIG. 844.—TRICHOMYCOSIS AXILLARIS NIGRA.

Macfie has described a subvariety of the red type, of less vivid colour: *fusca*. It is caused by *Cohnistreptothrix tenuis* plus a coccus which seems to be a variety of *M. castellanii*.

Diagnosis.—This is based on the presence of yellow, black, or red, rather soft, nodules on the hairs of the axillary regions, which, on microscopical and cultural examination, show presence of *Nocardia tenuis* (*Cohnistreptothrix tenuis*) alone, or with *Micrococcus* (*Nigrococcus*) *nigrescens* or *Micrococcus* (*Rhodococcus*) *castellanii*.

Differential Diagnosis.—The condition must be differentiated from the other nodular parasitic conditions of the hair, viz.:—

1. Trichosporosis tropica, or piedra.
2. Unna's trichosporosis, or piedra nostras.
3. Behrend's trichosporosis or 'nodular trichomycosis.'
4. Beigel's trichosporosis, or tinea nodosa.
5. Du Bois's trichosporosis.

1. Trichosporosis tropica, or piedra, generally affects the hair of the head. The nodules are extremely hard, hence the name 'piedra.' The fungus found belongs to the genus *Trichosporum* (*Trichosporum giganteum* Behrend, 1890).

2. Unna's trichosporosis, or piedra nostras, has been described by Unna in the hair of the moustache and beard. It is due to *Trichosporon ovale* (Unna, 1896).

3. Behrend's trichosporosis, or 'nodular trichomycosis,' described by Behrend, affecting the hair of the beard. It is due to *Trichosporum ovoides* (Behrend, 1890).

4. 'Beigel's trichosporosis,' or 'tinea nodosa,' discovered in London by Cheadle and Morris, and later in Breslau, Nancy, etc. It attacks the hairs of the head, and is due to *Trichosporum beigeli* (Rabenhorst, 1867).

5. Du Bois's trichosporosis of the hairs of the pubic region due to *Trichosporum glycophiles* (Du Bois, 1910).

Trichomycosis axillaris flava, rubra, and nigra has nothing to do with piedra or with any other form of trichosporosis, as no *Trichosporum* is found, the fungus being a *Nocardia* or more correctly a *Cohnistreptothrix*, with very thin, bacillary like mycelium. The types of the condition we have seen in Europe are very similar or identical with those we have seen in the tropics, except that in temperate zones we have never observed the black variety. The nodules were not very hard and the hairs not brittle, though European observers describe the European type as being characterized by the presence of hard nodules and the hairs becoming brittle.

Course and Prognosis.—The course is chronic, but the condition may subside or disappear on the patient going to a cold climate. The affection, if of very little pathological importance, has a certain practical interest, being much objected to by patients, especially by ladies.

Treatment.—The treatment originally used by Castellani is often efficacious. It consists in dabbing the hair two or three times daily with a solution of formalin in spirit (ʒi.-℥vi.) and applying at night a sulphur ointment (2 to 5 per cent.). Shaving, Tr. Iodi, and a salicylic alcoholic lotion, have been recommended.

RARER NODULAR AND GUMMATOUS AFFECTIONS OF HYPHOMYCETIC ORIGIN.

Hemisporosis.

Historical and Geographical.—Gougerot and Craven described a case of osteoperiostitis due to *Hemispora stellata* Vuillemin some years ago. Later Auvray and Bidot found the same fungus in a generalized nodular affection, and De Beurmann, Clair, and Gougerot found it in a gumma situated on the penis of a negro.

Ætiology.—The condition is due to a fungus, *Hemispora stellata* Vuillemin, the description of which is given on p. 1108.

Histopathology.—The histological lesions resemble those of tuberculosis cutis, as noted by Auvray and Bidot.

Symptomatology.—Gumma-like swellings are present, either single or multiple. These may later ulcerate. A chronic osteoperiostitis, with thickening of the tibia somewhat resembling the type due to syphilis, has been described. Mercury, however, had no effect.

Diagnosis.—This is based on isolating the fungus. The fungus microscopically is seldom if ever seen in the lesions, and cultures are necessary. These are carried out in the same manner as for sporotrichosis.

Treatment.—Potassium iodide given in full doses (gr. xv.-xx.) three times daily is very efficacious.

Acremoniosis.

There is only one case on record of this condition by Potron and Noisette in France. The condition is due to a fungus, *Acremonium potronii* Vuillemin, 1911, which has been described on p. 1121. The patient had fever, which was at first suspected to be typhoid, and several gumma-like swellings developed, which slowly ulcerated. They were not painful. The proximal glands were not enlarged.

Diagnosis.—This is based on finding the fungus by cultural methods.

Treatment.—In the only case known an intensive potassium iodide treatment cured the condition.

Enantiothamnosis.

Definition.—A nodular condition due to a fungus, *Enantiothamnus braulti* Pinoy, 1911.

Historical and Geographical.—This condition has been described by Brault in Northern Africa, who isolated the fungus, the complete botanical description of which we owe to Pinoy.

Ætiology.—The causative fungus is *E. braulti* Pinoy, 1911 (see p. 1096).

Symptomatology.—The condition in the only case so far known was characterized by the presence of nodules on the gluteal regions, the size of a pea to a small egg. The nodules had a central crateriform opening, from which some pus exuded.

Diagnosis.—This is based on cultivating the fungus from the lesions.

Treatment.—This is surgical, but first potassium iodide might be tried.

Cladosporiosis.

Definition.—A nodular condition due to *Cladosporium penicilloides* Gueguen, 1911.

Remarks.—There is another tropical condition due to a fungus of the genus *Cladosporium*—viz., tinea nigra—but this affection is clinically so different that we do not give it under the heading Cladosporiosis. We have given a separate description of it (see p. 1101).

Historical.—Fontoynont isolated the fungus from a case in Madagascar. Gueguen placed it in the genus *Cladosporium* and named it *C. penicilloides* Gueguen, 1911, and Verdun called it *C. madagascariense* Verdun, 1913 (*vide* pp. 1100 and 1101).

Symptomatology.—In the only case so far known, that of Fontoynont, gummatous nodules were present on the leg, some of which slowly ulcerated.

Treatment.—Potassium iodide has apparently very little efficacy in this condition.

Scopulariopsosis.

This condition is due to *Scopulariopsis blochi* Matruchot, 1911, and *S. koningii* Vuillemin, 1912. Two cases have been reported so far from France. The patients presented gummata and verrucose patches on the skin. Lymphangitis was noted in one case. The diagnosis is based on finding culturally the fungi. The treatment consists in giving large doses of iodides.

It is to be noted that Pinoy and other authorities doubt the pathogenic rôle attributed to *S. blochi*.

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CHAPTER XCIII

MYCETOMA AND PARAMYCETOMA

General remarks--The mycetomas--The maduromycoses--The actinomycoses--The paramycetomas--The pseudomycetomas--Actinomycosis of the body--Nodular actinomycosis--Trench foot--References.

GENERAL REMARKS.

THE subject of the mycetomas has for years been in an exceedingly confused condition, because there has been no clear conception as to the exact meaning of the term, and no scheme whereby the fungi associated with the disease could be identified. Further, the curious relationship of the disease to malignant growths of various descriptions does not appear to have been realized until lately. The labours of Pinoy, of Brumpt, and those of Chalmers with Archibald and Christopherson, systematically continued for years, have enabled a certain amount of information to be gathered together in understandable form.

There are three distinct conditions which require to be studied - viz., the Mycetomas, the Paramycetomas, and the Pseudomycetomas--and detailed references to the fungi associated with these forms will be found in Chapter XXXIX. (p. 1035), which deals with the Fungi Imperfecti; in addition, a few remarks are necessary with regard to actinomycosis of the body.

THE MYCETOMAS.

Synonyms.--Madura foot, the Fungus disease of India, Godfrey and Eyre's Tubercular disease, Endemic degeneration of the bones of the foot, Morbus tuberculosis Pedis, Morbus Pedis Entophyticus, Podelkoma, La Maladie de Ballingall, Slipada, Hatty-ka-Pung, Keerenagrah (signifying a dwelling of worms), Kirudeo (signifying a dwelling of worms), Ghootloo Mahdee (signifying eggs of insects probably so called from the small bodies found in the discharge).

Nomenclature.– In 1846, Colebrook of Madura said that the disease was commonly known in some parts of Southern India as 'Madura foot.'

In 1860, Vandyke Carter applied the term 'mycetoma,' or fungus tumour (μύκης, a fungus, and οἴδημα, a tumour), to that variety of Madura foot which contained black granules, and one year later included under this name the white or yellow variety of the same complaint with which he had become acquainted.

Definition.—The term 'mycetoma' includes all growths and granulations which produce enlargement, deformity, or destruction in any portion of the tissues of man or animals, and which are caused by the invasion of the affected area by fungi belonging to different genera and species, which produce bodies of varying dimensions, colour, and shape, composed of hyphæ, and sometimes chlamydospores, embedded in a matrix. These bodies, which are capable of giving rise to mycelial filaments, on germination, are termed 'grains,' and are found either embedded in the pathological tissue forming these growths and granulations, or escaping freely in the discharge therefrom. In addition, eosinophile bodies can usually be seen.

Early History.—According to Waring, as quoted by Collas, the Sanscrit work 'Vaweda,' by which is probably meant, 'At'harvavéda,' describes a disease of the foot termed 'padavalmicum,' which causes swelling and the formation of little fleshy tumours, which, after an interval of a year from the commencement of the disease, discharge a peculiar fluid.

This disease is distinguished from another malady of the foot which is called 'slipatham,' or elephant foot.

If the above is a correct quotation from the 'At'harvavéda,' then the Ancient Indian surgeons must have distinguished elephantiasis of the foot from such conditions as might have been produced therein by mycetoma, yaws, etc.

It is, however, curious that, like Collas, we have been unable to find any account of such a disease in the writings of Suśruta.

The term 'perical,' used by Kaempfer in 1712, is applicable to any enlargement of the foot, whether caused by elephantiasis, mycetoma, or yaws, but the Pondichéry missionary of 1714 appears to have seen the disease mycetoma, and possibly the actinomycotic variety, because he describes under the term 'fourmilière des vers' an incurable disease of the foot in which numerous small ulcers form, which intercommunicate by means of canals full of worms. These canals are described as being peculiar in that if one closes another opens.

Heyne probably recognized some sort of a mycetoma, in 1806, in the foot of the Rajah's brother at Cuddapah, and Brett's 'adipose sarcoma,' described in 1840, may have been of the same nature.

Madura Foot Period.—With the closing years of the last period it will be noticed that it began to dawn upon the medical men of India that there existed in that country a peculiar disease of the foot, and this was emphasized by Gill of Madura, who, in 1842, described a condition of that member which was characterized by marked deformity and fungoid excrescences, from which flowed an offensive ichorous discharge, while internally the disease produced a condition resembling fibro-cartilage, and destroyed joints, cartilages, and ligaments.

Four years later, Colebrook, Gill's successor at the Madura Dispensary, confirmed these observations, and stated that the disease was commonly known in some parts of India as 'Madura foot.' As no mention is made, as far as we know, by these authors of any black pigment being present in their cases, we conclude that probably they saw the actinomycotic variety of mycetoma.

It is interesting to note that about this time (1845) von Langenbeck, in Kiel, made illustrations of some curious bodies which he considered to be fungal in nature, and which he found in the pus from a case of spinal caries. Unfortunately he never published this observation, which was made known by Israel one year after Bollinger's discovery, which will be mentioned below.

In 1848, Lebert found some peculiar spherical yellowish bodies, about the size of a pin's head, in some thick gelatinous pus which Louis had obtained from an abscess associated with much swelling of the thoracic wall in a man, aged fifty years, in Paris. These bodies were carefully examined, both microscopically and chemically, and drawings were made which were subsequently published by Lebert (1857).

We have examined copies of these drawings, and they represent in a typical manner the fungus of an actinomycosis. Lebert, however, failed to recognize their fungal nature.

In 1855, Smith, in London, made some drawings for Paget of a tumour of the upper jaw, in which an organism resembling a ray fungus is portrayed. These drawings were published by Kanthack (1896).

Also in 1855, Ballingall, in India, described a disease of the foot, in the discharge from which he found bodies composed of large cells with transparent fringes containing irregular spicules, or simply composed of radiating spicules without cells. In 1858, Rustomji described a variety of Madura foot in which he found small, soft, yellowish granules, and which he distinguished from another variety of the same disease, in which he found a dark, soft, thick substance. Rustomji's first variety we call *yellow actinomycosis* and his second variety *black maduromycosis.*

We will now consider the subject of the Maduromycoses.

THE MADUROMYCOSES.

Definition.—The Maduromycoses are those forms of mycetoma which possess grains composed of large segmented mycelial filaments, possessing well-defined walls and usually chlamydospores.

History.— Excluding some ancient references discovered by Collas, to which Corre has drawn attention, and which will be considered when we discuss that author's writings, the history of the black maduromycoses commences in 1845 in India, where Garrison-Surgeon Godfrey, in his Departmental Report of the Public Dispensary at Bellary, described the occurrence of a considerable black deposit, much resembling fragments of coal, in a foot which had been amputated because it was affected by a disease which was commonly known as 'ulcus grave,' because the ulcers and sinuses produced such a serious condition that amputation became necessary. This disease he had described in the same report for the preceding year, designating it 'morbus tuberculosis pedis,' because, though he recognized it to be dissimilar from other recorded diseases, he looked upon it as a local tubercular affection, and, influenced by this view, he considered the black particles mentioned above to be accidental, and not essential parts of the disease. He also mentions that it was known to the natives as 'ghootloo mahdee,' from the tubercular irregularities being supposed to resemble eggs.

This first case of black maduromycosis occurred in a native aged about thirty years, and had existed four to five years before amputation was performed. The morbid appearances are described as being similar to those fully set forth in his 1844 report, with the addition of there being in this instance one cyst (or excavated tubercle) containing melanotic matter about the size of a small walnut, and extending from the plantar to the dorsal aspect of the foot, between the metatarsal bones of the great and second toes, which were in part absorbed. The integuments were not involved in this mass, which when recent had an angular and brilliant black appearance much resembling a fragment of coal, and was considered to be an accidental product in this peculiar case.

Carter says that the second volume of the 'Indian Annals' (probably dated about 1849) on p. 706 contains an account of dark granular or black gritty particles being found among the bones and in the sinuses of a diseased foot, but we have been unable to refer to this work, and are ignorant of the name of the discoverer and of the date and place in which this observation was made. The particles in question were examined microscopically, and were believed to consist entirely of dried blood, a belief which lasted for many years.

It may perhaps be advisable at this point to draw attention to the fact that Ballingall's celebrated observations do not refer to the black, but to the yellow variety of mycetoma, and hence do not enter into this history.

Sub-Assistant Surgeon Bazonji Rustomji (1858), of the Bhoo's Dispensary, in the Province of Kutch, drew attention to the fact that there were two forms of the disease—viz., one in which there was no granular deposit, but only a substance dark in colour and soft and thick in consistence; while the other showed small, soft, yellowish granules. This is the first occasion, as far as we know, when a differentiation was made between the melanoid and the ochroid varieties of the disease, but Rustomji did not recognize the fungal nature of the bodies in question.

Eyre (1860) states that in every foot examined by him there were numerous minute tubercles resembling fish roe, which were found lying beneath the muscles and extending from the bones to beneath the skin, with nodules of the same appearance and often black in colour. This paper deals with the external characters of the disease, its previous history, natural course, morbid anatomy, aetiology (which was doubtfully thought to be somewhat tubercular), and treatment.

In 1860, Vandyke Carter began a series of classical observations upon the black and yellow forms of Madura foot, which he continued until 1874, and during which he firmly established the fungal nature of the disease.

His first paper (1860) was entitled 'On a New and Striking Form of Fungus Disease affecting the Foot and Prevailing Endemically in Many Parts of India.' In his second publication (1860) he clearly differentiated between the white or ochroid division of the Mycetomas, which to-day we call 'actinomycosis,' and the black or melanoid variety, which we now name 'black maduromycosis.' He demonstrated that the black grains were of true vegetal nature, with a black friable rind composed of clear, orange-tinted, ovoid or angular cells and beaded fibres closely arranged so as to form a compact structure, and in addition larger vesicular bodies (seemingly comparable to gemmules or sporangia), which he thinks may arise at the extremities of the compressed beaded fibres by gemmation and expansion. The pale reddish-brown central part of the larger sclerotes was composed of slender, pale, flattened, and branching fibres arranged in bundles and intermixed with numerous granules and a few large beaded fibres, the septa of which were sometimes absent.

He placed some black particles, taken from a foot, on cotton soil moistened with animal juices and enclosed in a stoppered bottle, which he left unopened for two and three-quarter years, when he found a thin reddish film had appeared. Other black particles sown on rice paste for the same length of time remained unchanged, but on opening the bottle a red mould speedily made its appearance.

With reference to this mould, he says: 'It had not, however, a clear connection with the fungus particles, but seemed to spring up independently of them upon the rice whenever this was exposed to the air.'

This statement is of importance, as he grew a fungus from the white variety which was pink in colour, and produced sporangia resembling those of a species of the genus *Mucor* Micheli, 1729, but differing therefrom in the absence of a columella, which should have brought it under the genus *Morticrella* Coemans, 1863; but Berkeley, who examined the growths from a botanical point of view, classified it under the genus *Chionyphe* Thienmann, 1839, calling it *Chionyphe carteri* Berkeley, 1862, and defining it as:—'Hyphasmate ex albo flavorubroque, sporangiis demum coccineis, sporis breviter fusiformibus.'

The genus *Chionyphe*, however, was never recognized by mycologists generally, as its species came under the genera *Mortierella* or *Mucor*, while *Chionyphe carteri* was most undoubtedly a contamination, as its connection with the black or white grains was never proved, as we have noted above with regard to the former.

Thus we may conclude that although Carter gave the first proof of the parasitic nature of the grains, he was unable to produce growths by cultivation from either the black or the white varieties.

In 1860, Minas wrote upon 'keereenagoah' of the foot, as seen in the Punjab. The term used is a vernacular word signifying worm disease. He states that the characteristic symptom of the complaint is gradual enlargement of the foot, usually starting with a swelling in the sole associated with the presence and constant discharge of small particles, either soft or black and hard, from fistulous openings.

Collas (1861) described black maduromycosis as seen in Pondichéry. He recognized the little bodies of blackish or reddish brown colour, which in their clearer parts seemed to be formed of small transparent cells, which he could not sufficiently study. He called the disease 'dégéneration endémique des os du pied.'

H. J. Carter (1862) came to the conclusion that the fungus of black maduromycosis was nearly allied to *Mucor stolonifer* Ehrenberg, 1818, the spores of which in an amœboid state he considered entered the body through the sudorific ducts. Berkeley (1862) mentioned the fungus in question; he gave it the name *Chionyphe carteri*, a nomenclature which he subsequently repeated (1865).

In 1867, Moore reported an important early case, in which he effected a cure by cutting and scraping away all the diseased tissues, and he augmented this in 1873 by recording two more cases of a similar nature, treated in the same way with a like result.

In 1870, Holmsted, of Hyderabad, Sind, found a thorn of irregular shape and ½ inch long in a case of black mycetoma, in which it had been embedded for two years. In the same year, Bristowe described and figured the fungus seen in the black particles of a foot from a case of black maduromycosis amputated in Cantoor, and demonstrated to the Pathological Society of London by Tilbury Fox. Bristowe's descriptions and figures are excellent, and amply confirm Vandyke Carter's work. Thudichum chemically examined the black pigment of this case, and showed that it was not derived from blood.

Hogg (1872) described a black maduromycosis from India, in which he was able to observe the fungal threads and to resolve them into jointed dissepimented cells, some branching out and attaining a considerable length, while others terminated in an enlarged ovoid head. He, however, believed that the fungus was a secondary product, which might greatly aggravate but did not originate the disease, and suggested that it might be introduced at the time of the first accident when the foot was struck against a stone, or by the poultices used as treatment in a later stage.

Vandyke Carter (1874) published his monumental and classical work 'On Mycetoma, or the Fungus Disease of India,' which concluded his long-continued labours at this complaint.

Lewis and Cunningham (1875) admitted the fungal nature of the black particles, but not of the yellow granules. They showed that *Chionyphe carteri* had nothing to do with black or yellow grains.

In 1876, Berkeley came to the conclusion that *Chionyphe carteri* had nothing to do with mycetoma, a point which can be easily judged from the passages quoted above.

Notwithstanding all these researches, a great deal of confusion still existed with regard to the disease, which can be judged by a study of Fox and Farquhar's (1876) report. It was admitted that the black granules were fungal in nature, but it was contended that they were not causal in effect, because all the essential features of mycetoma were found to be present without any black fungal particles, and because there was not sufficient evidence forthcoming at the time in proof of the vegetal character of the yellow grains, which were believed to be essentially fatty in nature. It was, however, admitted that Moore's observation showing that the black variety could be cured by excision of all the particles at an early stage of the disease was a strong argument in favour of the parasitic nature of mycetoma.

Though Carter had found black, yellow or white, and red grains, still the general belief was that these were one and the same process, and, moreover, observers of this period must have seen the pseudomycetomatous conditions mentioned above, because competent workers appear to have met with cases in which they were unable to find any grains, although the clinical appearances resembled mycetoma.

Corre (1883) placed in order, completed, and revised the notes of researches made by Collas since his publication, already mentioned, in 1861. In these notes, which were published after his death, Collas desired his previous name for the disorder to be altered to 'La Maladie de Ballingall,' and states that the earliest references to the disease with which he is acquainted can be found in Waring's paper, and in one of the sacred books of the East which he calls 'Vaweda' (Ushta wunga hrethayum), which appears to us to be the 'Atharvavéda.' In this latter work, 'slipatham,' or elephant foot, is distinguished from 'padavalmicum,' which refers to an incurable malady of the foot associated with swelling and the formation of fleshy tumours, from which, about a year after the appearance of the first symptoms, there exudes a peculiar fluid. He also points out that the words 'perikal,' 'anaikal' (Tamil: this means Cochin leg —'slipada' (Bengalese), 'hatty ka-poung' (Deccan), are applicable to elephantiasis as well as to Madura foot, and, therefore, should not be specially applied to the latter, as they really mean the 'leg of an elephant.' In Ballary, he says, the disease was called 'gootloo mahdee,' because the swellings on the foot were thought to be like eggs; while in Rajputana it was called 'krimagras,' or the dwelling-house of worms, because the sinuses were considered to be like the cavities often occupied by the larvæ of flies. He also says that in 1714 a missionary described under the name of "fourmilière des vers' a disease of Pondichéry which was incurable, and in which numerous ulcers intercommunicated by means of small canals full of worms, which were peculiar in that if one closed another opened. This information Collas obtained from vol. ii., p. 167, of a book published in Paris in 1812, and entitled 'Mémoires sur les mœurs et coutumes de l'Inde par un missionaire.' Collas also points out that in 1806 Heyne saw the brother of a Rajah at Cuddapah in Hyderabad with a foot in a leprotic state, but which was considered to be distinct from leprosy, although it was not known what the nature of the disease might be. Collas thinks that this must have been mycetoma, and draws attention to Brett's 'sarcomes adipeux,' in which he says it is difficult not to recognize Ballingall's disease.

With reference to the above names, it will be noted that they apply to any form of mycetoma, and not especially to black mycetoma. The name 'Ballingall's disease,' in our opinion, is not applicable to the black mycetomas, because, as already indicated, he was not acquainted with the disease.

In 1886, Carter gave up his pink mould, and drew attention to the similarity between the fungus of actinomycosis and that of mycetoma.

Kanthack (1893) studied both the yellow and black mycetomas, and came to the conclusion that the former agreed morphologically and structurally with actinomycosis, but with regard to the black grains his position was curious, for although he found them to consist of an olive-brown, glassy, or finely granular material, in which hollow filaments, radially arranged, were embedded, still he regarded these as degeneration changes, and sought to prove that the granules were an organism allied to the actinomycosis fungus which he had found in the yellow variety. Thus, like Vandyke Carter, he believed both varieties to be fungal in nature and to be caused by the same fungus, but he attempted to show that the fungus of the yellow variety existed in the black, while the former observer believed the reverse to be true. He named the fungus *Oöspora indica* Kanthack, 1893, and distinguished the two varieties as *O. indica* var. *flava* and *O. indica* var. *nigra*. Unna, to whom he sent specimens, however, did not make this error, but says:- 'A whole series of important distinctions separate the two fungi, and there is no question of their identity.'

Boyce and Surveyor (1894), in a most important paper, first definitely proved that the fungi existing in the black and yellow varieties were quite different, and thus definitely established the two main divisions of mycetoma, which to day we call maduromycosis and actinomycosis. They showed that the black grains were composed of a large, septate, branching fungus embedded in a brown pigmented ground substance, which was readily bleached by eau de Javelle. They did not observe spore formation, nor was cultivation attempted.

In the same year Boccaro also differentiated between the white and the black varieties of the disease.

Chatterjee (1911) observed that grains placed in agar and glucose agar tubes increased in size some seven to eight times in four days, and were surrounded by fine hair-like structures which were composed of delicate branching mycelial threads, which were seen to come from the thick black threads. On potato, the growth was dry and black. In broth, small white colonies composed of radiating threads were found sticking to the walls of the tube. No diffuse growth was seen, nor did any scum form on the surface. Animal experiments were negative.

Mackenzie, in the same year, appeared to obtain similar cultures on agar: at first the growth was white and translucent, with radiations from the centre, later it became greyish yellow, there being a central granule surrounded by a clear zone and an indented margin. After a week the colony became a deep mahogany, and under the microscope exhibited mycelial structures.

Semon (1915) reported a case of black maduromycosis which occurred in a native Indian soldier serving in France. He left India about October, 1914, and in January, 1915, he injured one of his feet by the fall of an ammunition box. The patient attributed the disease to this cause, but Semon considers, probably correctly, that he must have been infected before leaving India. A typical mycetoma developed in about six months, and the pus contained black particles in which a central mass of mycelium obscured entirely by black pigment could be made out, but no proper demonstration of the fungus *in situ* could be made The foot could not be amputated, but sections were made of some of the tissue, which showed marked vascular hypertrophy, polymorphonuclear, plasma, and connective tissue cells, but no endo- or periarteritis and no giant cells. Growths were obtained at 35 C. on agar-agar, maltose agar, and Raulin's fluid. The fungus formed a central black portion with a peripheral zone of white or grey, and in the course of ten days or less became black

In 1916 Chalmers and Archibald grew a fungus allied to that described by Semon from a case of black maduromycosis found in the Anglo-Egyptian Sudan, and in 1918 defined and classified the Maduromycoses.

Climatology.- The Maduromycoses are known to occur in Europe, Africa, Asia, and America, but not in Oceania.

The climatology has been most thoroughly studied for black maduromycosis, which occurs in the Anglo-Egyptian Sudan, where the disease was first described by Balfour in 1904, and the northern part of which is hot and arid. He gives the native name for mycetoma as 'Napt Hindi Nabit,' and states that the black variety is most frequently encountered, and that the foot is the part principally affected, while the inguinal glands are often involved. In 1908, Wenyon noted its presence at Bor, which is hot but not arid, while Balfour's researches in 1911 have already been noted in the historical section. According to our inquiries, the word most commonly used by natives in the Sudan is 'en-nabt,' which means 'the growth.'

In addition to the Anglo Egyptian Sudan, the following is a list of African places from which cases of black maduromycosis have been reported: Algeria, Tunisia, Somaliland, Madagascar, Transkei (South Africa), Senegal, and the French Sudan.

In Asia the disease is recorded from the Yemen, various parts of India, Ceylon, and possibly from North Borneo.

In America it has been described in the United States by Wright, and in the West Indies by Scheult.

In Europe it has so far only been found in Italy, Macedonia, and Southern Germany.

This distribution, according to political geography, has but little meaning when the object being studied is a fungus, and for further details we turn to plant geography. According to Drude, climatic and local conditions permit the division of the surface of the world into six zones of vegetation, viz.:—The Northern Glacial Zone, the Northern Cold Winter Zone, the Northern Hot Summer Zone, the Tropical Zone, the Southern Hot Summer Zone, and the Southern Cold Zone.

The black maduromycoses occur in the Northern Hot Summer Zone, which includes Spain and Italy, North America, the Sahara, Indo-China, Malay Archipelago, the United States (roughly south of Utah), and Mexico. The general characters of this region are:—Very hot summer temperatures with cold nights and no real winter, but with varying rainfall. It contains very dry climates: it also contains wet areas. The black maduromycoses are most commonly met with in the dry parts of this area

The Tropical Zone, which appears to be the real home of these fungi, is generally humid, but contains arid regions bordering upon the preceding. In this zone comes the Anglo-Egyptian Sudan, in the northern or more arid part of which black maduromycoses are common, and the same remarks apply to Somaliland, while West Africa is mostly moist.

It also includes the greater part of India, in which the distribution of mycetoma, according to Boccaro, is interesting.

This observer states that Major Prain divided India into six floral regions, viz.: India Deserta, India Diluvia, India Aquosa, India Vera, India Sub-Aquosa, and India Littorea, while black maduromycosis is found in only India Deserta and India Vera, and is practically almost absent in other regions.

India Deserta includes the Indus Plain Region—*i.e.*, Sind, Rajputana, and the Punjab: while India Vera includes the Deccan Region, consisting of the dry but not desert triangle between the Western and Eastern Ghats, with its apex at Tinnevelly and its base at the borders of the plain of the Ganges.

The white varieties of mycetoma are also found in this area, but are outnumbered by the black maduromycosis, while in India Deserta the preponderance of the black maduromycoses is even more marked than in India Vera.

In Madura and adjoining districts of Tinnevelly, Palmcotta, and Coimbatore, situate in India Vera, mycetoma is very common, and the climate is hot and arid.

The Southern Hot Summer Zone includes South Africa, where the disease has been recorded, but where it is apparently rare.

This is as far as the present state of our knowledge permits us to go with regard to geographical distribution, and more research on this part of the subject is required, but from the above it is obvious that heat and aridity are favourable conditions for the fungi which cause black maduromycosis.

Botanical and Zoological Distribution.—Unfortunately, we are in complete darkness as to the characters which the fungi causing black maduromycosis assume when not living in animals or on artificial culture media.

Even with regard to those forms of black maduromycosis due to an aspergillus, we are quite ignorant as to whether this particular fungus lives on soil or on plants.

Ætiology.—The outstanding feature of microscopical specimens prepared from a case of maduromycosis is the presence of coloured granules, black in *black maduromycosis*, whitish or yellowish in *white or yellow maduromycosis*, and red in *red maduromycosis*.

These coloured granules are called 'grains,' a term which has been defined by Chalmers and Archibald as follows:—

'The term "granum" or grain has been given to differently coloured bodies of varying consistence, size, and shape, found in mycetomas, and composed of hyphæ, with sometimes chlamydospores, embedded in a matrix and giving rise to mycelial filaments on germination.'

The ætiological importance of these grains and their contained fungus rests upon the fact that they are present in all forms of maduromycosis and are co-extensive with the disease, while their complete removal effects a rapid and complete cure.

Animal inoculations have been successful in some varieties, thus affording, in these instances, a full and convincing proof of the ætiology of the fungus—*e.g.*, Pinoy's and Pepere's varieties.

The ætiological features of the various forms of maduromycosis are set forth below in a list which shows the Maduromycoses classified —firstly, by the colour of the grain; secondly, by the geographical distribution; and thirdly, by the discoverer's name or names.

I. The *black maduromycoses*, with black grains.

II. The *white or yellow maduromycoses*, with white or yellowish grains.

III. The *red maduromycoses*, with red grains.

I. THE BLACK MADUROMYCOSES.

These may be divided into:—

A. The *European black maduromycoses.*
B. The *African black maduromycoses.*
C. The *Asian black maduromycosis.*
D. The *American black maduromycoses.*

A. THE EUROPEAN BLACK MADUROMYCOSES.

(1) *Bassini's*, *Kölner's*, and *Schmincke's black maduromycoses*, respectively found in Padua, Italy, and in Kissingen, and of which the nature of the ætiological fungus is unknown.

(2) *Bovo's black maduromycosis*, found in Genoa, and of which the causal agent is called *Madurella bovoi* Brumpt, 1910, but this identification must be accepted with reserve, as the fungus has never been cultivated, and may not agree with the definition of the genus Madurella, as altered by Pinoy in 1912 subsequent to the cultivation of *M. mycetomi* and *M. tozeuri*.

(3) *Pepere's black maduromycosis*, found at Domusnovas in the Province of Cagliari in Sardinia, and caused by *Scedosporium sclerotiale* Pepere, 1914.

B. THE AFRICAN BLACK MADUROMYCOSES.

(1) *Brumpt's black maduromycosis*, caused by *Madurella mycetomi* (Laveran, 1902).

(2) *Nicolle and Pinoy's black maduromycosis*, caused by *Madurella tozeuri* (Nicolle and Pinoy, 1908).

(3) *Bouffard's black maduromycosis*, caused by *Aspergillus bouffardi* Brumpt, 1905.

(4) *Chalmers and Archibald's black maduromycosis*, caused by *Glenospora khartoumensis* Chalmers and Archibald, 1916, which has now been recovered three times in the Anglo-Egyptian Sudan.

These African black maduromycoses may be differentiated from one another as follows:—

A. Microscopical preparations show aspergillar heads—*Bouffard's black maduromycosis.*
B. Microscopical preparations do not show aspergillar heads; on culture the following types of spore are obtained:—
  1. The aleuriosporal form of conidium—*Chalmers and Archibald's black maduromycosis.*
  2. The arthrosporal form of thallospore.—
    (*a*) Mycelium greyish-white, when old, yellowish and darkening the media in sugar cultures. Spores varying in dimension from 2 to 5 microns. Grains black and sterile, with a diameter from 0·5 to 1 millimetre, formed in the depths of the medium in cultures. Can invade the skin, bone, muscles and connective tissue of man, giving rise to black grains which are small, hard, round, and more or less warty, and which morphologically resemble the grains formed in the cultures. Up to the present the inoculation into animals is negative. Very widely spread in Africa. Isolated by Brault from a mycetoma with black grains in Algeria—*Brumpt's black maduromycosis.*
    (*b*) Mycelium white, becoming yellowish with age, and darkening the medium in sugar cultures. Spores generally small, 2 microns or sometimes even 5 microns in diameter. Grains are only rarely produced, and then they appear on the surface of the medium. Occasionally it gives rise to a mycetoma in man, in which it forms black amorphous grains which are often made up of mycelial rings enclosing some degenerate cellular elements which are impregnated with the pigment of the fungus, and also of small diffuse masses formed solely by the filaments of the fungus which have a yellow membrane. Inoculation into pigeons positive. Isolated by Nicolle from a mycetoma at Tozeur—*Nicolle and Pinoy's black maduromycosis.*

C. The Asian Black Maduromycosis.

There is only one type known at present—viz., *Carter's black maduromycosis*, caused by *Glenospora semoni* Chalmers and Archibald, 1917, which can be readily differentiated from *Glenospora khartoumensis* Chalmers and Archibald, 1916, by the following characters:—

(1) Grown on clear maltose agar in Khartoum after twelve days in an uncapped tube at 30° C.:—

G. semoni produces a cupola-shaped, large, central black mass with an outlying fringe of white.

G. khartoumensis produces a black growth, consisting of a central crumpled ridge or hillock placed on a grooved black plateau, and with hardly any white fringe.

(2) and (3) Grown on glucose agar and blood serum; there are marked differences between the two fungi.

D. The American Black Maduromycoses.

(1) *Wright's black maduromycosis*, which was found in the United States in an Italian woman who had left Italy, where black maduromycosis occurs, an indefinite number of years before the onset of the malady. The systemic position of the causal fungus is unknown.

(2) *Scheult's black maduromycosis*, which was found in the West Indies in a native of India, who had left that country twelve years before the onset of the malady. The nature of the causal organism is unknown.

II. THE WHITE OR YELLOW MADUROMYCOSES.

These may be divided into:—

A. The *European white maduromycoses*.
B. The *African white maduromycosis*.
C. The *Asian white maduromycosis*.

A. The European White Maduromycoses.

(1) *Brumpt and Reynier's white maduromycosis*, caused by *Indiella reynieri* Brumpt, 1906, with a large *soft* grain, found in Paris.

(2) *Tarozzi and Radaeli's white maduromycosis*, caused by *Scedosporium apiospermum* (Saccardo, 1911), with a small, *rather hard*, and yellowish grain, found in Sardinia and Italy.

B. The African White Maduromycosis.

Nicolle and Pinoy's white maduromycosis, due to *Sterigmatocystis nidulans* (Eidam, 1883), with grains of size varying from those which are almost microscopic to others about the size of a pea, of rounded or polyhedral form, and of variable colour, being dirty white or yellowish-white, and *soft* in consistence, and found in Tunisia.

C. THE ASIAN WHITE MADUROMYCOSIS.

Brumpt's white maduromycosis, due to *Indiella mansoni* Brumpt, 1905, with very small and very hard white grains, found in India.

The differentiation of the white maduromycoses may be effected as follows:—

A. *Grains soft*:—
  1. Sterigmatocystic heads found in grains and in cultures. Grains *not* like a ribbon rolled on itself—*Nicolle and Pinoy's white maduromycosis*.
  2. No such heads to be found in the grains, which are like a ribbon rolled upon itself—*Brumpt and Reynier's white maduromycosis*.

B. *Grains hard*:—
  1. Grains small, yellowish, not reniform; spore of the type of a conidium—*Tarozzi and Radaeli's white maduromycosis*.
  2. Grains small, whitish, reniform; spore of the type of an arthrospore—*Brumpt's white maduromycosis*.

III. THE RED MADUROMYCOSIS.

Only one form is known *Balfour and Archibald's red maduromycosis*, which was possibly due to an aspergillus, because aspergillar like heads were found in the grains It occurred in the Anglo-Egyptian Sudan

Pathology.—The causal fungus is introduced into some part of the body by a wound produced by a thorn, a splinter of bamboo or other wood, by a sharp stone, knife, etc., but once introduced into the subcutaneous tissues, it commences to grow, the original wound in the meantime healing. Usually the growth is slow; but if Kemper and Jamieson's case was true mycetoma, it may be rapid, and, indeed, this is supported by Musgrave and Clegg's inoculation of *Nocardia asteroides* into a monkey's feet, in which the swelling developed in ten to sixteen days, and was quickly followed by suppurative lesions. As the fungus grows, it destroys the tissues of the foot, and meets with but little reaction on the part of the body, and no attempt is made to repair its ravages. The reaction on the part of the body confines itself to a lymphocytic infiltration around the fungus, and later the formation of granulation tissue, with epithelioid and giant cells at times; while, finally, fibrous tissue is formed around the fungus and its surrounding cells, and the vessels become blocked by an endarteritis and periarteritis. This appears to be an attempt to encapsule and prevent the spread of the parasite, as well as to damage it by cutting off its food-supply.

At the same time the cellular exudate becomes a thin, oily, occasionally stinking, pus, and works its way to the surface, forming apertures, and carrying the parasite with it. This must be considered to be an attempt to rid the body of the fungus.

In the meanwhile the parasite, if of certain species, forms special club-shaped hyphæ considered to be chlamydospores, which at first serve for extracting nutrition from the surrounding leucocytes, but later, breaking free from the main mass, form means of asexually propagating the fungus in the foot. Some of these separated clubs are attacked and engulfed by leucocytes, and though it is possible that in this way many may be destroyed, still, Brumpt's researches show that the leucocyte, with its enclosed club, may wander away from the diseased area into healthy tissue, and may be killed by the club, which, being set free, grows into a new mass of fungus. In this way the fungus may be disseminated by means of the phagocytes.

When surrounded by pus, the fungus gathers itself into granules, the so-called sclerotia, which show externally radially arranged fibres or clubs, and internally a mass of mycelium with crystals and débris, the latter being most marked in the centre. These granules escape to the exterior, and form the yellow, black, or pink granules in the discharge. As the fungus grows in the foot the connective tissues and the muscles undergo vitreous degeneration, and break up into débris, amongst which pieces of nerves and tendons may be found, while even the bone in some cases becomes attacked by a form of degeneration and disappears. The result is that the foot appears much swollen externally, and shows the openings of the sinuses, through which the pus and the fungoid granules escape; while internally the normal structure may have completely disappeared, being replaced by degenerated tissue, débris, sinuses, and fibrous sacs containing the fungus and the pus.

The result is, however, not merely destruction of the foot, but also great bodily waste, due to the continuous discharge, so that the patient becomes emaciated, and may finally die of cachexia.

Morbid Anatomy.—The pathological anatomy of black maduromycosis has been the subject of a fair amount of investigation. Kanthack merely drew attention to the fact that the black masses were always to be found embedded in dense fibrous tissue, while a few pus and granulation cells were to be seen in most cases. In the fibrous wall yellowish-brown or black pigment could be found, while fuchsin bodies were present in most specimens. Unna's example, obtained from Kanthack, only showed fibrous and some granulation tissue. Boyce and Surveyor drew attention to the presence of small round cells, macrocytes, and giant cells surrounding the fungus in cases of black maduromycosis. Their microphotographs are, however, mainly devoted to the fungus, while their Fig. 22 evidently depicts a very young piece of fungus surrounded by giant cells.

Wright (1898) stated that the nodules consisted of more or less atypical connective tissue, in the cavities of which the granules lay surrounded by polymorphonuclear leucocytes, loose epithelioid cells, and cellular detritus. The cavities were lined by either a wall of vascular granulation tissue or by masses of epithelioid and multinucleated giant cells, while these cells closely invested other granules, and outside of this tissue lay lymphoid and plasma cells. He gives in his original paper four excellent low-power photographs, of which

Figs. 4, 5, and 6, though older, if examined with a lens, will be seen to agree more or less with Boyce and Surveyor's Fig. 22.

Oppenheim's description in 1904 mainly deals with the fungus, but Brumpt's account of the histological changes induced by *Aspergillus bouffardi* covers all the important points—viz., the polymorphonuclear leucocytes, the lymphocytes, the giant and epithelioid cells, the connective tissue, the cells containing brown pigment, and the endarteritis. On Plate XIX., Fig. 7, and Plate XX., Figs. 1 and 2, he shows appearances resembling those described by Boyce, Surveyor, and Wright in a young grain in which the giant cells are situate close to the fungus.

Boccaro, writing in 1909 in general terms for the encapsulated form of both white and black mycetomas, says:—

> 'The fungal hyphæ are surrounded by round cells, held together by a delicate network of fine bloodvessels, the cells being located in the meshes of a fibrillar, transparent, reticulated substance. On the inner side of the group of round cells, between them and the central hyphal mass, is a collection of *finely granulated débris*, and on the outer side, in most preparations, may be seen large nucleated cells, giant cells, and phagocytes.'

This description, which unfortunately is not illustrated, agrees well with our observations.

Balfour, in 1911, published photomicrographs of black maduromycoses believed to be due to *Madurella mycetomi* and to *Aspergillus bouffardi*, but did not describe them.

Babès (1913) gave a well-illustrated account of Indian black maduromycosis, in which he observed far less cells than we have noticed in immediate relationship to the fungus, from which the giant cells were separated by fibrous connective tissue. He drew attention to violet and reddish rounded bodies enclosed in cells.

In 1916 Chalmers and Archibald gave an account of the histology of a case of black maduromycosis, and this is followed in the description given below.

Fig. 845 shows the general appearance of black maduromycosis very slightly magnified. It will be observed to be largely composed of fibrous tissue containing black particles—the grains—and some spaces, which are formed by the falling out of some of the black granules during preparation. The spaces demonstrate the character of the lacunæ occupied by the grains and their surrounding cells.

FIG. 845.
BLACK MADUROMYCOSIS.

The fungal mass lies embedded in cellular tissue, as is shown in Fig. 846. The spaces are artefacts produced in making the section, which otherwise is as natural as possible—*i.e.*, is not bleached or softened in any way. The cracks in the black mass are also artefacts. Around the fungus lies a mass of small cells, and on the upper and left side of the grain are seen some giant cells, which also occur in other parts, but are not in such close relationship to the fungus; then comes some fibrous tissue containing a number of cells, bloodvessels, and lymph spaces, the last mentioned being situate towards the top of the photograph and being markedly dilated. At the very top of the figure, and only partially shown, comes the dense fibrous connective tissue which is continuous with

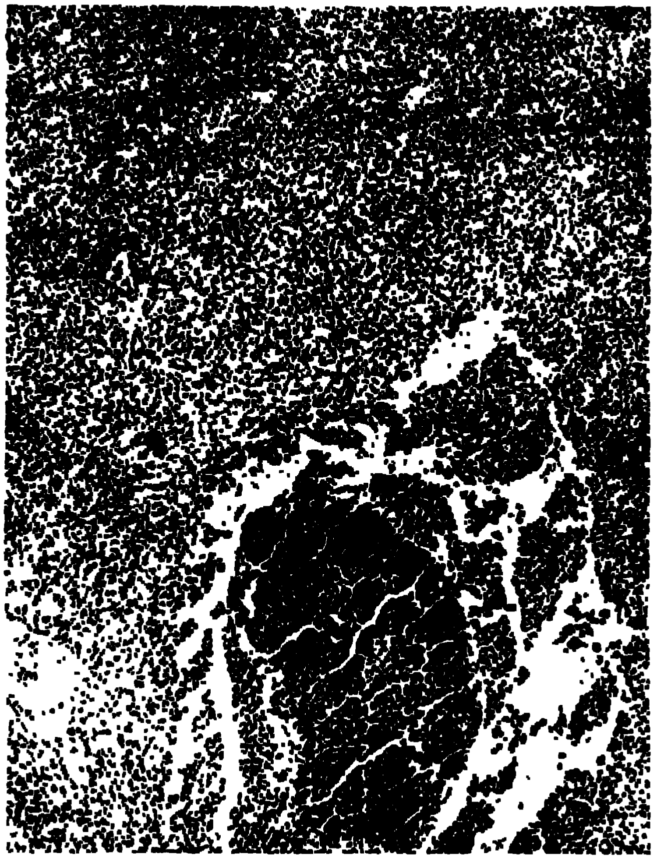


FIG. 846.—BLACK MADUROMYCOSIS

the dense tissue, depicted in Fig. 846, which permeates and surrounds the growth. Therefore the main features of the tumour may be summarized as follows:—

1. Fungus.
2. Small cells.
3. Giant cells and large cells.
4. Small cells, connective tissue, bloodvessels, and lymph spaces.
5. Dense connective tissue.

The cells are separated by a variable amount of fine connective tissue, which also supports large lymph spaces and bloodvessels. Débris and pigmentary granules can also be seen. A special rare feature of this layer is the presence of mononuclear cells containing one or more eosinophile rounded bodies, which were first observed in this pathological condition by Kanthack, and subsequently by nearly all the other workers on the morbid histology of the black maduromycoses, to which they are, however, not confined. Their exact nature is unknown, but they are probably in some way due to the fungus.

On inspecting the upper part of the cellular mass, it will be observed that the white fibrous tissue increases in amount, but is still loose and contains many cells in its meshes, while more externally, and situate at the top of the photograph, is seen the denser and less cellular connective tissue, which is continuous with that separating one fungal mass from another and surrounding the whole tumour. In this connective tissue, cells containing yellowish granules are frequently observed.

There are also many lymph spaces and bloodvessels, but the latter at times show signs of endarteritis or periarteritis, by which means the lumen of the vessel may be considerably diminished or even closed.

Very rarely do the fungi invade the body, and rise to a general infection.

The peculiarity of the pathology is the slight reaction which the body makes against the invasion by the fungus, and the entire absence of any attempt at repair.

The black varieties of mycetoma owe their colour to a dark substance which the fungi secrete. The nature of this black substance is not known. It is soluble in hot sulphuric acid, forming a yellowish-red solution, but is not soluble in cold sulphuric acid nor in potash solutions. According to Thudichum, it does not contain hæmoglobin in any form, though a small quantity of iron is present.

In more advanced cases the swollen foot shows nodules and openings externally, the latter of which lead into the sinuses. In sectionizing the foot it will be noticed that the sinuses which run in various directions are communicating, and end in small cavities containing pus and the fungus, and that these cavities are embedded in degenerated tissue and débris.

The bone may or may not be affected, but if it is, the whole foot can be easily cut by a knife.

Microscopically the tissues show degeneration and débris, with fibrous tissue formation, endarteritis, and periarteritis, and at times absorption of the bone.

The microscopical examination of sections of the tissues typically affected—viz., of alveolar appearance--and containing mycotic grains, show a central roundish mass—the mycotic grain– a clear circular space, and the surrounding degenerated tissues. The clear space is due to the fact that the thin purulent matter in which the granule is embedded contracts during fixation with alcohol. The mycotic granule is composed at the centre almost exclusively of mycelial elements with a few leucocytes; more externally there are masses of amorphous substance, staining lightly purplish with eosin, in which a few mycelial threads may be seen. The periphery shows a polymorphonuclear infiltration. The walls of the alveolar cavities containing the granules are formed of young connective tissue with numerous plasma cells and occasionally giant cells; there is a marked proliferation of bloodvessels.

Symptomatology.—The disease usually begins in the foot, more rarely in the hand, and still more rarely in the leg, knee, neck, or trunk. There may or may not be a history of a cut or injury some time previously. In any case, this primary injury will have healed long before the disease is well established.

The incubation period in well-recorded cases would appear to be short; thus, in Musgrave and Clegg's case, one month after the primary injury the wound reop[illegible]l and discharged pus, and in their experiments on monkeys [illegible]ppeared to vary from ten to sixteen days. Further researc[illegible] on this point are, however, required.

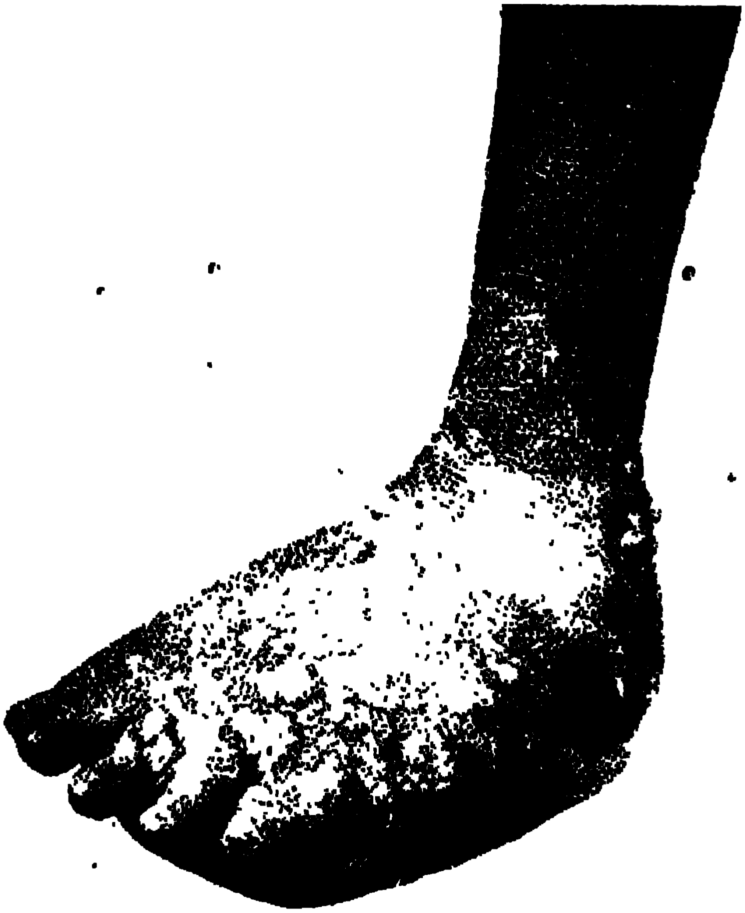
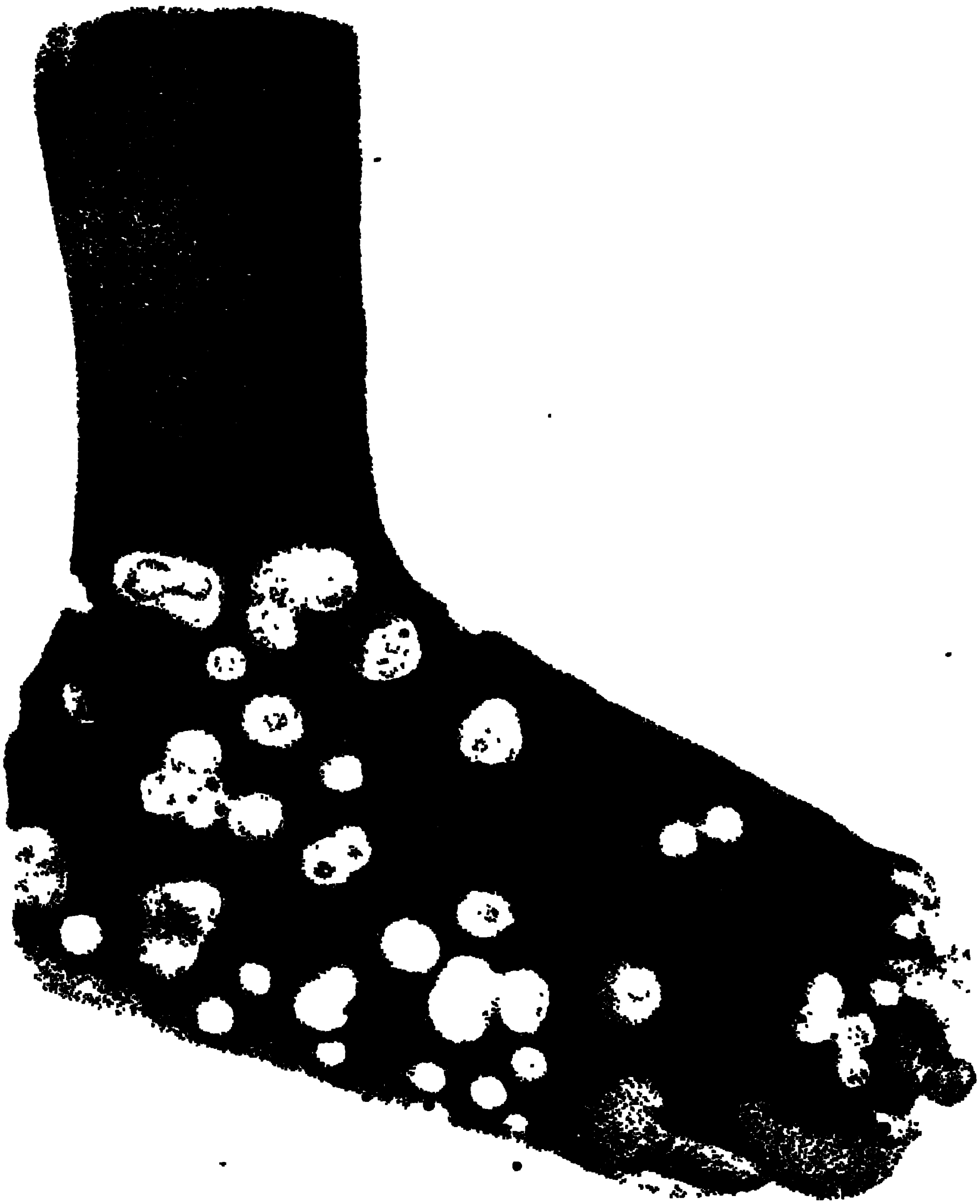


FIG. 847.- MYCETOMA.

The earliest signs are either pain or swelling in the region of the original injury, which is usually on the sole of the foot, between the toes, or on the instep. The swelling becomes a hard lump, on the surface of which a bleb may form, which bursts and reveals a small opening discharging an oily, rarely sanious, thin, offensive pus, in which the granules characteristic of the fungus may be found.

PLATE XIII.



MYCETOMA.

Some new indurations and nodosities appear in various parts of the foot, and new openings are formed, while the whole foot begins to swell in a very characteristic manner. First the arch of the foot fills up and disappears, the whole sole becoming so swollen and convex that the toes are no longer able to touch the ground, and may be pushed apart, but are usually not affected by the disease. At the same time the dorsum of the foot becomes studded with nodules and openings. The colour of the integument may be normal, but is usually darker than in the healthy skin. It is rarely œdematous. The openings, when examined by a probe, are found to lead into sinuses, which penetrate deeply into the tissues, and at times even into the bones of the foot. The quantity of the discharge varies from time to time, being increased by motion. On palpating the affected area, it is found to be elastic, and the sensibility to be normal. The inguinal glands are often enlarged and hard.

As the disease progresses, pain, which at first was slight, becomes more marked, especially in cold weather. The patient ceases to be able to place the foot to the ground, and is compelled either to walk on the heel or to use a support. The leg begins to waste, and after a long time the patient becomes weak and anæmic from the constant drain on the system by the discharge, and possibly also by toxins produced by the fungi. General constitutional disturbance of a febrile nature is rare.

The disease is very chronic, and has no tendency to heal, and if not treated, will eventually cause the death of the victim, from exhaustion or diarrhœa, after lasting some ten or twelve years.

Diagnosis.—The peculiar swelling of the foot, with a filling-up of the arch, and the formation of sinuses from which a discharge containing the typical grains is escaping, enables the disease to be diagnosed with certainty from elephantiasis or tubercular disease of the foot.

The variety of the fungus may be determined by examining the grains or the scrapings of the sinuses microscopically, culturally, and by inoculations in animals.

It is to be noted that the typical grains may for a time be absent from the purulent liquid exuding from the sinuses. In such cases squeezing of the nodules may make the grains appear, or a nodule which has not yet opened may be incised and the contents examined.

Prognosis.—If the growth is observed when young, small, and lying subcutaneously, so that it can be completely removed, the prognosis is good, as the wound heals readily and the growth does not recur.

If, however, the growth has lasted some time, and has involved the bones, the prognosis is not good, and is worse if the lymphatic glands are also implicated.

Treatment.—Remove the growths at an early stage and as completely as possible. In later stages amputations well above the seat of any lesion, together with the removal of any enlarged lymphatic glands, is the only possible treatment.

Potassium iodide may be tried, but as a rule internal medicines and vaccines are useless for this form of mycetoma.

Prophylaxis.—The wearing of boots and shoes and not walking barefoot are apparently good and sensible methods of prophylaxis.

THE ACTINOMYCOSES.

Definition.—The Actinomycoses are those forms of mycetoma with grains composed of very fine non-segmented mycelial filaments, in which usually the walls are not clearly defined from the contents, and in which chlamydospores are absent.

History.—This period opens with Bollinger's epoch-making work in 1876 on the lumpy-jaw of cattle, a disease which had been recognized since 1785, and in which he found the constant presence of a branching organism. This fungus was examined by Harz (1877-78), who gave it the name *Actinomyces bovis*, but, most unfortunately, this generic name cannot stand, because, unbeknown to Harz, it had already been used by Meyen (1827) for a fungus which he called *Actinomyces horkelii*, which is in no way related to the group of fungi which we are considering. This mistake launched the generic name applicable to these organisms on to a sea of change, and led to much confusion.

1. *Nocardia bovis*.—The correct name for Bollinger's organism is *Nocardia bovis* (Harz, 1877). The fungus appears to have been first seen in man by Israel in 1878. Corre (1883) was the first to draw attention to the similarity between actinomycosis and the ochroid variety of mycetoma, while Acland (1886) was the second observer to demonstrate the presence of actinomycosis in man; and as Israel's name is associated with quite a different human actinomycosis, we propose to name this variety *Acland's actinomycosis*. In 1886, Vandyke Carter, as we have already stated, also drew attention to the likeness between actinomycosis and mycetoma. Finally, in 1891, Bostroem grew *N. bovis* from eleven cases of actinomycosis in man, and since that time it has often been cultivated and described. It is a *nocardia* with radially arranged filaments, which show club-like enlargements of their extremities, caused by a protective thickening of the walls in animals and less commonly in man, and having abundant Gram-positive but not acid-fast hyphæ, some of which end in chains of arthrospores.

It grows well aerobically at 22° C., but better at 37° C. Anaerobic growths are, as a rule, but poorly developed.

It may form a dry pellicle on the surface of broth, but more usually it gives rise to cohering colonies at the bottom of the tube, and in either case the medium remains clear.

It grows slowly on gelatine, producing a yellowish-white growth and slow liquefaction, beginning about the seventh day. The resulting fluid may or may not be dark coloured. On blood serum it produces poor growths, and no liquefaction or pigmentation of the medium.

On agar and glycerine agar it forms hard, spherical, white colonies, which give rise to an undulating crateriform growth, having a yellowish or greyish tint, which in its turn becomes a lichenoid ashen grey or yellowish mass with a powdery efflorescence. On maltose agar it forms discrete fawn-coloured colonies, later becoming yellow, dark brown, or even black, while the medium may be slightly darkened.

On potato it forms confluent, hard, raised, variously coloured masses, at first white, but becoming greenish-yellow, brown, greyish-black, or even black, with more or less erosion and pigmentation of the medium to which the growth is very adherent. No diastatic action has been observed.

Litmus milk is first reddened, but later it becomes a clear brown alkaline liquid. It is pathogenic for man, ox, horse, pig, and other animals, while experimentally rabbits and guinea-pigs have been infected by intraperitoneal inoculation.

2. *Nocardia asteroides.—Nocardia bovis* (Harz, 1877) is not the only organism known to cause actinomycosis in man, for in 1890 Eppinger obtained an organism which he called *Cladothrix asteroides*, and which is now known as *Nocardia asteroides* (Eppinger, 1890), from the lesions in a case of pseudo-tuberculosis of the lungs and pleura, with old caseous nodules in the apices and calcareous degeneration of the bronchial and supraclavicular glands, together with a cerebral abscess which had ruptured into the ventricles. The fungus was Gram-positive and acid, but not alcohol-fast, and grew aerobically on laboratory media, and was pathogenic for laboratory animals. It was afterwards recognized by Almquist, in 1890; by Sabrazès and Rivière, in 1894; by Aoyama and Miyamoto, in 1900, in Tokio; by MacCallum, in 1902, in America; and by Schabad, in 1903, in Russia. It is also the same as the fungus described by Musgrave and Clegg (1907), in a case of mycetoma in the Philippine Islands, under the name *Streptothrix freeri*.

In 1909, Lindenberg, in Brazil, isolated a fungus from a case of mycetoma of the left leg, which began in the popliteal space, and to this organism he gave the name *Discomyces brasiliensis*.

He was very careful to separate it from *N. bovis* and from *N. maduræ* (*N. indica*), but he does not appear to have done so with regard to *N. asteroides*. We therefore offer a comparison between the two organisms in the table on p. 2132.

The inoculations into animals are not comparable, as Lindenberg did not use monkeys. He was unsuccessful with a guinea-pig, but does not say how he inoculated it, while Musgrave and Clegg were successful by means of intraperitoneal inoculations.

The differences as set forth between *N. brasiliensis* and *N. asteroides* appear to us to be very slight, and therefore we are able to agree with Pinoy in his belief that they are one and the same organism.

Also Cranwell, Bachmann, and Del Pont (1909) gave an excellent and well-illustrated description of a yellow mycetoma in Buenos

Aires. Unfortunately, they did not grow it on inspissated blood serum, but, as far as we understand their account, we should classify this organism, which they did not name, as *Nocardia asteroides*.

Nature of Test.	*N. asteroides from Musgrave and Clegg.*	*N. brasiliensis Lindenberg.*	*Result of Comparison.*
Seat of disease	Mycetoma of foot	Mycetoma of leg	Difference unimportant.
Grains	Consistency dough-like, colour yellowish-white; size 0·25–0·5 mm. in diameter.	Consistency soft, colour yellowish-white; size 0·1–0·5 mm. in diameter.	No important difference.
Clubs	Usually absent.	Absent.	Agree.
Bacillary and coccal forms	Numerous bacillary and coccus-like varieties.	Bacillary and coccal forms present.	Agree.
Optimum temperature	Slower growth at 30° C. than at 37° C.	Better growth at room temperature than at 37° C.	Slight disagreement.
Anaerobic cultivation	Does not grow	Does not grow.	Agree.
Broth	Floating flat particles which later fall to the bottom Medium not affected	Small particles which later fall to the bottom of the tube. Medium not affected	Agree.
Gelatine	No liquefaction	No liquefaction	Agree.
Sabouraud's glucose agar at 37° C.	Centre yellow periphery pink to pinkish white.	Colonies rose violet	Slight disagreement.
Potato	At first delicate pink and later yellow ochre centre with pinkish or white periphery, the medium becomes darkened	At first a rose colour, and later a yellow-orange colour; the medium becomes brown.	Agree.
Serum	Growth slower Colonies at first white, later diffuse pink.	Grows very badly at 37° C. Colonies white.	Later pink not mentioned in *N. brasiliensis.*
Milk	Yellowish mass. No coagulation	Yellowish-orange pellicle. No coagulation.	Agree.

Nocardia asteroides possesses Gram-positive, acid, but not alcohol-fast hyphæ, which are without club-like enlargements. It produces restricted growths aerobically and usually anaerobically at 22° C. and 37° C., but nothing is stated in the literature we have consulted with regard to any odour arising from these cultures. It does not liquefy gelatine or blood serum, nor has it any diastatic action. It reddens litmus milk, which later becomes alkaline, but is not coagulated or cleared. It grows on the agars and on potato, producing reddish (often brick red) growths. It is pathogenic for monkeys, rabbits, and guinea-pigs.

3. *Nocardia liquefaciens.* This fungus was obtained by Hesse in 1892 from a man in Germany with a left inguinal abscess which communicated with the rectum. Subsequently other abscesses formed on either side of the dorsal spine. The pus from these abscesses discharged soft yellowish grains about the size of a millet seed, which contained a Gram-positive fungus which did not possess clubs. On cultivation it grew readily, and was found to be strictly aerobic. In gelatine stabs it formed a nail-shaped growth, which at room temperature in Europe was only visible on the third day, while liquefaction, beginning on the fourth or fifth day, was complete by the end of the week. The liquefied gelatine was not discoloured, and if the growth stuck to the glass it was yellowish, with a whitish covering. On blood serum it formed small cloudy granules of the same colour as the medium, in twenty-four to forty-eight hours. Liquefaction begins at the end of the first week and proceeds slowly, the liquid remaining quite clear and colourless, and only after some six months turning to a reddish-yellow colour. In broth it forms delicate flakes which fall to the bottom of the tube, and consist of a lower surface which is yellowish-white, and an upper surface which is snow white. The medium remains quite clear. No surface growth is mentioned.

On agar the colonies at first form separate rosettes, which remain distinct for a time. These colonies appear to resemble the gelatine culture, being yellowish below and having a white envelope. The growth on glycerine agar is more vigorous than on ordinary agar.

On potato it forms small yellow nodules by the second day, which later become covered with a snow-white efflorescence, which does not alter. Apparently it was not grown on glucose agar, milk, or eggs. Intravenous, intraperitoneal, and subcutaneous injections into rabbits, guinea-pigs, and white mice were negative.

Hesse gave it the name *Cladothrix liquefaciens*, which now becomes *Nocardia liquefaciens* (Hesse, 1892), and it appears to be the same organism as that named *Streptothrix buccalis* by Goadby in 1903, and found by him in 1899 in the mouth in cases of pyorrhœa. Goadby's form showed clubs, or club-like swellings. It precipitated the casein in milk, which became clear.

4. ***Nocardia indica.***—Kanthack, 1893, studying specimens of black and yellow mycetoma which came from India, concluded that the

latter variety was a true actinomycosis, and attempted to show that the former was the same, only in a degenerated condition.

He only examined the specimens microscopically, as no cultures were possible, and named the fungus in question *Oōspora indica* Kanthack, 1893, calling his two varieties *O. indica* var. *flava* and *O. indica* var. *nigra*. The name of this fungus, translated into more modern nomenclature, becomes *Nocardia indica* (Kanthack, 1893).

Boyce and Surveyor (1894) clearly proved that the melanoid variety was due to quite a different fungus from that causing the ochroid variety, which latter they considered in some, but possibly not in all, cases to be an actinomyces, a conclusion in which they were supported by Hewlett and by Boccaro. The latter analyzed one hundred cases of Madura foot, of which the vast majority were black mycetomas, while seventeen had evidence of pricks with an acacia (Babul) thorn, in several of which it was found present on examination.

Kanthack's name appears to have been overlooked, but it certainly has priority as regards the fungus of an actinomycotic nature causing the ochroid variety of mycetoma as seen in India, but difficult of recognition in that it was not cultivated.

In 1892, Gémy and Vincent described a parasitic disease of the foot in Algeria, which they considered analogous to, if not identical with, the ochroid variety of Vandyke Carter's mycetoma.

In 1894, Vincent, still working in Algeria, met with a streptothrix in a similar case. This fungus, which was first known as *Streptothrix maduræ* Vincent, 1894, is believed to be identical with the fungus found by Boyce in London in an agar tube inoculated in India from a case of the ochroid variety of mycetoma.

This streptothrix found by Boyce is, of course, an entirely different organism from the mucor-like fungus called *Chionyphe carteri* mentioned above, which therefore cannot be placed in the list of synonyms of *N. maduræ*, as has been done by some authors.

Boyce's culture showed a fungus without club-shaped extremities which grew very slowly on agar, glucose agar, and glycerine agar, at a temperature varying between 35° C. and 37° C. No formation of pigment was observed, but it was remarked that the organism closely resembled that of actinomycosis.

In 1904, Cornwall reported the cultivation of Vincent's organism in India. He washed the grains in six changes of sterile salt solution, and then planted them on agar in tubes. After an interval of one or two months a growth appeared, which in some cases assumed a pink colour and in others remained a dull white. In subcultures it grew more freely, preserving its characteristics, one of which was to adhere so closely to the medium that each nodule had to be literally dug out when it was required to transfer it to another tube. Puff-balls formed in broth and hay infusions, while it was noted that the fungus required plenty of oxygen for its growth and only occasionally formed the pink pigment.

This description by Cornwall leaves no doubt in our minds that he met with Vincent's organism in a case of the ochroid variety of mycetoma, and if this is correct, then Kanthack's name assumes its priority and Vincent's becomes a synonym, and the correct name of the fungus is *Nocardia indica* (Kanthack, 1893), and this is supported by Strong's culture of the same fungus from an Indian mycetoma in 1908.

With regard to the remaining history of the fungus, it should be noted that in 1898 Legrain, and in 1899 Brault, again described its presence in Algeria, while in 1901 Albertini and Desvernine reported its presence in Cuba, and in 1902 Brumpt discovered that it existed in Abyssinia, while Sommer y Greco demonstrated its presence in the Argentine in 1904, and Williamson in Cyprus in 1905, in which year Brumpt, in his classic on Mycetomas, stated that he had obtained it from India, Somaliland, and Senegal.

In the same year, Pelletier described a case of mycetoma with red grains which he saw in Saint Louis, in Senegal. The grains were very small, from 0·4 to 0·5 millimetre in diameter, and of a beautiful vermilion red colour. In the same year Laveran published a paper upon Pelletier's mycetoma, in which he says that it was possible on making sections of the tumour to easily discern therein little red spots of variable size which stood out from the surrounding neoplasm. These grains contained a large number of Gram-positive micrococcal-like bodies embedded in a ground substance. These bodies, which measured 0·7 micron in diameter, were never found isolated, but always in masses or short chains. No trace of a mycelium could be seen, and for this reason he gave it the name of *Micrococcus pelletieri* Laveran, 1906. But coccal-like forms are commonly found in nocardial infections, and in 1912 Thiroux and Pelletier reported that this red mycetoma was fairly common in Senegal, where one of them had met with eight cases, from one of which, a suppurating tumour of the right side of the chest, they obtained cultures on Sabouraud's medium which very much resembled those of *N. maduræ*, but differed therefrom in the following particulars:—

1. The growths were ruby red from their commencement.
2. It had only so far been grown on Sabouraud's gelatine.
3. The growths did not penetrate into the gelatine, and were easily detached.
4. In the parasitic stage the organism takes the form of a micrococcus in zooglea.

They renamed the parasite *Oöspora pelletieri*. In the discussion on this paper, Laveran agreed with Thiroux and Pelletier's finding, and Pinoy pointed out that the only real differences between it and *N. maduræ* were the greater intensity of the red colour and the more abundant sporulation. Further, he suggested that the correct name was *Nocardia pelletieri*. Under these circumstances, *N. pelletieri* would become simply a synonym of *N. indica*, of which the full list of synonyms has been given on p. 1058.

Clegg and Hobdy (1916) described *N. indica* in a native woman in Hawaii.

Nocardia indica, with yellow or red grains, possesses Gram-positive but not acid-fast hyphæ, without clubs. It forms restricted growths under aerobic surroundings at 22° C. and 37° C., but will not grow under strict anaerobic conditions. The cultures are without any distinct odour. It is usually said not to liquefy gelatine or blood serum, but Koch and Stutzer say that it has a peptonizing effect after a long time. Milk is not coagulated, but after some time is cleared. Pinkish colonies are produced on the agars and on potato. It is non-pathogenic for animals, as far as is known.

5. *N. garteni*.—Garten, 1895, met with an organism in cases of actinomycosis in man which he called *Cladothrix liquefaciens* No. 2, in order to distinguish it from Hesse's fungus, which he called *Cladothrix liquefaciens* No. 1; but Brumpt, in 1910, altered Garten's name to *Discomyces garteni*, which now becomes *Nocardia garteni* Brumpt (1910).

This fungus was grown in 1895 by Garten from the lesions of a case of necrosis of vertebræ and ribs, which was associated with abscesses, sinus formation, and empyema. The grains were composed of a tangle of ramified filaments without club formation.

The organism was an aerobe which grew easily on various media, producing on gelatine fine greyish-white points. On the fourth day liquefaction commenced, and was completed by the eighth day. Nothing is said as to the liquid being coloured in any way, and, therefore, we must assume that it was not tinted. On agar, glycerine, and glucose agar it formed a greyish-white growth, which became somewhat wrinkled on the surface after two to three days. The wrinkles are deep folds on glycerine agar.

On serum it forms a white layer, which becomes wrinkled and folded after forty-eight hours, when commencing liquefaction may be noted. On the third day the liquid has increased considerably, and by the sixth day the whole serum is reduced to a perfectly clear fluid. On potato it gives rise to white colonies, while the surrounding medium becomes greenish in colour. It apparently was not grown on eggs, milk, broth, or peptone solutions. It is pathogenic for rabbits and guinea-pigs.

6. *N. krausei*.—In 1896, Krause found an organism in an abscess of the lower jaw, in a man in Germany, which was characterized by having long and short rods and club-like forms resembling the diphtheria bacillus.

It did not grow at 22° C. nor on gelatine or potato, but it was a facultative anaerobe which formed slightly yellowish colonies on glycerine agar and was not pathogenic for rabbits, guinea-pigs, or mice.

This fungus was named *Streptothrix krausei* by Chester, 1901, which name has become changed to *Nocardia krausei* (Chester, 1901).

Allied to, or identical with, this species are the fungi causing the conditions described by Mosetig-Moorhof, Dor, and Poncet, and often called 'pseudo-actinomycosis' or the mycoses with yellow grains, which are larger than those of the ordinary actinomycosis, while they are less numerous in the pus. Microscopically they show a tangle of filaments longer and larger than those of ordinary nocardias, between which lie micrococcal-like débris. They never show clubs at the periphery, and do not grow on solid media like gelatine. They grow quickly in broth, forming a skin on the surface. Cultures on serum give clavate forms like the diphtheria bacilli.

The fungus causing the above conditions was named *Nocardia ponceti* by Verdun in 1913, and may be a synonym for *N. krausei* (Chester, 1901) for the following reasons:—

A. The pseudomycetomatous condition of Poncet does not differ from the definition of actinomycosis given at the commencement of this paper.

B. *N. ponceti* only differs from *N. krausei* in the following details:

1. *Broth is rendered turbid and has a bad odour*, but Foulerton has pointed out that this turbidity, together with the odour which was described as being associated with these growths, may have been due to the pus not being collected aseptically, and therefore the turbidity and odour may have been due to contamination, as in addition to these characters *N. ponceti* forms a typical puff-ball, just like *N. krausei*, in which the turbidity and odour are absent.
2. *According to Verdun, it does not grow on agar.* It is not known whether *N. krausei* grows on plain agar, but it can grow on glycerine agar and (according to some authors) on glucose agar.

C. They resemble each other in:—

1. Morphology.
2. They both possess clavate forms like the diphtheria bacilli.
3. Both grow on serum.
4. Neither grows on gelatine.

Other reactions are given for one, but not for both organisms, and are, therefore, useless for purposes of comparison.

We therefore, at present, see no reason why *N. ponceti* should be considered as a species distinct from the older *N. krausei*, of which its name becomes a synonym.

7. *Nocardia somaliensis.*—Bouffard observed two cases of a mycetoma at Jibouti, in French Somaliland, which appears to be peculiar both in its histological appearances and in its cultural characters. Brumpt, in 1906, classified this fungus in his new genus, *Indiella* Brumpt, 1906, calling it *I. somaliensis* and pointing out that, judging by the descriptions given by older writers in India of the macroscopical appearances of some of the ochroid varieties of

mycetoma, this variety might be found to be more common than Vincent's *N. maduræ* (=*N. indica* of Kanthack).

Balfour (1911) reported the presence of the same causal agent in a case of mycetoma of the hand in the Anglo-Egyptian Sudan, and gave a photomicrographic illustration of the growth; and in the same year Fülleborn described and gave excellent illustrations of a case from South-West Africa, which occurred in a Herero aged twenty years. A study of Fulleborn's preparation induced Brumpt to alter his generic diagnosis for the fungus which, in 1913, he classified as *Discomyces somaliensis*, which, converted into our present nomenclature, becomes *Nocardia somaliensis* (Brumpt, 1906), but he is inclined to think that it ought to form a separate genus or subgenus, for which he proposes the name *Indiellopsis* Brumpt, 1913, because it secretes around itself in the grain a hard sheath, insoluble in potash and in eau de Javelle, which no other nocardia is known to do.

In 1916 we met with this fungus in a mycetoma of the foot in Khartoum.

The grains are hard, 1 millimetre in diameter, and being of a reddish-yellow colour, resemble the eggs of fish. The fungus will not grow on hay or on dura broth, but it quickly produces a white, lichen-like, folded growth, becoming yellow on the fifth to sixth day on potato, but this growth never becomes red like that of *N. indica.*

Genus Cohnistreptothrix.- In 1891, Wolff and Israel published a beautifully illustrated account of a streptothrix, which they had isolated from two cases of actinomycosis in man— viz., from the lungs and from a retromaxillary growth. This organism was considered to differ from *N. bovis* in that it grew best anaerobically, that branching was absent, and that its injections into animals were regularly positive in their result. These three characteristics induced Kruse, in 1896, to make a new species for it under the name *Streptothrix israeli.* In 1911, for reasons presently to be set forth, Pinoy founded a new genus, *Cohnistreptothrix*, with Israel's organism as the type species, and therefore its name becomes *Cohnistreptothrix israeli* (Kruse, 1896).

It appears to us to be of importance that the reader should clearly understand the nature of the organisms included in this genus, and, therefore, we digress from our main subject in order to give a brief history.

Lachrymal concretions have been known since Césoin described them in 1670. In 1848, Gruby, examining one of these objects, found it to be composed of a fungus, which he believed to be the same as that causing favus; but Cohn, in 1875, examining another such concretion, also saw a fungus, for which he created a new genus, Streptothrix, calling the fungus in question *Streptothrix foersteri* Cohn, 1875, which may be the same organism as *S. aureus* Du Bois de Saint Sévérin, 1895, and must be closely related to *Nocardia tenuis* Castellani, 1911, which belongs to the same genus, and as its colonies on agar are 'cerebriform,' it may possibly be the same or related to *Streptothrix radiatus* and *S. cerebriformis*, both described from cases of keratitis by Namyslowski in 1909, as well as the more aerobic hyphal form of Silberschmidt's organism.

Unfortunately, a mistake was made, for Cohn was not aware that the same streptothrix had already been given by Corda, in 1839, for another and quite different fungus, which is known as *Streptothrix fusca* Corda, 1839, and which is to be found in all works of any importance on systemic mycology. Therefore, as streptothrix is not available, after many changes, the generic name has become *Cohnistreptothrix* Pinoy, 1911, and to this genus Israel's human organism belongs. It differs from Bollinger's type of fungus in growing best anaerobically, in being difficult to cultivate, and in not producing arthrospores. Other allied organisms are *Cohnistreptothrix thibiergei* (Ravaut and Pinoy, 1909), also found in actinomycosis in man; *Streptothrix spitzi* Lignières, 1903, found in cattle, and probably identical with *C. israeli*, as may be Doyen's streptothrix; while *Nocardia carougeaui* Gougerot, 1909, in juxta-articular nodules, and *Streptothrix cuniculi* Schmorl, 1891, probably also belong to this genus, as well as the streptothrix recently discovered in a liver abcess in America by Bloomfield and Bayne-Jones (1915), as we have consulted the authors upon this point, with which they are in agreement. Perhaps the bacillus described by Sawtschenko, in 1896, as the causal agent of a pseudomycetomatous condition may also belong to this genus, and it is also possible that the *Coccobacillus pseudo-actinomycosis polymorphus* Berestneff, 1898, may be the same as the chromogenic anaerobic streptothrix obtained from human pus by Neschezadimenko in 1908, and carefully described.

8. *Cohnistreptothrix israeli.*—This organism appears to be of increasing importance in human pathology, for, according to Pinoy, it appears to affect man more often than *Nocardia bovis*. It was first discovered in man, as mentioned above, by Wolff and Israel in Germany, and has since been found in thirteen cases in the United States by Wright. It has also been found in cattle by Lignières and Spitz (1904) in the Argentine, and by Pinoy (1913) in France.

It is composed of short and long rods, some of which show club-like swellings, while in old cultures spores which resemble cocci in appearance can be seen. It grows but poorly in the presence of air, but much better anaerobically at 37° C. on agar, on which it forms dew-like drops, which later become yellowish and generally remain discrete. In broth it forms a deposit of small scaly particles. It does not grow on gelatine at the room temperature of Europe, but egg cultures show typical branched filaments with club-like ends, which later break up into bacillary and coccal forms, but true arthrospores (*i.e.*, resistant spores) are not produced. It forms granulation tumours when inoculated intraperitoneally into rabbits and guinea-pigs, after an interval of four to seven weeks. In these tumours typical actinomycotic grains can be found, containing branched filaments with clavate ends.

9. *Cohnistreptothrix thibiergei.*—This fungus was discovered in 1909 by Ravaut and Pinoy in a case of actinomycosis which produced generalized subcutaneous and intramuscular nodules in a man in France.

The nodules opened and discharged blood-tinged pus, in which the fungus was seen sometimes in isolated bacillary form and sometimes as very small white grains, which in the tissues might measure some 80 microns and be composed of a radiating mycelium with or without fine club forms. It grows well aerobically and anaerobically, but the former produces more bacillary and the latter more filamentous forms. The optimum temperature is about 37° to 38° C. It does not appear to be pathogenic for laboratory animals.

Climatology.—The geographical distribution of this variety of mycetoma is as follows:—

I. *Black actinomycosis :* Only one variety of this is known—viz.:—

Babès and *Mironescu's black actinomycosis,* found in Roumania and caused by an unknown fungus.

II. *Yellow actinomycosis :* This form is well known in North America, and Sutton, of Kansas City, in 1913, in addition to drawing attention to four previously described cases, added two from his own practice. The usual microscopical appearances shown in yellow actinomycosis are depicted in Fig. 848, but the only method, known to us, of distinguishing the nine forms of actinomycosis classifiable under this heading is by cultivation, as will be indicated below. The nine varieties known to us are:-

1. *Israel's yellow actinomycosis,* found in Europe and America (North and South), and caused by *Cohnistreptothrix israeli* (Kruse, 1896).
2. *Ravaut* and *Pinoy's yellow actinomycosis,* found in France, and caused by *Cohnistreptothrix thibiergei* Ravaut and Pinoy, 1909.
3. *Acland's yellow actinomycosis,* found in Europe, but the distribution of this form requires further investigation. It is caused by *Nocardia bovis* (Harz, 1877).
4. *Bouffard's yellow actinomycosis,* found at Djibouti, in French Somaliland, in the Anglo-Egyptian Sudan, and in South-West Africa, and caused by *Nocardia somaliensis* (Brumpt, 1906).
5. *Krause's yellow actinomycosis,* found in Europe, and caused by *Nocardia krausei* (Chester, 1901).
6. *Garten's yellow actinomycosis,* found in Europe, and caused by *Nocardia garteni* (Chester, 1901).
7. *Hesse's yellow actinomycosis,* found in Europe, and caused by *Nocardia liquefaciens* (Hesse, 1892).
8. *Chalmers* and *Christopherson's yellow actinomycosis,* found in the Anglo-Egyptian Sudan, where it appears to be not uncommon, and caused by *Nocardia convoluta* Chalmers and Christopherson, 1916.
9. *Eppinger's yellow actinomycosis,* found in Europe, America (North and South), Asia, and Africa, and caused by *Nocardia asteroides* Eppinger, 1890.

III. *Red (sometimes yellowish) actinomycosis :* Only one form of which is known:

Carter's red (sometimes yellowish) actinomycosis, found in, India, Hawaii, Argentina, Cuba, Senegal, Algeria Cyprus, and Somaliland, and caused by *Nocardia indica* (Kanthack, 1893), synonym, *Streptothrix maduræ* (Vincent, 1894).

This organism has red or yellowish grains, which produce pinkish colonies on the agars (Plate VI., Fig. 8) and on potato. Kanthack's name was overlooked until recently.

Ætiology.—The fungi causing actinomycosis belong to the genera Cohnistreptothrix and Nocardia, and are best arranged by considering the different varieties of the disease, classified, like the Maduromycoses, according to the colour of the grain and the name of the discoverer.

They may be divided into:—

I. The *black actinomycosis*, with black grains.
II. The *white* or *yellow actinomycoses*, with white or yellow grains.
III. The *red* (sometimes *yellowish*) *actinomycosis*, with red (sometimes yellowish) grains.

I. THE BLACK ACTINOMYCOSIS.

Only one variety, found in Europe, is known—viz., *Babès and Mironescu's black actinomycosis*, of which the fungus has never been classified.

II. THE WHITE OR YELLOW ACTINOMYCOSES.

These may be differentiated by the characters of causal organisms into:—

A. Fungus difficult of cultivation, grows best anaerobically, arthrospores absent—Genus 1, *Cohnistreptothrix*.
  (*a*) Yellow grains:—
    1. *Israel's yellow actinomycosis*, caused by *C.* ***israeli*** Kruse, 1896.
  (*b*) Very small white grains:—
    2. *Ravaut and Pinoy's yellow actinomycosis*, caused by *C. thibiergei*.

B. Fungus grows readily aerobically and produces arthrospores—Genus 2, *Nocardia*.
  (*a*) Clubs present:
    3. *Acland's yellow actinomycosis*, caused by *N. bovis* Harz, 1817.
  (*b*) Clubs absent.
  (*c*) Hard sheath around grains:
    4. *Bouffard's yellow actinomycosis*, caused by *N. somaliensis* Brumpt, 1906.
  (*f*) Hard sheath absent.
  (*m*) No growth on gelatine.
    5. *Krause's yellow actinomycosis*, caused by *N.* ***krausei*** Chester, 1901.
  (*n*) Growth on gelatine.
  (*o*) Blood serum not liquefied:—
    6. *Eppinger's yellow actinomycosis*, caused by *N. asteroides* Eppinger, 1890.

(*p*) Blood serum liquefied.

(*w*) Pathogenic for laboratory animals:—

7. *Garten's yellow actinomycosis*, caused by *N. garteni* Brumpt, 1906.

(*x*) Non-pathogenic for laboratory animals.

(*y*) Gelatine liquefied:—

8. *Hesse's yellow actinomycosis*, caused by *N. liquefaciens* Hesse, 1892.

(*z*) Gelatine not liquefied:—

9. *Chalmers* and *Christopherson's yellow actinomycosis*, caused by *Nocardia convoluta* Chalmers and Christopherson, 1916.

III. THE RED (SOMETIMES YELLOWISH) ACTINOMYCOSIS.

There is only one known variety—viz., *Carter's red* (sometimes *yellowish*) *actinomycosis*, of which the causal organism is *Nocardia indica* (Kanthack, 1893).

The reasons for believing that these are the causal organisms of the disease are the same as for maduromycosis, and need not be repeated.

Pathology.—This is much the same as in maduromycosis.

Morbid Anatomy.—A young growth removed *in toto* can be divided into two portions, viz.:—

1. A dense matrix.
2. A number of irregularly shaped darker bodies, 'the fungal masses,' embedded in the matrix.

THE MATRIX.—When the matrix is studied by the aid of higher magnifications, it will be seen to be composed of white fibrous connective tissue containing a large number of connective-tissue corpuscles, and here and there a bloodvessel or a small group of bloodvessels which may or may not be associated with a collection of cells, and, in addition, lymph spaces and small collections of fat cells mostly associated with the bloodvessels. When these vessels are studied more carefully, some will be observed to be more or less normal, while others show signs of periarteritis or endarteritis of varying degree, which produce diminution and even occlusion of the lumen.

Connected with many of these vessels, and often more or less surrounding them, lie dense masses of cells, which when carefully studied appear to be all mononuclear. They are not all of the same category, however, for some, judging by their nuclei, appear to be derived from the endothelial cells of the vessels. Another type of cells is characterized by a darker staining nucleus, and appearing when cut in certain directions as though it possessed very little cytoplasm, but, when seen more correctly, has a relatively fair quantity of cytoplasm in proportion to the size of the nucleus. The nucleus being placed excentrically, and the cytoplasm being non-granular and not eosinophile, this cell agrees with Unna's description of a healthy *plasma cell* as seen in actinomycosis.

A third type of cell shows a large vesicular nucleus situate excentrically in a relatively large quantity of cytoplasm, which is either eosinophile or contains eosinophile granules, and corresponds exactly with Unna's description of degenerating plasma cells as seen in actinomycosis.

FUNGAL MASSES.—The darker irregular bodies seen embedded in the matrix, if examined by the aid of higher magnification, can be seen to consist of fibrous tissue and cells surrounding a portion of the fungus, and have, therefore, for purposes of distinction, been termed 'fungal masses.'

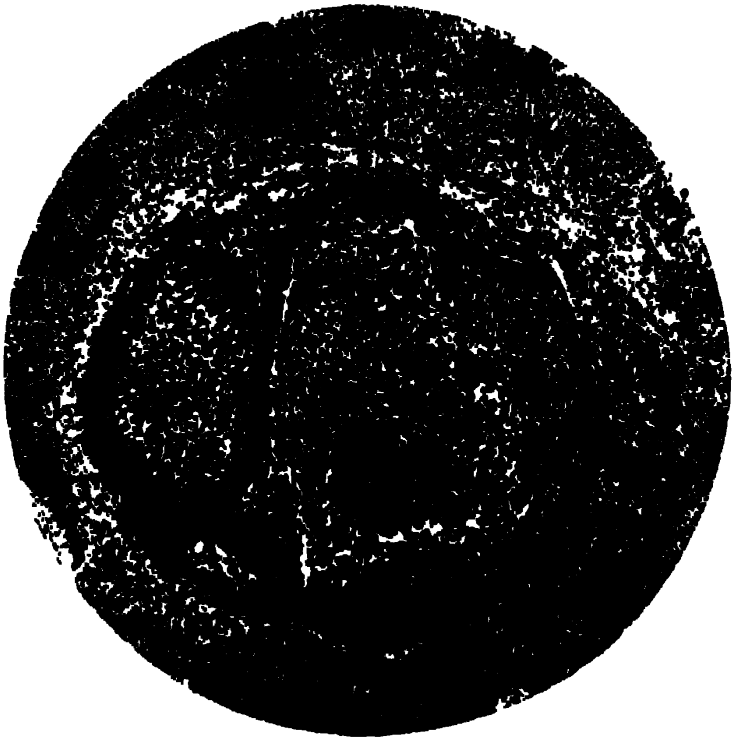


FIG. 848.—ACTINOMYCOSIS.

When a typical fungal mass is examined by means of a moderately high magnification, it can be seen to be composed of several distinct areas, which, working from the fibrous tissue matrix towards the fungus, lie in the following order:—

1. *The Fibrous Sheath.*—This is continuous with the fibrous tissue forming the matrix of the whole growth, as already described.

2. *The Fibrocellular Layers.*—Directly under the dense fibrous tissue there lies a thicker or thinner area composed of loose fibrous tissue, containing in its meshes cells and thin-walled vessels; this area may be termed the fibrocellular layers.

3. *The Cellular Sheath.*—Internal to the fibrocellular layers comes a mass of cells which may be called the cellular sheath.

4. *The Grain.*—Situate in the cellular sheath there lies a more or less distinctly or indistinctly striated body, of varying shape, and often with irregular edges, which is the grain, and is composed of the fungus and its surrounding matrix.

FIBROUS SHEATH.—When the fibrous connective tissue forming the matrix is examined, in the vicinity of a fungal mass, it will be observed to show collections of cells at intervals.

FIBROCELLULAR LAYERS.—These layers are composed of loose fibrous tissue, holding in its meshes plasma cells, healthy and degenerating polymorphonuclear cells, giant cells, and bloodvessels.

With regard to the giant cells, they may be seen to contain fungal masses, or these may be observed escaping therefrom, or the giant cells may be remarked to be separated from the fungal mass by a little distance and to be damaged, while polymorphonuclear cells lie near the fungus, and the adjacent layers of the fibrocellular tissue may be observed to be arranging themselves circularly so as to circumscribe the new fungal growth, and so to commence the formation of a new fungal mass.

When two fungal masses lie in close approximation to one another without the intervention of dense fibrous tissue, it will be observed that small areas of the fibrocellular layers adjoining the two masses show signs of granular degeneration.

Another interesting feature, but by no means confined to the fungal masses, is the presence of cells containing one or several, small or large, rounded eosinophile globules. These were called fuchsin or Russell bodies by Kanthack, and botryomycotic bodies by Archibald (1911), who published some excellent illustrations thereof in Plates XV. and XVI. of the medical volume of the Fourth Report of the Khartoum Laboratories. They are a product of the fungus, and are frequently seen in nocardial infections lying in cells at a distance from the fungus, in which case they are a great aid in diagnosis, as indicating the probable presence of a fungus somewhere. They are also seen in masses cut longitudinally and lying in lymph spaces. They have been recorded by all workers at actinomycosis and maduromycosis since the days of Kanthack, and appear to us to be probably the same material as that forming the club-like dilatation of the extremities of the hyphæ in *N. bovis* and other nocardias, and that they may possibly be a protective substance excreted by the fungus which only under certain conditions consolidates into the eosinophile form and into the clubs of certain species of nocardia.

THE CELLULAR SHEATH.—All our observations tend to support Brumpt's view that primarily the fungus is enclosed in a cell which in the younger fungal areas near the older area is always multinuclear.

Further, in the present specimen, there can be no doubt that the fungus is not destroyed by the giant cell, but, on the contrary, grows and escapes therefrom and starts life as a little fungal mass of its own, in which instance the polymorphonuclear leucocytes now

appear upon the scene, and the fibrocellular coat begins to circumscribe the cells and the fungus, while the damaged remains of the giant cell are seen retiring towards the periphery.

Later, the mononuclear cells mentioned above appear, and these **various cells,** together with detritus from the destruction of similar **cells** situate in a granular network, form the cellular sheath of the **grain,** as shown in our specimens. This description, although varying in detail, does not differ materially from a composite picture such as can be derived by a study of the writings of Carter, Acland, Kanthack, Boyce and Surveyor, Unna, Schlegel, Foulerton, Brumpt, and other authors who have studied the reaction of the body against different species of the genus Nocardia.

In more advanced cases the morbid anatomy is like that described in maduromycosis, with, of course, the difference in the grain.

Symptomatology, Diagnosis.—These are the same as for maduromycosis.

Treatment.—Vaccines have not given good results in our hands. The correct treatment is removal whenever possible, but, failing this, iodide of potash in large doses may be administered.

Prophylaxis.—This is the same as for maduromycosis.

THE PARAMYCETOMAS.

Definition.—A paramycetoma is a disease which includes all growths and granulations producing enlargement, deformity, or destruction in any part of the tissues of man which are caused by fungi of any nature whatsoever, but in which grains are either absent or so few and so small as to escape observation without prolonged search.

History.—In 1917, Chalmers and Archibald first proposed this differentiation, and followed it up in 1918 by a further communication.

Clinical Remarks.—The Paramycetomas, as already stated, cannot be recognized without microscopical assistance, because they present a varied group of clinical forms comprising chronic ulcers which may seem to be non-malignant, doubtfully malignant, or malignant, of growths which appear to be innocent or which are capable of diagnosis as doubtful carcinomata, epitheliomata, or sarcomata, or with reference to which no doubt is entertained in the mind of the surgeon attending them.

If removed in the more innocent forms or in the early stages they probably do not recur, but in the later stages of the malignant forms they do recur, but probably then as true malignant growths.

As a diagnosis cannot be made clinically, it behoves us to inquire upon what it is to be based.

Diagnosis.—The recognition of a paramycetoma is based entirely upon microscopical examination, and consists in finding one or more of the following features:—

(a) Peculiar eosinophile bodies.
(b) Fungal filaments.
(c) Minute grains.
(d) Cultures and animal experiments.
(e) Minor points.

(a) PECULIAR EOSINOPHILE BODIES.—These are single bodies enclosed in cells, or several large and apparently free bodies.

In our opinion these bodies are composed of a chemical substance, apparently formed in human tissues by several different kinds of fungi, but more particularly by the nocardias. The substance may be noted lying in a lymphatic, or in the form of these bodies in cells at a considerable distance from the site of the fungus. Hence their importance in diagnosis and the necessity on discovering them for further search in the tissues, or the patient, for a fungus.

(b) FUNGUS FILAMENTS.—The most common filament to be found in a paramycetoma is the *nocardial hypha*. These are easy of recognition to the trained eye, but are apt to be mistaken by persons not acquainted with mycology and to be recognized as bacilli, while their spores, if present, may be considered to be micrococci.

Other forms of fungi, however, may cause a paramycetoma—*e.g.*, fungi of the type of a leptothrix.

It will thus be seen that just as we divided the mycetomas into the actinomycoses and the maduromycoses, so can the paramycetomas be divided by the nature of the hyphal filaments into the paractinomycoses and paramaduromycoses.

(c) MINUTE GRAINS.—These grains are very minute in size, and very few in number, and, in our experience, are most difficult to find, and, indeed, are perhaps often absent when the case may be due entirely to hyphal filaments not collected into grains.

(d) CULTURES AND ANIMAL EXPERIMENTS.—We have been unfortunate with our attempts at cultivation and in our animal inoculations, but the success attained by the Leytons indicates that these can be done at all events with certain species of fungi. Our climatic difficulties must be remembered in connection with our failures.

(e) MINOR POINTS.—Among minor points which are worth noting are the presence of many plasma cells either in good condition or degenerated.

The condition of the vessels, which often show endarteritis or periarteritis, just as in mycetoma, is also worthy of note.

Another minor point is a peculiar glassy or vitreous macroscopical appearance, which is due to a degeneration of the tissues of a glassy nature, and must not be mistaken for hyaline degeneration.

For certain diagnosis the fungal filament should be found, but, failing this, the eosinophile body is of the utmost importance. These bodies, if associated with many plasma cells, degenerated plasma cells, and changes in the bloodvessels and glassy degeneration, are almost pathognomonic of the presence somewhere of a parasitic fungus.

The differentiation from mycetoma is not difficult, as the grain is readily found in this growth, which it certainly is not in a paramycetoma.

The differentiation from malignant growth is at the same time very easy and very difficult. Very easy because at once the specimen appears somewhat different from the typical malignant growth simulated, and very difficult because it may require prolonged search before definite evidence of the presence of a fungus is found.

Prognosis.—This depends upon the site and age of the tumour and its association with malignant characters or not. If the last feature is absent, and the growth is small and can be completely removed, the prognosis is good, otherwise it is bad. If glandular excision is performed, the presence or absence of infection is of the utmost prognostic value.

Treatment.—The only known satisfactory treatment is the early and complete removal of the growth associated with glandular excision.

THE PSEUDOMYCETOMAS.

Definition.—A pseudomycetoma resembles a mycetoma clinically in the presence of swelling, ulceration, and discharge, but differs therefrom in the absence of grains, and from a paramycetoma in the absence of eosinophile bodies.

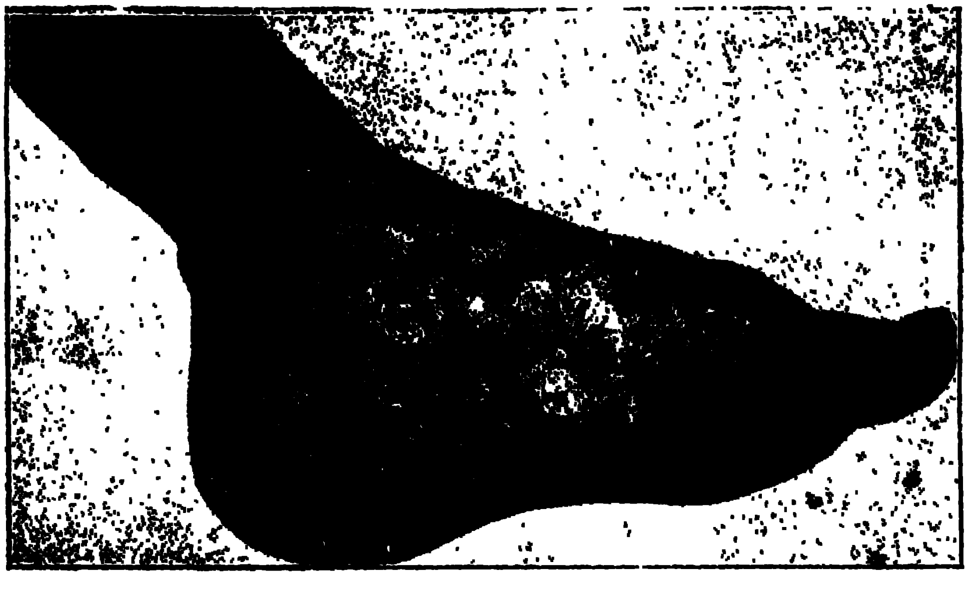


Fig. 849.—Pseudomycetoma of Frambœsial Origin.

History.—The name *pseudomycetoma* was first used by Castellani to indicate a peculiar tertiary condition of yaws, which he described as clinically somewhat resembling mycetoma. The term was adopted by us in the second edition of this work.

Remarks.—This condition is now well-known to occur in the tertiary stage of frambœsia tropica (yaws), and is not unfrequently seen in Ceylon. Breinl, in New Guinea, has described a similar condition, known to the natives by the names 'roaki,' 'buno,' or 'auma,' which he considers is a separate clinical entity from yaws. He says that the foot closely resembles Madura foot, without the presence of the typical grains in the pus.

A similar condition is known to occur in sporotrichosis. The foot in this case is swollen and painful, and shows subcutaneous and deep gumma-like swellings. Fistulæ discharging pus are also present.

A similar condition has been described by Austregesilo as being due to an angiokeratoma in the foot of a negro in Brazil. The foot was much enlarged, with several nodules, from which white material exuded. Microscopical sections enabled a correct diagnosis to be made. The whole condition, however, resembled a mycetoma, but neither grains nor fungal hyphæ could be found. His paper contains an excellent illustration.

ACTINOMYCOSIS OF THE BODY.

Remarks. The fungi producing Madura foot may occasionally invade other parts of the body instead of, or in addition to, the foot. They may attack the skin and deeper tissues of the hands, trunk, mammæ in females, and also the deep organs, lungs, heart, liver, brain. For such conditions the term 'mycetomiasis' may be used, and when the fungi found are *Nocardia bovis* and *Nocardia israeli*, the term 'actinomycosis' is generally employed. These two fungi, in fact, seldom attack the foot. Some authorities used the term 'pseudo-actinomycosis' to indicate the condition induced by *Nocardia poncelii* Verdun, 1912, *N. liquefaciens* Hesse, 1892, *N. garteni* Brumpt, 1910.

Symptomatology.- The lesions resemble, to a certain extent, those found in the foot. The condition generally begins with indolent nodules in the skin or subcutaneous tissues, the skin over them becomes tense and glossy, and finally the nodules break down, with formation of sinuses, from which a purulent liquid exudes, containing the characteristic granules, of various sizes and colour, as described in Madura foot. Occasionally the ulcerated lesions become fungoid and large, and papillomatous purplish tumours may develop. The location of the lesions varies. The type caused by *Nocardia israeli* Kruse and *N. bovis* Harz, or *true actinomycosis*, as found also fairly frequently in temperate zones, is in most cases situated on the lower region of the face and neck, especially in the tissues under the jaw. In cattle it produces the well-known condition known as wooden tongue. It is characterized by the presence of sulphur-yellow grains in the pus. Of actinomycosis, besides the cervico-facial situation, which is the commonest, the following types have been described: The parietal, attacking the walls of the thorax and abdomen, the broncho-pulmonary, the abdominal (liver, etc.); the cerebral (very rare), in addition to the rare type situated on the foot (actinomycotic mycetoma).

Prognosis.- This depends greatly on the species of fungus causing the malady. The types due to *Nocardia bovis*, *Nocardia israeli*, or true actinomycosis, answer well to a potassium iodide treatment.

Diagnosis.—This is based on the presence of indolent or nodular masses, breaking down with formation of pus, in which grains containing the fungi are found.

Treatment.— Potassium iodide in full doses (gr. xx.) three or four times a day should always be administered.

Nodular Actinomycosis of Pinoy and Ravaut.

Historical and Geographical.—This condition and its fungus were studied by Pinoy and Ravaut in France.

Ætiology.—The condition is caused by a *Cohnistreptothrix*. Only one case is known, described by Pinoy and Ravaut, and due to *C. thibiergei* Pinoy and Ravaut, 1909 (see p. 1000).

Symptomatology.—In the only case on record there were numerous subcutaneous and intramuscular gummatous nodules, which had developed very slowly; they slowly softened, some ulcerating. In the pus the fungus was found.

Treatment.—Potassium iodide is to be recommended.

Other nodular actinomycoses of nocardial origin, and characterized by the presence of abscesses, or gummata in which fungi of the genus *Nocardia* are found, have been described by Rivière and others, and very ably in England by Foulerton.

Nocardial Abscesses.

Species of the genera *Nocardia* and *Cohnistreptothrix* may, at times, give rise to abscesses in various parts of the body. One such case was described by Broughton Alcock as being due to *Nocardia asteroides* Eppinger.

TRENCH FOOT.

Remarks.—Trench foot is not a tropical disease, but as it has been considered to be of hyphomycetic origin and ætiologically related to Madura foot by Raymond and other recent observers, we propose giving a short account of the condition.

Ætiology.—There can be little doubt that damp cold plays a very important rôle in the ætiology of the disease, but there is much difference of opinion on the point whether a low temperature is the real ætiological factor or merely a predisposing cause. Many authorities hold that trench foot is a separate entity from ordinary congelation conditions. Raymond and Parisot believe that the true ætiological agents of the malady are fungi, principally *Scopulariopsis koningii* Oudemans and *Sterigmatocystis versicolor*.

According to Castellani's researches, cocci, bacilli, and various fungi of the genera *Scopulariopsis* Bainier, *Aspergillus* Micheli, *Sterigmatocystis* Cramer, *Penicillium* Link, *Monilia* Gmelin, are often found, but they are probably secondary invaders. Castellani has noted in several cases a spirochæte. Certain authorities consider the affection to be a form of avitaminosis.

Among the predisposing causes one may mention the *race*—black troops in the trenches being much more prone to develop the condition than white troops—*fatigue and mental depression, and the wearing of puttees*.

Symptomatology. In a well-marked case the whole foot is œdematous, swollen, often of a dark red colour, and painful on pressure. Bullæ may develop, and after a variable period of time a gangrenous process may set in; but this is far from being a constant feature, and can be frequently avoided if a proper treatment is carried out. There are, however, fulminating gangrenous cases. A feature of the condition which has apparently escaped the attention of most observers is the presence in many cases of a low intermittent fever, even when there is no sign whatever of gangrene.

Prognosis.—This should be always guarded, as even if symptoms of gangrene do not occur the affection may run a very long course.

Treatment.—Raymond and Parisot recommend a boracic camphorated lotion, and in mild cases camphorated oil. Castellani has used as routine treatment, with good results, the following:—Calcium lactate in 5 or 10 gr. doses is given three times a day, and the affected parts are painted once or twice daily with an ichthyol lotion (ichthyol 1 dr., aq. ad 1 oz.), and very lightly wrapped in cotton-wool. It is advisable to keep the affected foot slightly raised by means of cushions. In severe gangrenous cases a surgical treatment is necessary.

Prophylaxis.—Trenches should be kept clean, dry, and sanitary as far as conditions permit. Officers and soldiers should receive instructions to keep the feet scrupulously clean, and wear rubber boots in wet weather when possible. In our opinion, putties should never be worn.

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CHAPTER XCIV

DERMATITIS VENENATA

Definition — Remarks — Historical — Climatology — Ætiology —Symptomatology — Diagnosis — Treatment — Prophylaxis — Varieties — Rhus group — Euphorbia group - - Urtica group — Tectona group—Rue group —Buffalo bean group— Little-known group— Doubtful group—References.

Definition.—The term 'dermatitis venenata' includes a number of inflammatory skin lesions caused by the irritative action of poisonous principles contained in certain plants.

Remarks.—By the above definition it will be observed that the term 'dermatitis venenata' is here used in the restricted sense of being only caused by plants, leaving the dermatitis caused by animals to be treated in the chapter dealing with the Dermatozoiases (p. 2200). Neither does the definition include *dermatitis medicamentosa*, which is due to drugs administered internally or externally, nor does it include *dermatitis factitia*, which is caused artificially—*e.g.*, beggars rubbing in *Ranunculus scleratus* Linnæus to produce sores for the purpose of inducing pity and the money usually associated therewith or recruits or soldiers utilizing various plants for purposes of malingering.

Historical.—From very ancient times it has been known that certain plants have stinging properties—*e.g.*, many species of the genus Urtica, of which *U. urens* Linnæus and *U. dioica* Linnæus are well known in Europe—but the effects of which are slight in comparison with the results produced by the species found in the East Indies—*e.g.*, *U. urentissima* Comm, *U. crenulata* Roxburgh, *U. stimulans* Linnæus, and *U. ferox* Forster. One of the earliest remarks on the subject is to be found in Kaempfer's 'Amœnitatum exoticarum,' which was published in 1712, and in which he refers to the action of lacquer varnish on the skin.

From that time onwards scattered references may be found in books on travel, on botany, materia medica, poisons, as well as in textbooks on skin diseases. Thus in 1862 Van Hasselt made some references to the subject, as did Bazin in the same year, while Piffard in 1881 made many references to plants supposed to be causal agents.

In 1887 White gathered the whole subject together in his work on 'Dermatitis Venenata,' and following this there was a leading article in the *Lancet* on the dermatitis produced by *Primula obconica*

Hance, 1880. In 1898 Blanchard made an excellent contribution with regard to *Arundo donax*, and was followed by Havard in 1899, Reynault in 1902, who detailed facts with regard to the disease as seen in Indo-China, and by Wellman in 1907, who considered the stinging plants of Angola. Then came publications by Balch (1906), Sabouraud (1908), and the Imperial Institute (1909), the last-named discussing satin-wood. After this there are the papers by Kamgiesser in 1911, Fordyce 1912, Santa Maria 1913, Whitfield 1914, and Letcher's book with the account of the buffalo bean of Rhodesia. In 1914 Hornsey gave a good account of the 'rungus poisoning' as seen in British North Borneo.

In 1916 Vadala again referred to *Arundo donax*, and in 1917 Chalmers and Pekkola gave an account of a Sudanese dermatitis venenata caused by a member of the Rutaceæ.

Climatology.—With regard to *geographical distribution*, it is a cosmopolitan complaint, being found in all parts of the world. It, however, requires further study in the tropics, and it is for this reason that we have specially brought it forward in connection with skin diseases.

Ætiology.—The causation of dermatitis venenata depends upon:—

I. The plant.
II. Personal idiosyncrasy.
III. Confirmatory test.
IV. The active principle.

I. *The Plant.*—The following list, largely compiled from White's book, but altered so as to agree with our definition of dermatitis venenata and to include tropical plants, gives those known to us to cause the complaint:-

Anacardiaceæ: *Rhus venenata* De Candolle.
Rhus toxicodendron Linnæus.
Rhus diversiloba Engler.
Rhus vernicifera De Candolle.
Semecarpus anacardium Linnæus.
Ampelidaceæ: *Cissus pruriens* Welwitsch.
Apocynaceæ: *Nerium oleander* Linnæus.
Araceæ: *Arisæma triphyllum* Schott.
Symplocarpus fœtidus Nutt.
Araliaceæ: *Aralia spinosa* Linnæus.
Artocarpaceæ: *Antiaris toxicaria* Leschenault de la Tour.
Aurantiaceæ: *Citrus vulgaris* Risso.
Berberidaceæ: *Podophyllum peltatum* Linnæus.
Bignoniaceæ: *Catalpa bignonioides* Walter.
Borraginaceæ: *Borago officinalis* Linnæus.
Cactaceæ: *Cactus grandiflorus* Linnæus.
Compositæ: *Erigeron canadense* Linnæus.
Lappa officinalis=*L. majus* Gaertner.
Leucanthemum vulgare Lambert.
Solidago odora Hooker and Arnold.

Coniferæ: *Abies excelsa* Link.
Juniperus virginiana Thünberg.
Juniperus sabina Linnæus.
Connaraceæ: *Thuija occidentalis* Linnæus.
Cnestis corniculatus Lam.
Crassulaceæ: *Sedum acre* Linnæus.
Euphorbiaceæ: *Euphorbia corollata* Linnæus.
Hura crepitans Linnæus.
Hura brasiliensis Willdenow.
Hippomane mancinella Linnæus.
Jatropha urens Linnæus.
Stillingia sylvatica Linnæus.
Leguminosæ: *Andira araroba* Aguiar.
Leucanthemum vulgare.
Mucuna pruriens De Candolle.
Stizlobium stans Kuntze.
Linaceæ: *Linum usitatissimum* Linnæus.
Loasaceæ: *Mentzelia oligosperma* Nuttall.
Mentzelia lindleyi Torrey and Gray.
Loganiaceæ: *Gelsemium sempervirens* Aiton.
Malvaceæ: *Malache hirsuta* Kuntze.
Orchidaceæ: *Cypripedium pubescens* Willdenow.
C. pubescens Salisbury.
Papaveraceæ: *Sanguinaria canadensis* Linnæus.
Phytolaccaceæ: *Phytolacca decandra* Linnæus.
Polygonaceæ: *Polygonum hydropiper* Linnæus.
Polygonum acre Hooker and Bentham.
Ranunculaceæ: *Aconitum napellus* Linnæus.
Anemone nemorosa Linnæus.
Anemone patens Linnæus.
Clematis virginica Thünberg.
Delphinium consolidum Linnæus.
Rubiaceæ: *Cephælis ipecacuanha* Richard.
Cinchona bark and quinine.
Rutaceæ: *Ailanthus glandulosa* Desfontaines.
Haplophyllum tuberculatum (Forskal, 1775).
Pilocarpus pennatifolius Engler.
Ruta graveolens Linnæus.
Scrophulariaceæ: *Verbascum thapsus* Linnæus.
Solanaceæ: *Datura stramonium* Linnæus.
Thymelaceæ: *Daphne mezereum* Linnæus.
Tropæolaceæ: *Tropæolum majus* Linnæus.
Umbelliferæ: *Thapsia garganica* Linnæus.
Laportea canadensis Gaudichaud-Beaupré.
Urticaceæ: Many species of Urtica.

This is a long list, but all its members are not natives of the tropics, in which the more important families are the Ampelidaceæ, the Anacardiaceæ, the Apocyanaceæ, the Artocarpaceæ, the Connaraceæ, the Euphorbiaceæ, the Leguminosæ, the Malvaceæ, the Rubiaceæ, the Rutaceæ, the Tropæolaceæ, and the Urticaceæ, the genera and species of which are indicated above.

II. *Personal Idiosyncrasy.*—When the poisonous principle is contained in the juice of cultivated plants, the poisoning is largely met with among gardeners, florists, and people associated with plants in some way; when, however, the poisoning is due to a principle contained in some special hairs of a plant, whether cultivated or not, it is obvious that anyone may be affected; and when it is due to principles contained in the dust from dry wood, it is also obvious that carpenters and persons who cut or saw this wood will be most liable to be affected.

With regard to the first series of cases, in our experience, there can be no doubt that some people are more liable to the affection than others, and it would appear that certain people suffering from any form of seborrhœa or allied condition, no matter how mild, are especially liable to be troubled by dermatitis venenata.

As stated in the previous editions of this book, we should not be surprised if, in the future, it will be found that certain forms of dermatitis venenata are due in reality to some parasitic micro-organisms living in the plants or woods, and which get inoculated. The fact that, for instance, satin-wood dermatitis appears several weeks after handling the satin-wood sawdust is rather in favour of there being some *contagium vivum* which requires some time to develop and multiply sufficiently to cause symptoms of disease.

III. *Confirmatory Test.*—The crucial ætiological test is to remove the patient from the district in which the plant grows, to cure his dermatitis, and then, after a lapse of time, to test him experimentally with the suspected plant, which, if the genuine causal factor, should reproduce the eruption.

IV. *Active Principle.*—Unfortunately at present hardly anything can be said upon this subject. We know that drugs like quinine can cause eruptions, and therefore we conclude that quinine is the active principle causing the eruption produced by boiling cinchona bark; but with regard to the majority of the plants, we are entirely or almost entirely ignorant of the chemical nature of the active principle.

Symptomatology.—Sometimes the symptoms consist merely of itching, with or without an erythematous blush. At other times there may be marked erythema, with œdematous swelling in the affected part, which is often the face or the hands, or both. In more severe cases a true dermatitis may be present with papules, vesicles, or pustules, with or without such general symptoms as fever and enlargement of the local lymphatic glands.

The onset is generally sudden, and the affected person may previously have been in excellent health. The termination is in quick recovery, especially if the causal agent is removed.

Diagnosis.—The case presents the ordinary appearance of an acute dermatitis, and it requires patience and acumen to trace this to its correct cause.

The characteristics of the disease are:—

1. Acute dermatitis appearing suddenly and often without apparent cause in a previously healthy person.
2. The history of the association with some plant by handling or being affected by the odour, or even of being in the neighbourhood thereof.
3. There may be history of previous similar attacks when in the vicinity of the suspected plant.
4. The rapid recovery on removal from the causal plant.
5. The return of the symptoms when again exposed to the plant.

The differential diagnosis has to be made from other forms of dermatitis, which can usually be done by the history and by finding the causal plant, but this will not help with certain forms of acarine dermatitis when the mite infests the plant.

In such a case the only possible method of diagnosis is to examine the plant and the patient carefully, so as to exclude the presence of these insects, and to reproduce the disease by means of a plant found to be quite free from mites.

Treatment.—The essential feature of the treatment is to remove the plant from the patient or the patient from the plant, whichever may be most convenient. The next point is to remove all irritating substances by copious bathing of the whole body in water, and in some cases to recleanse the affected area with alcoholic solutions. Lastly, soothing lotions such as calamine lotion should be applied to the inflamed area.

Strickler has tried in certain types the injection of minute doses of the poisonous principles extracted with absolute alcohol.

Prophylaxis.—When the patient knows that he is susceptible to the influence of a given plant, care should be taken to avoid it.

Varieties.—Dermatitis venenata may be divided into several groups as follows:—

I. *The Rhus Group.*—Plants in which the poisonous principle is contained in a clear watery fluid.
II. *The Euphorbia Group.*—Plants in which the poisonous principle is contained in a thick milky fluid.
III. *The Urtica Group.*—Plants in which the poisonous principle is contained in fluid in special hairs.
IV. *The Tectona Group.*—Plants and dried hard woods, the dust of which contains the poisonous principle.
V. *The Rue Group.*—Plants in which the poisonous principle is apparently volatile, but acts mainly when the plants are handled.
VI. *Buffalo Bean Group.*—Plants in which the causal agent is innumerable minute hairs which penetrate into the skin.
VII. *The Little-Known Group.*—This is a group containing plants which apparently cause dermatitis venenata, but about which information is very defective.
VIII. *The Doubtful Group.*—This contains plants which probably do not produce dermatitis venenata, but perhaps harbour a mite which may be the causal agent.

I. THE RHUS GROUP.

This group includes all those plants in which the poisonous principle is contained in a clear, watery juice.

The ivy or sumac belongs to the genus *Rhus* Linnæus, which is classified either as a genus belonging to the superfamily Anacardioideæ in the family Terebinthaceæ, or more simply as belonging to the family Anacardiaceæ. The genus *Rhus* includes about 120 species, growing in nearly every part of the world; but fortunately only a few are poisonous to man, and they may be distinguished, as a rule, by their inconspicuous flowers being in loose, slender clusters or panicles in the axils of the leaves, and by their greyish-white or yellowish dry fruit.

They may be arranged in two sections, according to the structure of their leaves:—

1. Leaves trifoliate.
    Rhus radicans Linnæus.
    Rhus toxicodendron Linnæus
    Rhus diversiloba Torrey and Gray.
2. Leaves pinnate.
    Rhus vernix Linnæus.
    Rhus pumila Meerburg.
    Rhus vernicifera De Candolle.
    Rhus succedanea Linnæus.

Rhus radicans Linnæus is by many authorities considered to be merely a variety of *R. toxicodendron*. It is common in the Northern United States, while the latter is more common in the Southern United States. It has ovate or lozenge-shaped leaflets, which are either entire or toothed and pointed, while *R. toxicodendron* has obtusely crenated, lobed leaves.

Rhus diversiloba is the Californian poison ivy or poison oak, with rounded, obtuse leaflets.

Rhus vernix (synonym, *R. venenata*) is the poison elder or poison sumac of the United States, and is a large shrub or small tree. It is very poisonous.

Rhus pumila Meerburg is a small erect shrub, found in the Southern United States.

Rhus succedanea Linnæus is the Japanese wau-tree, and is well known in Tonkin and in South China.

Ætiology.—The poisonous principle is an oil (*Toxicodendrol*), which occurs in all parts of the plant and at all seasons, and not toxicodendric acid, which is merely a synonym of acetic acid, as was formerly thought to be the case.

Symptomatology.—After an incubation of one to nine days, there is at first itching in the affected area, which gradually increases in intensity, and is associated with all the signs of inflammation, producing an appearance not unlike erysipelas, and sometimes going on to vesiculation. The parts most commonly affected are the eyelids, face, and neck, but it may also occur on the hands and feet. Left to itself, the eruption remains well marked for some four to five days, and then gradually subsides, serum discharges from the vesicles, and after some desquamation the affected area returns to normal after some ten to twenty days.

Treatment.—Wash the affected parts thoroughly with soap and water, and then clean with a lotion of alcohol and ether, and finally apply the ordinary lead and opium lotion or a solution of acetate of aluminium. In mild cases calamine lotion is very efficacious.

Prophylaxis.—Remove the poisonous ivy. This can only be performed by digging up the roots.

THE LACQUER POISON.—*Rhus vernicifera* De Candolle is the lacquer or varnish-tree of Japan. Lacquer poisoning has, however, been described on p. 191, and need not be repeated here.

THE PARSNIPS. In the same group with the poisonous ivies come the parsnips, of which *Pastinaca sativa* Thomas, the common parsnip, and *Heracleum lanatum* Mich (*H. giganteum* Fischer), the cow parsnip, cause symptoms analogous to those described above. The treatment is similar.

II. THE EUPHORBIA GROUP.

The Euphorbia group is placed in the non-volatile division, because, although it is definitely known that the milky juice if it touches the skin causes dermatitis, it is not so evident that any volatile principle contained therein can act at a distance, though it is possible that it does so. The subject requires further investigation.

In this group the poisonous principle is contained in a thick milky juice, the latex, which is contained in special lactiferous cells.

Hippomane mancinella Linnæus (Euphorbiaceæ), which is the celebrated manchineel-tree of the Grenadine Islands, is also found in Colombia, South America, where it is called 'Pedro Fernandes' or 'mansanillo.' It causes very severe pruriginous and painful urticaria in people who rest under its shade. According to Martinez Santa-Maria, this eruption usually disappears in about twenty-four hours, but occasionally it may last for two or three days, or even longer.

THE EUPHORBIAS.—All euphorbias possess more or less irritating juices, which, if rubbed into the skin, cause inflammation. The thick milky latex is acid, and contains a dense oil, which is very irritating. As an example of this group may be mentioned *E. pilulifera* Linnæus or *E. resinifer* Bergmann. The former is common in many parts of the tropics, and the latter occurs in North Africa.

Hura crepitans **Linnæus, of Central America and the West Indies, and** ***H. brasiliensis*****, of Brazil, possess a milky juice, said by Piffard to cause severe swelling of the face, while the latter was employed in Brazil as a treatment for leprosy.**

III. THE URTICA GROUP.

URTICA SUBGROUP.—This is characterized by containing its poisonous principle in hairs.

This group includes the nettles which belong to the genus *Urtica* Linnæus, of which *U. urens* is the common European type, while *U. ferox* Forster is found in New Zealand, and *U. pilulifera* Linnæus occurs in the Mediterranean littoral.

Laportea Gauducheau is an allied genus, of which *L. crenulata* Roxburg in Bengal, *L. stimulans* Weddel in Java, and *L. gigas* Weddel in New Holland, produce severe urticarial eruptions, associated with pain lasting for several days.

The genus *Urera* Gauducheau belongs to the same family, being found in tropical Africa and America, while the genus *Girardinia* Gauducheau is found in tropical Africa and Asia, and both contain species with markedly urticarial properties.

In all these the poisonous principle, which is said to be of the nature of an aldehyde, is contained in a special poison apparatus, which consists of secreting cells which pour their secretion into awl-shaped filaments, or hairs which are filled with an acrid, non-volatile, albuminoid, acid liquid. These hairs penetrate the skin, and the tip, being broken in the process, discharges the poison into the dermis. The poison quickly produces the well-known urticarial eruption associated with itching, tingling, and even pain.

PRIMULA SUBGROUP.—In the same group come quite a different series of plants—viz., the primulas, primroses, etc.—which belong to the family Primulaceæ. In the tribe Primuleæ there is a section called 'Sinesis,' which contains *Primula obconica* Hance, *P. sinensis* Sabine, *P. sieboldii* E. Moir, and *P. cortusoïdes* Linnæus, which possess poison glands associated with hard poisonous hairs, contact with which produces acute dermatitis, which often begins as an erythema on the face or back of the hands, and spreads quickly to other regions. Soon the erythema becomes œdematous and swollen, and vesicles may at times appear. The general aspect of the patient with the red and swollen eyelids, red and swollen face, and the similar eruption on other parts of the body, closely resembles erysipelas, and is, without doubt, one of the forms of the complaint often called 'the rose'—*i.e.*, a non-contagious erysipelas.

It must, however, be admitted that some of the recurrent eruptions described on the hands and face of persons believed to be suffering from this or ivy-poisoning are suggestive of pellagra (see p. 1700). The erythema of pellagra is, however, generally confined to areas exposed to the light, and is usually associated with some intestinal or nervous symptoms. It is, however, as well to bear in mind the possibility of pellagra in cases of dermatitis on the hands and face recurring in the spring or autumn.

The usual treatment is to apply calamine lotion, to which a little menthol or opium is added.

ORCHID SUBGROUPS.—*Cypripedium spectabile* Salisbury, of the Orchidaceæ, is also said to possess venomous hairs, while *C. pubescens* Willdenow is also known to cause a dermatitis.

Jatropha urens Linnæus, var. *stimulosa* Pohl, growing from Virginia southwards, has stinging bristles and is called '*tread softly*.'

Malache hirsuta Kuntze (Malvaceæ), called by the natives of Angola '*utiete*,' which name it shares with other stinging species of the Malvaceæ in the same locality, has been investigated by Wellman, who finds it to be armed with hairs containing a very irritating substance. Other examples in the same locality are species of the genera *Sida* and other species of *Malache*.

Cisus pruriens Welwitsch (Ampelidaceæ) is another of Wellman's stinging plants. The fruit is covered with stinging hairs. It also has an irritating juice around the seeds, which burns the throat if an attempt at mastication is made.

Cnestis corniculatus Lam. (Connaraceæ) is a vine common in Angola and called sakupolopolo. Wellman had an unpleasant experience with the hairs from a pod.

Several other species belonging to the same genus and to *Rourea* have stinging bristles on the fruit.

Stizlobium stans Kuntze and *S. pruriens* De Candolle—synonym, *Mucuna pruriens* (Leguminosæ), and called by the natives of Angola 'eyumbi'—are armed with stinging pelose hairs: *Mucuna pruriens* is the cowhage of the East and West Indies.

IV. THE TECTONA GROUP.

This group includes trees, the handsome wood of which is used for the ornamentation of saloons, and also for making furniture. The dried hard wood gives off dust, which is extremely irritating to some people, while others appear not to be affected. One attack appears to render the sufferer more liable to the complaint, and although certain authorities claim that immunity may be acquired by attacks, there appears to be considerable doubt on this point, and, in fact, the evidence points to quite the reverse being true. The best known of these dermatites was, until recently, that caused by the wood of *Tectona grandis* Linnæus, commonly called 'teak,' which gives off a dry essential oil in the dust created by sawing, and this produces a severe form of dermatitis in carpenters and joiners, which tends to become generalized, and may be of long duration, lasting sometimes for months.

The effect of the dust of 'satin-wood'—*i.e.*, the wood of *Chloroxylon swietenia* De Candolle from Ceylon and the East Indies, or the wood of *Fagara flava* (synonym, *Zanthoxylum flavum*) from the West Indies is to produce a dermatitis. These woods contain a crystalline alkaloid ('chloroxylonne,' $C_{22}H_{23}O_7N$), which has been carefully studied by Cash, who finds that twenty-two days after application for the first time it causes a dermatitis which, beginning with itching, gives rise to papules, vesicles, and oozing points on the inoculated limb, which in due course becomes brawny and pits on pressure. In a little time the swelling spreads to the eyelids and face, ears, lips, and nose, and great discomfort is experienced. In a few days a nasal catarrh and a laryngeal cough appear. This cough is of an explosive nature, as though a hair had become lodged in the throat, and although the secretion at first is slight, later it becomes more abundant. The experimental illness lasted about forty days. Another application of the active principle produced a relapse in forty minutes.

In the ordinary way the first attack is of slow development, the symptoms appearing some six weeks after the first handling of the wood, but a relapse is of rapid development.

The illness begins with the development of an acute inflammation of the skin of the hands, wrists, face, and neck, producing an appearance somewhat resembling erysipelas, but without fever or concomitant sickness. The inflamed surfaces discharge, dry, and finally desquamate. The most suitable treatment, according to Cash, is to apply the unguentum glycerinis plumbi subacetatis of the British Pharmacopoeia every four hours, to administer bromides to allay the irritation, and opium to relieve the laryngeal cough.

Other woods with similar properties are ebony (*Diospyrus ebenum* Koni), found in Ceylon and India originally, and rosewood (*Dalbergia latifolia* Roxburg), found in India.

Andira araroba Aguiar (Leguminosae), the Goa powder tree of Brazil, produces an irritating dust when the wood is cut or sawn, so that workmen have to protect their faces.

V. THE RUE GROUP.

HAPLOPHYLLUM DERMATITIS.—This has been described by Chalmers and Pekkola as occurring in the Anglo-Egyptian Sudan. It is caused by a rue named *Haplophyllum tuberculatum* (Forskal, 1775), synonym *Ruta tuberculata* (Fig. 850), which was proved to be the causal agent by producing the dermatitis in the susceptible person by bringing him experimentally into contact with the plant for a few seconds some time after he had been cured of the original attack. At the time of the experiment the person in question was staying in a place far distant from the area where the plant grew, from which it had to be fetched for purposes of the experiment. The experimental eruption (Fig. 851) appeared in about eighteen hours after rubbing the forearm for a few seconds with the leaves and flowers, which were partially dry after their long journey. The plant only affects susceptible people.

In the original attack the incubation period was thirty hours, and began as small red papules on the hands, feet, and legs, which became swollen, red, and itching, and were associated with headache and pain in the epigastric region, but no fever. The lips, lobules of the ears, and eyelids became red and swollen, and there was much itching. Later the face became swollen, the lips cracked and oozed, and the lymph glands under the jaw and in the groin enlarged. All the symptoms rapidly disappeared when he ceased to work among these plants.

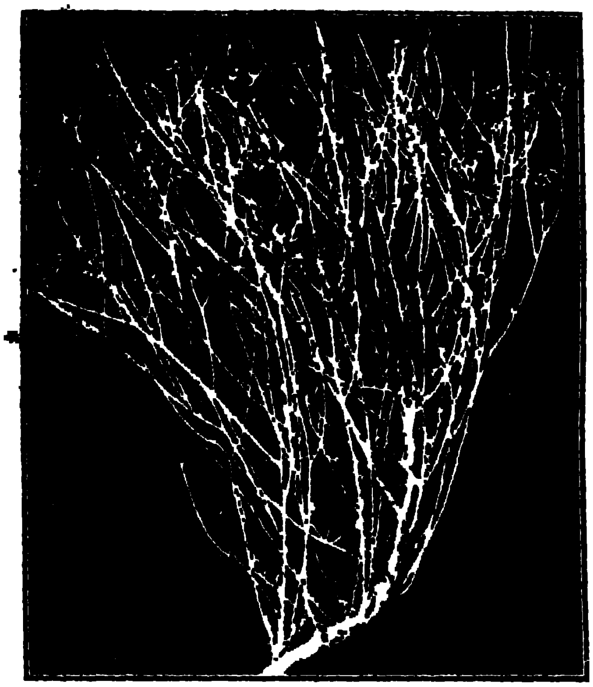

Fig. 850.—*Haplophyllum tuberculatum.*

The treatment adopted was to wash the whole body after removal from the endemic area and to apply calamine lotion.

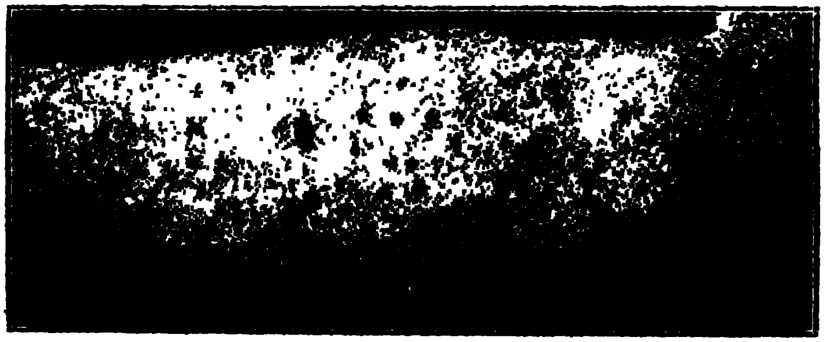

Fig. 851.—Experimental Eruption.

Other Rues.—According to Bentley and Trimen, *Ruta graveolens* causes redness, swelling, and even vesication of the skin if much handled, while Le Maout and Decaisne state that *R. montana*, found in Spain, produces erysipelatous-like conditions and ulcerating pustules on the hands of those who gather it.

VI. THE BUFFALO BEAN GROUP.

Letcher has written an interesting account of the sufferings produced by the minute hairs of the pods of the Buffalo bean. This bush, with its silky green pods, lives along the Luia River in Portuguese South Africa. The little hairs settle on the skin and set up violent irritation and burning, lasting about one hour despite remedies. Natives plaster themselves all over with mud. This laconic description by no means expresses the views of sufferers who look upon the tree as one of the ' choicest creations of the devil.'

VII. THE LITTLE-KNOWN GROUP.

This group includes dermatitis due to:—

1. Cashew nut.
2. Cinchona quinine.
3. Nasturtium.

Oleander.
Rungus.
Upas.

Semecarpus anacardium Linnæus (Anacardiaceæ), the common cashew nut of the tropics, a native of Tropical America and naturalized in Africa and Asia, is said to cause fumes when roasted which may blister the face. The mere handling of the plant does no harm.

Cinchona (Rubiaceæ) [Quinine].—Although the cinchona tree itself is harmless, yet workmen preparing quinine by boiling the bark, those who make the sulphate, and those who bottle the powder, are apt to suffer from erythema, vesicles, and pustules, which appear upon the hands, forearms, and genitalia in susceptible persons. It is believed to be due to emanations from the drug acting upon susceptible persons, who should not be longer employed at this work. The rash disappears in two to four weeks after ceasing to work with quinine.

Nasturtium.—*Tropæolum majus* Linnæus (Tropæolaceæ), which is a native of Peru, will cause a dermatitis in susceptible persons when handled.

Oleander.—*Nerium oleander* Linnæus (Apocyanaceæ), the oleander of Palestine and the East, may, in susceptible people, cause symptoms like those produced by the Rhus group, but this requires confirmation.

Rungus.—This is a curious affection, described in British North Borneo by Hornsey, and is caused by contact with any part of the tree called rungus or ringus by the natives, and said to be capable of being spread from a victim to uninfected persons. Within twenty-four hours of handling the tree itching sets in, and this is followed by a papular rash associated with fever and malaise. The rash appears first on the parts which have been in contact with the tree. The papules become vesicles and then bullæ, filled with a serous fluid, and these if secondarily infected may give rise to foul ulcers. Some people are immune. The condition heals naturally.

Upas Tree.—*Antiaris toxicaria* Lesch (Artocarpaceæ), according to Loudon, causes cutaneous eruptions when wounded, while Hasselt says that it affects the Javanese after the manner of the Rhus group when they come in contact with it. This requires confirmation.

VIII. THE DOUBTFUL GROUP.

The irritant poisoning caused by kaju-rugas, the juice of which produces painful bullæ, by kaju buta-buta, which causes violent dermatitis and conjunctivitis, have not been well studied, neither has the poisonous properties of the well-known daffodil; in fact, the whole subject requires further study.

CANE DERMATITIS.—A peculiar dermatitis is found in people handling and cutting reeds (*Arundo donax* Linnæus) in Provence, some parts of Italy, some districts of Greece, and other countries. The dermatitis was studied by Blanchard and many observers, among whom Thiebierge, Berlese, Brigi, Aravandinos, Sfameni, and Vadala, may be mentioned. It starts with severe itching and erysipelatoid eruption, associated with the formation of blebs, generally on the uncovered parts of the body, but also on the genital organs, which may become greatly œdematous, and febrile symptoms with signs of coryza may appear. After a few days the rash disappears, and is followed by desquamation.

The **Ætiology** is doubtful. Some authorities consider it to be due, to the plant itself, others to a fungus (*Ustilago hypodytes* Schlecht) and still others to a mite (*Aclerda berlesi*).

Treatment consists in applying calamine and lead lotions.

VANILLA DERMATITIS.—This is often called Vanillismus, and is due to *Vanilla planifolia*, which is a native of Eastern Mexico, but which also grows naturally in Tropical America and is cultivated in many parts of the tropics. Workmen when handling the beans suffer from itching of the hands and face, while the skin becomes covered with a pruriginous eruption and reddens, swells, and desquamates. It would, however, appear that this is not due to the plant, but to some mite thereon, as it does not occur in some works. It is said that only persons with dry skins should work with vanilla, as the least drop of perspiration or moistening of the beans causes their destruction by fungal growth. The whole matter requires further investigation.

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CHAPTER XCV

ULCERATIONS

Cutaneous leishmaniasis (Oriental sore)—Muco-cutaneous leishmaniasis (Espundia)—Indian oro-pharyngeal leishmaniasis—Ulcus tropicum—Ulcus interdigitale—Ulcus infantum—Remarks on ulcers in the tropics—Granuloma inguinale—Papilloma inguinale—References.

CUTANEOUS LEISHMANIASIS (ORIENTAL SORE).

Synonyms.—Delhi boil; Aleppo boil; Biskra boil; Bagdad boil Ulcera de Bauru (Brazil); Bouton d'Orient; Ulcère d'Orient; Chancre du Sahara; Dermite Ulcereuse Circonscrite (Corre); Endemische Beulenkrankheit: Bottone d'Oriente: Godownik, *i.e.*, 'yearly boil' (Caucasus); the Tartar name is 'Il-jarassy' ('il' = year, 'jarassy' = boil); Tschiban, *i.e.*, 'yearly sore'; Dous-el-Kourmati, *i.e.*, 'date disease' (Turkish); Ghisud (Abyssinia); Habb-es-Sanawi, *i.e.*, 'yearly boil'; Habb-es-Sanah, *i.e.*, 'boil of the year'; Bess-el-Temür, *i.e.*, 'date disease' (Arabian); Salek, *i.e.*, 'annual' (Persian); Pascha-churdj, *i.e.*, 'fly-bite'; Afghan Jara *i.e.*, 'Afghan plague'; Jaman Dyscharagan, *i.e.*, 'malignant ulcer' Taschkent Jarassi, *i.e.*, 'Tashkent ulcer' (Tashkent); Mycosis Cutis Chronica (Carter); Lupus Endemicus (Lewis and Cunningham) Endemic Boil Disease (Scheube); Granuloma Endemicum (Brooke) Furunculus Orientalis (Crocker); Pian-Bois (Guiana); Sudan nodules Cutaneous leishmaniasis; Leishman nodules; Parasitic granuloma (Ferguson and Richards).

The so-called Nile boil has been demonstrated by Modder and Archibald to have nothing to do with Oriental sore, being of pyogenic origin. The so-called Bucharest boil, also, has apparently nothing to do with Oriental sore.

Definition.—A specific ulcerative affection of the skin caused by *Leishmania tropica* Wright and its varieties.

History.—The earliest account of the disease is to be found in Russell's description of Aleppo boil in 1756, in which he states that the inhabitants believed that it was caused by the drinking-water. The disease was also described by Hasselquist in 1762, Holland in 1780, Volney in 1787, Alibert in 1832, and Guillon in 1835. Tholozan, in 1866, appears to have been the first to doubt the ætiological value of the drinking-water; but Virchow is said by Hirsch to have been the first to suggest that the true cause might possibly be a parasite.

Smith in 1868 and Fleming in 1873 claimed to have found eggs of a species of *Distoma* in the sections of specimens of the tissues derived from cases of Delhi boil. Carter in 1875 described a mycelial fungus and spores. In 1880 Laveran stated that the virus of Oriental sore was probably carried by flies. Depéret and Boniet, Duclaux and Heydenreich cultivated various cocci in 1884. In 1885 Cunningham described some peculiar parasitic organisms of various size and shape, often endocellular, easily brought in evidence by staining with gentian violet. Cunningham inclined to regard these bodies as representing various stages of the development of a mycetozoal parasite, probably belonging to the group of the Monadidæ.

Riehl (1886) isolated a capsulated micrococcus. Finkelstein and Chantemesse (1887) also cultivated a micrococcus similar to the organism described by Duclaux. Poncet in the same year described a coccus in sections and a very delicate bacillus. Le Dantec and Auché in 1894 found in a case of Biskra boil a streptococcus and the *Staphylococcus albus*. In 1897 Nicolle and Nourry Bey found a streptococcus which they believed to be specific. The organism was very slightly virulent. Attempts to inoculate monkeys with the disease did not succeed. In the same year Brocq and Veillon cultivated a streptothrix from a case of Aleppo boil. Crendiropuolo isolated in numerous cases a bacillus, probably belonging to the Proteus group. Firth in 1891 stated that he had been able to confirm the presence of the Cunningham parasitic bodies in numerous cases of Delhi boil. He proposed for the parasite the name of *Sporozoon furunculosum*. In 1898 Borowsky constantly observed in twenty cases of Sarten ulcer some peculiar organisms which he thought to be protozoa. In fresh preparations the bodies were very actively motile, and presented a spherical shape; sometimes they were spindle-shaped. The maximum diameter varied from 0·5 to 3 μ. The cell-body stained very faintly. The nucleus was placed eccentrically. No chromatin bodies could be put in evidence. Schulgin in 1902 confirmed Borowsky's results, and suggested that the disease might be conveyed by mosquitoes. In 1903, in a case of tropical ulcer occurring in a boy from Armenia, Wright described bodies very similar to those found in cases of kala-azar. These bodies may possibly be identical with those seen by Cunningham in 1885. Wright's discovery has been confirmed by Mesnil, Nicolle, James, Strong, Plehn, Nattan-Larrier, Splendore, Carini, Cardamatis, Wenyon, Gabbi, Lacava, Balfour, Archibald, and others, who have greatly extended our knowledge of the disease. Marzinowsky and Bogrow state that, independently from Wright, they found similar bodies in cases of Pendjeh ulcer from Persia. In 1908 C. Nicolle and A. Sicre succeeded in cultivating the organism. In the same year and 1910 C. Nicolle and his co-workers reproduced the disease in monkeys and dogs, and in 1913 to 1914 Gonder, Row, and Laveran infected mice and other rodents. In 1917 Laveran published a most useful and complete treatise on the malady and other leishmaniases.

Geographical Distribution.—The disease is endemic in many tropical and subtropical regions. It is found also in temperate zones. In Africa it is found in Morocco, Tunis, Tripoli, Algeria, and Sahara (Biskra, Gafsa), Egypt, Sudan, Congo, West and East Africa, and South Africa; in Asia it is common in Syria and Asia Minor, in Mesopotamia, Arabia, Persia, the Caucasus, Turkestan (Tashkent), in the Turkmene district (Pendhe). It is very common in some parts of India, especially along the Valley of the Indus, in the Rajputana States, and in the North-West Provinces (Delhi, Multan, Lahore). In Europe the affection occurs in the Crimea, Cyprus, Crete, and Greece. Cases have been reported by Gabbi, Lacava, and others from Italy. It is known also in Brazil and other countries of South America, and in French and British Guiana, where it is known as Pian-bois, or forest yaws, and has been observed by Darling in Panama, so that the name 'Oriental sore' is somewhat misleading,

It is generally much more common in large towns than in the country. In some cities it is so prevalent that even visitors of a few days only may not escape it. Its occurrence appears to be influenced by the seasons, as, according to Hirsch, in the tropics it is most prevalent at the beginning of the cool season, and in more temperate climates at the end of summer. Laveran says that in Biskra, from September to October inclusive, the slightest wound tends to become transformed into the 'bouton.' In some years it has been found to be more prevalent than in others.

A peculiarity of the geographical distribution of the disease is that in the countries where it is endemic its distribution is not general, but is confined to certain districts only; hence the numerous local names given to the malady, as Aleppo boil, Bagdad boil, etc.

Ætiology.—The disease is caused by *Leishmania tropica* Wright, 1903. In the first edition of this book we expressed the belief that future investigation would show that there are several varieties of *L. tropica*, each giving rise to a slightly different clinical type of the affection, and this has come true, several species and varieties having been described, though not yet generally accepted. The description of *L. tropica* and its varieties is found in Chapter XIX., p. 378. Nicolle and Manceaux, Laveran and others have occasionally succeeded in producing in monkeys and dogs Oriental sore by inoculation of cultures. Row, by inoculating cultures of *L. donovani*, has produced cutaneous lesions in monkeys, but such lesions differ histologically from true Oriental sore.

Mesnil, Nicolle, and Remlinger have observed the parasites to be present occasionally in true polymorphonuclear leucocytes, besides being found in the mononuclear leucocytes as usual. Mesnil has observed in some cases a typical 'bacillary' form.

The medium used by Nicolle for the cultivation of the parasite is a modification of Novy-McNeal medium, and is composed as follows:—

Agar	14 grammes.
Salt	6 „
Water	900 c.c.

This is dissolved in a large flask in a Koch's stove, and then distributed in tubes. After sterilization, to each tube is added one-third rabbit-blood, collected with all aseptic precautions. The tubes are kept aslant for twelve hours, then kept at 37° C. for five days, after which they are kept at the ordinary temperature for some days before using. This medium is often referred to as the N.N.N. medium. Row has introduced a simple hæmoglobinized saline culture medium.

Histopathology.—The histopathology of the disease has been studied by Unna, Leloir, Kumm, Riehl, Wright, Strong, Bettmann and von Vasielewski, Balfour, Archibald, Darling, and others. The histological lesions in the common ulcerative variety consist essentially in the atrophy and disappearance of the epidermis of the part, and in a very extensive cellular infiltration of the corium and papillæ by various kinds of lymphoid cells, plasma cells, and numerous large roundish cells containing a single faintly stained vesicular nucleus and large amount of cytoplasm. These large roundish cells, which are probably proliferated endothelial cells, contain often many Wright's bodies closely packed together, occupying most of the available space between the nucleus and the cell periphery. Darling in his case found that the corium and papillæ were infiltrated by newly formed cells, lymphoid, endothelial, epithelioid, giant, and plasma cells. There were no necrotic areas, and a polymorphic leucocytic infiltration was not noted. Many interpapillary downgrowths were seen in the rete. The squamous epithelium was surrounded by a mass of desquamated epithelium forming the crust. The lymphatic and blood vessels in the deeper layers of the skin were surrounded by collections of lymphoid cells. Balfour, Thomson, and Archibald, noted the following principal histological features in their cases:—presence of vertical epithelial columns extending deeply downward, with a few cell-nests and isolated masses of cell infiltration. The dermis is infiltrated with cells of the large round type, polymorphonuclear leucocytes, and large numbers of eosinophiles. This cellular infiltration may extend to the sebaceous glands and hair follicles.

Communicability.—The disease may be conveyed by direct infection from person to person, by absorption of the virus through some pre-existing abraided surfaces, or small wounds or ulcers of other nature present on the skin. The reservoir of the virus would be in the affected persons and in dogs, which, as noted as long ago as 1854 by Vuillemin, may suffer from a very similar or identical affection. Certain authors have suspected geckoes and lizards to be the reservoir, but this can hardly be, as these animals cannot be experimentally infected. Camels, too, have been suspected to be a reservoir of the virus. Insects, especially flies, probably play a certain rôle in the transmission of the disease. That flies convey the disease was first claimed by Seriziat (1875) and by Tscherepkin (1876).

Tscherepkin states that by the people of Tashkent the disease is called 'pascha-churdj,' meaning 'fly-bite.' Laveran thinks that flies carry the virus on their feet and proboscis, and thus convey infection. Schulgin and others believe the disease to be conveyed by mosquitoes. Ed. Sergent and Pressat have suggested that some 'Phlebotomus' may play a rôle in the transmission of the disease, while Balfour and Thomson suggest that the bed-bug may carry the infection. Fleas and lice have also been inculpated.

The disease is inoculable from man to man, as is clearly proved by the experiments of Marzinowsky and Wenyon. It is also auto-inoculable.

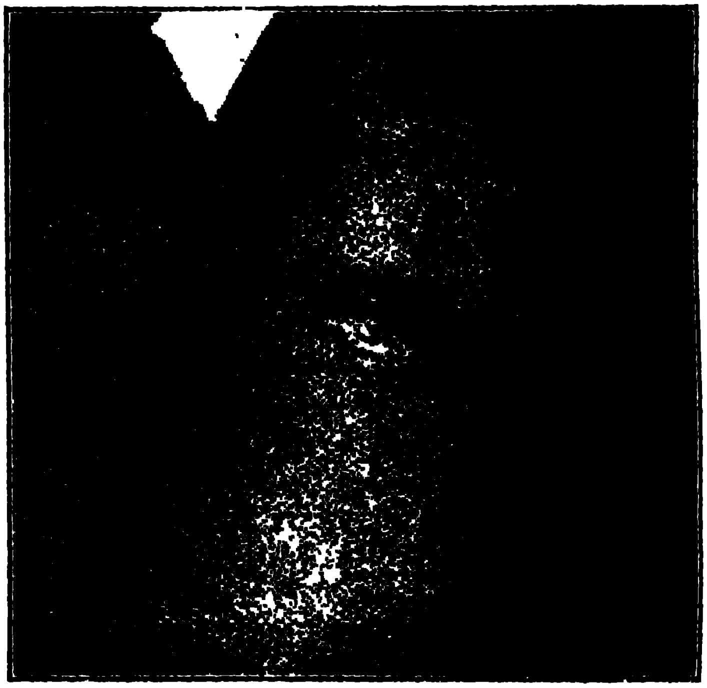

FIG. 852.—ORIENTAL SORE

Marzinowsky inoculated himself with Oriental sore by putting inside the bulla caused by an artificial burn on his hand some material (scraping) derived from an Oriental sore. After ten days from the inoculation he began to feel unwell and feverish, and suffered from headache and general debility. The fever lasted two weeks. With the beginning of these general symptoms a papule appeared at the seat of inoculation, which slowly developed into a typical Oriental sore. Scrapings contained many parasites. Wenyon has also inoculated himself, and he, too, presented fever before the skin lesion appeared. The Bagdad Jews, according to Colvilli, inoculated their children with the disease, as they thought that after having recovered once, there was no danger of getting it again.

Symptomatology.—After an incubation period varying from a few days to some weeks or several months, during which attacks of irregular fever often occur, one or several small pruriginous spots appear on the skin of uncovered parts of the body, not much dissimilar at the very beginning from mosquito-bites, for which they are often taken by the patients. The spots, however, instead of slowly fading, become red and shotty, with an inflamed areola; which later becomes markedly indurated. The papules slowly enlarge to the size of a pea or bean; the surface gradually loses its smooth and shiny appearance, and becomes covered with small thin scales. After a period of time, somewhat variable in length, but generally not exceeding three to four months, the ulceration of the nodule begins. At first the ulceration is very superficial, and exudes a yellowish secretion, which soon dries into a hard, adherent, darkish scab. Underneath the scab the ulcerative process and disintegration of the nodule continues slowly to spread. The tissues surrounding the ulcers may become œdematous. If later the darkish scab be removed, an ulcer is seen, about an inch or more in diameter, with sharp-cut, jagged edges and irregular fundus, with reddish-yellow, sometimes fungating granulations. The ulcer is generally indolent, or but slightly painful. The neighbouring lymphatic glands are not, as a rule, sensibly enlarged, unless there

Fig. 853.—Oriental Sore in a Persian Soldier.
(From a photograph of Drs. A. Bussière and Nattan-Larrier.)

is a secondary pyogenic infection. The examination of the blood taken from the finger shows often a distinct mononucleosis, and the coagulability is generally increased. The total number of leucocytes may be normal, or there may be leucopenia, or during the attacks of fever leucocytosis. In the blood taken from non-ulcerated lesions the mononucleosis is much more marked.

Healing generally sets in after six to twelve months by granulation, which begins in the centre of the ulcer, the unhealthy-looking, large, yellowish granulations giving place to healthy ones. A whitish or pinkish, often depressed and disfiguring, scar remains at the seat of the ulceration. After cicatrization, the sore may break down again.

Oriental sore may be single or multiple. Two or three are frequently found on the same patient, but occasionally there are many more, and may spread to the mucous membranes of the mouth and nose. The sores are auto-inoculable by scratching.

The seat of the ulcers is generally on uncovered parts—feet, legs, hands, arms, face. They are very seldom observed on the palms, soles, or scalp. The affection attacks people of any race, sex, and age, if they expose themselves to the infection.

Course.—The length of the incubation period is not known with certainty. It is generally stated that it varies between a few days and six weeks. Manson, however, has observed that it may be as long as five months, and Wenyon, who inoculated himself, observed that the first skin lesions appeared six and a half months after inoculation. Manson in one case made the interesting observation that the appearance of the sore was preceded several months by a fever of an irregular remittent type, not influenced by quinine, and having some features of the fever of Indian kala-azar. This fever was also noted by Marzinowsky and Wenyon, who inoculated themselves experimentally. Attacks of irregular fever during the incubation and the course have been recorded by several other authors. During one of these febrile attacks Neumann observed *Leishmania tropica* free in the liquor sanguinis of the patient.

The duration of the eruption varies from four or five months to twelve months and more. Relapses may occur, but true reinfections are rare.

Clinical Varieties.—The following clinical varieties may be distinguished:—

1. The common variety—*Oriental sore sensû stricto*—to which the description given above refers. This variety, which is the usual type met with in Asia, Africa, and South Europe, while comparatively rare in America, is characterized by the presence of one or several nodules, which slowly ulcerate, with or without symptoms of general infection, such as fever and enlargement of the spleen. Very rarely, in addition to the cutaneous nodules, there may be ulcerative lesions on the mucosa of the mouth and nose, as noted by Cardamatis in Greece and Lacava and Gabbi in Italy.

2. The *verrucose variety*, described by Ferguson and Richards,

and later by Archibald in Egypt and the Sudan, so called from the peculiar verrucose appearance of the lesions.

3. The *keloidform variety*. This is a non-ulcerative type described by Cambillet, Balfour, and Thomson, characterized by the presence of pinkish nodules, somewhat keloid-like, which never ulcerate. For this variety Balfour suggested the name 'Leishman's nodules' and Brumpt created a new species for the leishmania found in them —*L. nilotica* Brumpt, 1913.

4. The *frambœsiform variety*. This is characterized by the presence of numerous nodules capped with crusts and resembling yaws (see Fig. 854). It is fairly common in the West Indies, where it is known by the name of 'forest yaws,' 'Bosch-Yaws,' or 'Bush-Yaws.'

5. The *papillomatous variety*. This is found in South America, but very similar types seem to have been met with in North India. It is characterized by the presence of papillomatous masses, which are generally found on the lower limbs, and are designated by the Amazon natives with a word which means *sponge*. The natives believe that the same affection attacks horses, mules, and donkeys.

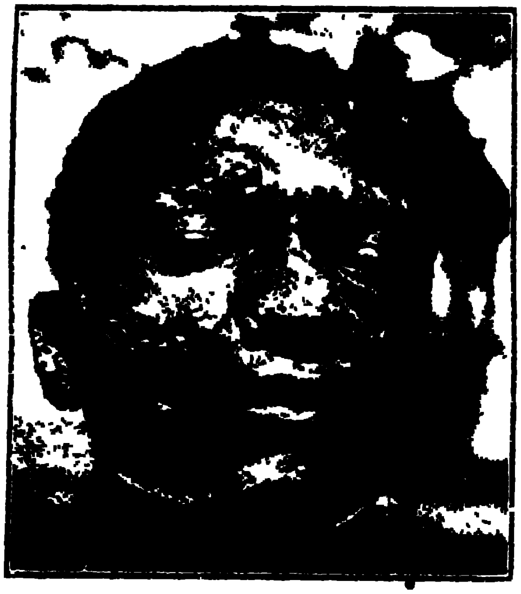

FIG. 854.—FOREST YAWS. (From a photograph by Sambon.)

This variety runs a much longer course than the common type of Oriental sore, lasting ten to fifteen years, and with very little or no tendency to spontaneous cure. It is probably due to a species of leishmania biologically different from *L. tropica*, and most authorities consider it to be due to *L. tropica* var. *americana*, the variety of leishmania which is the cause of espundia (see below).

6. The *deep ulcerative variety*. This is found in South America, and is characterized in most cases by the presence on various parts of the body of deep large ulcers running a very long course and with practically no tendency to spontaneous cure. In some cases the condition is localized to the ear, which may become perforated (*oreya de los chicleros*). One such case has recently been recorded by Low. This condition is often in reality the first stage of espundia, and is due to *L. tropica* var. *americana* (p. 380).

Diagnosis.—The diagnosis of all types of cutaneous leishmaniasis is made with absolute certainty only by examining microscopically the suspected lesions and finding the leishmanias. In numerous cases of the most common variety—*Oriental sore sensû stricto*—the diagnosis can often be made clinically, taking into account the following data:—

1. The patient comes from or is living in an affected area.

2. The few eruptive elements—often one single element—situated as a rule on uncovered parts of the body.

3. The course: a small papule which slowly enlarges into an indurated nodule, indolent, smooth, or slightly scaly, and after several months ulcerates.

4. The proximal lymphatic glands usually not enlarged.

The history, the absence usually of enlarged lymphatic glands and other symptoms of syphilis, and the uselessness of the mercurial treatment, will help in excluding syphilis. In framboesia there is a primary lesion, which, after a time, is followed by a general granulomatous eruption. We have, however, seen cases of framboesia patients who, after the general eruption has disappeared, have remained for months with a single or a few sores closely resembling the Oriental sore. In fact, we believe that in a certain number of cases it is very difficult to make the differential diagnosis between Oriental sore and ulcers of tubercular, syphilitic, or frambœtic origin: also, at times, from cancroid when the ulcer is single and situated on the face. In our experience, the only reliable way to come to a definite diagnosis in difficult cases is the microscopical examination. To do this the scab is removed, and a scraping is taken from the floor and edges of the ulcer. The preparation is then coloured with Leishman's or Giemsa's stain, or any other of the numerous modifications of Romanowsky's method, and examined for the presence of *Leishmania tropica*. The search must be prolonged in some cases, as the parasites may be very rare.

Prognosis.—In the common type the prognosis is good, *quoad vitam*. Very occasionally the disease may end fatally, owing to the ulcers becoming phagedænic, and to secondary septicæmic and pyæmic processes. In some rare cases, as observed by Cardamatis in Greece and Lacava and Gabbi in Italy, the ulcerative lesions may spread to the mucosa of the mouth. Sometimes the scars remaining after the ulcers have healed up shrink considerably, and if they are on the face, may give rise to serious disfigurement.

Treatment.—Tartar emetic is a specific. It is best given by intravenous injection, using a 1 per cent. solution in saline or simple distilled water. The solution should not be autoclaved; it should be filtered through a Berkefeld candle, or may be sterilized in flowing steam on two or three consecutive days. Five to ten c.c. of the solution are given daily for five to ten days, then every other day or twice a week until fifteen to thirty injections have been given. In children one-third or half doses are used. The intravenous injections should be given, taking all ordinary precautions and making sure that the needle is actually in the vein and that none of the liquid escapes into the surrounding tissues. Soon after the injection patients at times complain of metallic taste, giddiness, and nausea, but as a rule tolerance for the drug is easily established. Occasionally a prolonged treatment induces diarrhœa, and the patient may complain of great debility and muscular stiffness. Tachycardia has been noticed, exceptionally, and a few cases of sudden death have been ascribed to the action of the drug, which may produce a severe fatty degeneration of the heart, liver and kidneys.

Tartar Emetic Carbolic Solution.—This contains 1 per cent. tartar emetic and ½ per cent. carbolic acid, and does not need to be sterilized or passed through a Berkefeld filter.

Solutions for Intramuscular Injection.—Intramuscular injections are in certain cases very convenient, especially in children, in whom the superficial veins are often small. Unfortunately the usual solutions of tartar emetic and other antimonial salts are painful, and may induce the formation of an abscess. The following formulas will be found fairly satisfactory:—

Formula No. 1 (*Castellani*).—Tartar emetic, gr. viii.; ac. carbolici, ♏x.; glycerin., ʒiii.; aq. dest., ad ℥i.; ½ to 1 c.c. (8 to 16 minims) every other day in the gluteal region. At the time of the injection there is as a rule no pain whatever, but a few hours later in most cases there is a certain amount of pain and an infiltrated patch often develops, as after an intramuscular injection of quinine or of mercury perchloride. Care should be taken to give the injections in different spots, never giving a second one in the infiltrated part. If the pain and infiltration should be severe, hot fomentations will be found useful.

The solution is prepared in bulk in a sterile bottle, and tested for sterility forty-eight hours after preparation; it may then be put up in small 1 c.c. ampoules, which it is advisable to keep in a cool dark place. The presence of carbolic acid decreases the pain induced by tartar emetic and makes the solution sterile.

Formula No. 2 (*Castellani*).—Tartar emetic, gr. viii.; ac. carbolici, ♏x.; glycerin., ʒiii.; sodii bicarb., gr. ½; aq. dest., ad ℥i. This solution differs from No. 1 in being slightly alkaline. The results seem to be the same, and the pain induced by it appears to be about the same as with formula No. 1.

Formula No. 3 (*Martindale*).—Antimonii oxidi, gr. ⅒; glycerin., aq. dest., āā ♏xv. (for one ampoule). This preparation is good and is practically painless, but our impression is that the curative action of antimonium oxide is inferior to that of tartar emetic.

Oral Administration of Tartar Emetic.—The oral administration of the drug may be useful in conjunction with the intravenous or intramuscular injections. The following mixture is often very convenient:—

Tartar emetic, gr. v.; sodii bicarb., gr. xxx.; glycerin., ℥i.; aq. chlorof., ℥ii.; aquæ, ad ℥iii., ʒi. to ʒii. in water, three times daily, in children; double dose in adults. The presence of bicarbonate of soda and chloroform water decreases the emetic action of the drug.

Local Applications of Antimonial Preparations.—G. C. Low has used with satisfactory results a 1 per cent. antimonial ointment. A 1 per cent. antimonial lotion has been used by several authorities as a local application to the sores, and certain observers have used tartar emetic in powder, but this is extremely painful, and we do not recommend it.

Before the introduction of tartar emetic the treatment of Oriental sore was very unsatisfactory. Nitrate of mercury ointment, alum ointment, boric acid, and various antiseptics were recommended, with very poor results. Formalin often irritates the ulcer, and may produce a dermatitis. Röntgen rays have been tried, without any good results. An expectant treatment was generally advised. The scabs should be removed by boracic acid fomentation, and then the sores must be thoroughly disinfected once or twice daily with a 1 in 1,000 solution of perchloride of mercury or 2 per cent. carbolic acid, after which one of the ordinary antiseptic ointments (β-naphthol, gr. v.; vaseline, ℥i.; iodoform or europhen, gr. v.; ung. ac. borici, ℥i.; balsam. Peru., gr. v.; to vaseline, ℥i.) or an antiseptic powder (iodoform or xeroform or boric acid) is applied.

Salvarsan and atoxyl have been used without any good result.

Marzinowsky, after removing the crust and cleansing the ulcer with antiseptic lotion, applies a 10 per cent. lotion of ferropyrin to stop the bleeding, and then applies thoroughly a 50 per cent. lotion of chininum bimuriaticum daily. He says recovery takes place in between seven to eleven days.

Schulgin advises the freezing of the boil with ether. He used this method in 300 cases with good results.

Several French writers advise the use of permanganate of potassium, at first in powder form, and later as a 5 per cent. ointment.

Duncan advised placing a thin piece of lead over the ulcer, and then bandaging up.

Emily recommended the repeated applications of boric acid.

Oudiourminsky has applied to the treatment of Oriental sore Bier's stasis method, apparently with good results.

Chulguine recommended soaking the sore with a solution of methylene blue (10 per cent.).

Bussière advised dilute tincture of iodine (10 per cent.).

In other cases Bussière and Nattan-Larrier advised excision of the sore. Several physicians praise the use of silver nitrate.

Castellani had some fairly good results in two cases by washing the sores with a 5 per cent. solution of protargol, followed by the application of a 20 per cent. protargol ointment. The protargol ointment cannot be used on Europeans when the face is affected, as the protargol, after some time, induces a discoloration of the skin.

Lincoln and Aviss have obtained good results by painting the sores with a native gummy fluid, sold in native bazaars under the name of 'raurath.'

Timpeno injects 1 c.c. daily round the sore of a 1 per cent. solution of carbolic acid.

Prophylaxis.—The disease being very contagious, and being also probably spread by some blood-sucking insects, the slightest wound and any insect-bite should be thoroughly disinfected with carbolic acid 5 per cent., or tincture of iodine.

MUCO-CUTANEOUS LEISHMANIASIS (ESPUNDIA).

Synonyms.—Naso-oral Leishmaniasis, Uta, Chancre Espundique d'Escomel (Laveran and Nattan-Larrier), Leishmaniasis cancerosa (A. da Matta). Bubas Braziliana (Breda), Smith's disease, Breda's disease, Bueno de Miranda and Splendore's Leishmaniasis, American Leishmaniasis (Laveran and Nattan-Larrier).

Definition.—A chronic ulcero-granulomatous affection of the skin and mucosa of the mouth and nose due to *Leishmania tropica* Wright, 1903, var. *americana* Laveran and Nattan-Larrier, 1912.

Historical.—Espundia seems to have been present in South America since time immemorial. According to Tamayo espundia lesions are depicted on certain water vases of the ancient Incas. The malady has been known to local medical men for many years in Peru and other parts of South America, though it was often confused with framboesia and blastomycosis. Fairly good descriptions of the malady were given by Smith in 1840 and Tschudi in 1846, and later by several other observers. In 1895-1896 Breda described in a series of important publications the affection in Italy, in emigrants returning from Brazil, under the name of Bubas Braziliana, and considered it to be due to a bacillus the presence of which was confirmed by Fiocca, who claimed to have reproduced the disease in the lower animals by inoculating pure cultures of the organism. Breda's work was confirmed by Verrotti and De Amicis. The term 'boubas,' used by Breda, was a rather unfortunate one, as it led to much confusion, this term being generally used by tropical authors as a synonym for framboesia, while the natives, as noted by Splendore and others, use it indiscriminately to indicate various ulcerative lesions of widely different nature.

Escomel in 1911 gave a very good description of espundia as found in Peru. Further investigation has shown that the condition found in Brazil is identical with that found in Peru.

Bueno de Miranda and Splendore first found leishmania bodies in the ulcerative lesions, Splendore making a very complete pathological and clinical investigation of the condition, and succeeding in experimentally inoculating it in monkeys. Splendore called attention to the fact that in cultures the flagellum of the *Leishmania* found was generally longer than in *L. tropica*; he observed also that with Giemsa's reagent the parasite stained usually deeper than *L. tropica*. Laveran and Nattan-Larrier have made an important study of the parasite in tissues sent to them by Escomel, and noting the very frequent peculiarity of the nucleus being flattened, have created a new variety: *L. tropica* Wright, 1903, var. *americana* Laveran and Nattan-Larrier, 1912. Vianna had previously created a new species, *L. brasiliensis*, but this species has not been generally accepted. More recent important researches have been carried out by Horta, Carini, Lindenberg, Rabelo, Morales, Darling, Velez, Araujo, Chagas, Alfr. da Matta, Aragao, Strong, Tyzzer, Brues, Sellards, Gastiaburú, Flu, Migone, Torres, Christopherson, and many others.

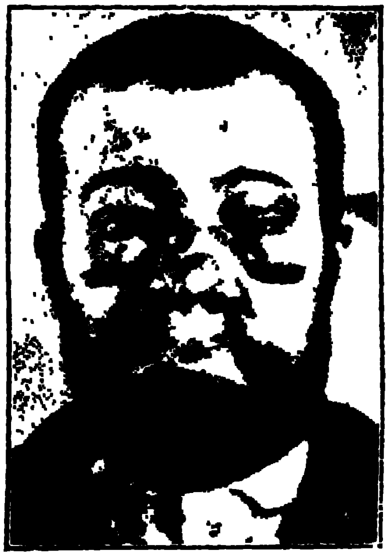

FIG. 855.—ESPUNDIA.
(After Splendore.)

Geographical Distribution.—The disease has been reported from Peru, Brazil, Paraguay, Argentina, Colombia, and other parts of South America. In Brazil it is especially common in the regions between the State of St. Paulo and the State of Matto Grosso, near the River Tiété; in Peru it is found in the regions of Caralaya and Sandia, and close to the River Madre de Dios. Cases have been reported from Panama and Mexico. It has been found in the Anglo-Egyptian Sudan by Christopherson.

Ætiology.—The disease is due to *Leishmania tropica* Wright, 1903, var. *americana* Laveran and Nattan-Larrier, 1912, which Vianna considers to be a separate species, *L. brasiliensis* Vianna, 1911 (see pp. 378, 379, and 380).

Morbid Anatomy and Histopathology.—Escomel, in a chronic case which died of cachexia, found the body extremely emaciated, and the espundial lesions extending from the oral cavity to the pharynx, larynx, and trachea. The œsophagus was also affected. The organs presented amyloid degeneration.

The histopathology of the disease has been well investigated by Breda, Escomel, De Amicis, Verrotti, Splendore, Carini, and recently very completely by Laveran and Nattan-Larrier. The lesions do not show any characteristic histological feature, the epithelial strata have disappeared, and are substituted by a fibro-leucocytic membrane; there is a large amount of granulation tissue, with numerous mononuclear leucocytes and plasma cells; a few macrophages may be seen.

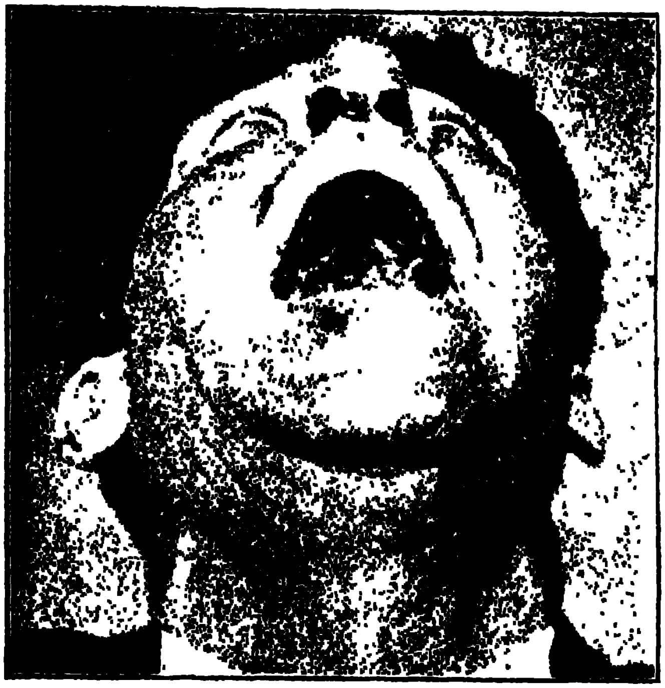

FIG. 856.—ESPUNDIA.
(After Splendore.)

Splendore has occasionally seen giant cells; no cell nests have been observed. The stroma consists of some fibrils, which are stained with difficulty. The lesions are not very vascular.

Communicability.—The infection may be conveyed by direct contact from person to person, the virus being absorbed through some abraded surface, fissure, or small wound. It may also be transmitted probably by some blood-sucking insect, most patients stating that the first lesion appeared at the place where they had been bitten by some insect. Mosquitoes, sand-flies, certain ticks and certain flies (especially tabanid) have been inculpated.

As regards the *reservoir* of the virus, certain observers suspect dogs, in which occasionally a similar or identical affection to the human one may be found. In Paraguay there is a popular belief that the rattle-snakes are the reservoir of the virus.

Darling and Townsend have brought forward the hypothesis that the

leishmania is an adaptation to man of insect flagellates. In this connection one may quote the interesting observations made by Fantham and Porter, Laveran and Franchini, (who have succeeded in infecting mammalia with certain flagellates found in fleas and mosquitoes (see p. 363).

Symptomatology.—The incubation period is unknown. The malady generally begins with a nodule on some uncovered part of the body, which fairly quickly breaks down, and an ulcer is formed. This first lesion is called by Escomel 'espundial chancre.' It is mostly found on the forearms, legs, chest, trunk, or more rarely on the face. The ulcer is generally atonic, roundish; there is very little or no pain, the fundus is granulating, and there is abundant purulent secretion which dries up, forming thick crusts. The ulcer after some months, or even one or two years, heals up, leaving a thick scar. While this primary ulcer is still open, but oftener after it has healed, the characteristic lesions occur on the mucosa of the mouth and nose, with or without the appearance of further ulcerative lesions on the skin of various regions of the body. The lesions on the mucosa of the mouth are ulcero-granulomatous, often frambœsiform, and may invade the hard and soft palate, the gums, the labial mucosa; they may form on the palate a diffuse granulomatous mass, with deep furrows. The mucosa of the nose is very often attacked, and destruction of the cartilages may take place, inducing a marked deformation of the nose. Alfr. da Matta has noted that the bones are not destroyed; the skin is often œdematous, and patches of hard œdema may be found below the eyes. The pathological process may extend to the pharynx and larynx. In some cases the patient may become aphonous, and complains of great pain during deglutition; his breath may be very offensive. There may be serotine fever.

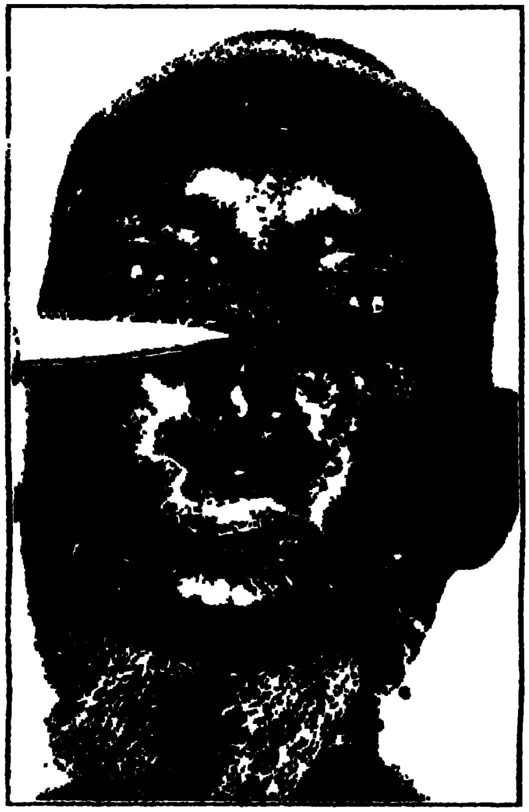

Fig 857.—Espundia A Sudan Case.
(From a photograph by Christopherson.)

The course is chronic; the disease may last for twenty to thirty years, death being generally due to some intercurrent disease. In a few cases the affection may attack mucosæ other than the naso-oral, and pharyngeal. For instance, a case of vaginal leishmaniasis has been recorded by Alfr. da Matta. In the last stage the patient becomes cachectic, and his appearance may be that of a carcinomatous patient.

Prognosis.—Before the introduction of tartar emetic by Vianna the prognosis used to be very bad, though occasionally when the diagnosis was made as soon as the primary cutaneous lesion appeared, and this was destroyed, the further progress of the disease was prevented.

Diagnosis.—The disease is distinguished from the usual type of dermal leishmaniasis (Oriental sore) by its very long course. Moreover, the latter invades the oral mucosa only exceptionally, though cases have been reported by Cardamatis in Greece, and Lacava and Gabbi in Italy. From blastomycosis it is distinguished by the presence of a leishmania, and absence of yeast-like or monilia-like fungi. From syphilis it can be diagnosed by the uselessness of the mercurial and salvarsan treatment; from morva by the absence of *B. mallei* Löffler and Schütz; moreover, morva is very rare or absent in those regions where espundia occurs. The condition is distinguishable from tuberculosis by the different histological lesions; from framboesia by the absence of the framboesiform eruption on the body, by the absence of the *Treponema pertenue* Castellani, and by the uselessness of the salvarsan treatment.

Treatment.—Tartar emetic, first used in the disease by Vianna, is a specific. The usual 1 per cent. solution in saline or distilled water, filtered through a Berkefeld candle, or sterilized in flowing steam, is given by intravenous injection (5 to 10 c.c. per injection) for several periods of five days each until twenty or thirty injections have been given. The same solution may be used as a local application to the sores, for syringing the nose, etc.

Strong solutions or tartar emetic in powder form should not be used, as they give rise to severe pain.

Mild antiseptic mouth-washes such as diluted glycothymolin and listerin or potassium permanganate (1 in 5,000) should be freely used.

According to Escomel, if the primary lesion be excised or destroyed, the further course of the disease is prevented.

Prophylaxis.—Abrasions, fissures, and any ordinary traumatic small sores, should be kept well disinfected and protected with antiseptic dressings, to prevent infection with the espundia virus. Any insect bite should immediately be touched with tincture of iodine.

INDIAN ORO-PHARYNGEAL LEISHMANIASIS.

Remarks.—It may be of interest to give a brief account of an ulcerative condition of the throat observed by one of us in two Europeans who had long been living in India.

Ætiology.—In one of the two cases observed, scrapings from the ulcers contained typical leishmania bodies very similar or identical to *Leishmania tropica* and *L. donovani*. In the other—which was the first case seen, and clinically identical to the second—no leishmania was found, but the patient had to go back to India, and no repeated examinations could be carried out. We are inclined to think that it was of the same nature. The condition may have been kala-azar, with ulcerations on the throat, though this manifestation of kala-azar has never been described; moreover, the general health was not so affected as in kala-azar of long standing. It was not Oriental sore with complications on the oral mucosa, as the skin had never been affected; moreover, Oriental sore does not run such a long course. It was not espundia, as there were no cutaneous lesions and the ulcers were not frambœsiform.

Symptomatology.—In the case in which leishmania bodies were found there was no history of syphilis or of any ulcerative lesion on the skin. He had been residing for a long time in India, and when he consulted one of us at Colombo, was going on a long holiday. He was a tall, rather stout man (European) of thirty-eight years of age, in apparently good general health, but he complained of intractable ulcers on the pharynx and soft palate, which, according to him, had been present for the last nine years, and which gave a certain amount of discomfort, though they were not very painful. No enlarged lymphatic glands could be detected. The local examination showed the presence of several ulcers on the posterior wall of the pharynx and on the soft palate; they were of various sizes, but not very large, mostly ½ to ¾ centimetre in diameter; they were roundish, and some of them not very deep. Some were covered by débris: none had a frambœsiform appearance. The patient had been treated in various ways, including a very energetic antisyphilitic treatment, without any effect. The microscopical examination of scrapings from the lesions showed leishmania bodies, apparently very similar or identical to *Leishmania donovani*. On inquiry the fact was elicited that the patient had been occasionally suffering from attacks of fever, believed to be malaria, for the last five years. The physical examination of the patient revealed nothing abnormal, but the spleen on percussion appeared to be slightly enlarged, and on deep inspiration was just palpable.

In a clinically identical condition seen in a previous patient no leishmania was found in the ulcers, but no repeated examinations could be carried out; he admitted having had many attacks of what he called 'malarial fever.' In that case the spleen was much enlarged, though the examination of the blood revealed absence of malarial parasites and pigment.

Prognosis.—The local ulcers were most intractable. The general health did not seem, however, to be very markedly affected.

Diagnosis.—This is based on the microscopical examination. Care should be taken to make a deep scraping of the ulcer.

Treatment.—This should be the same as for espundia.

ULCUS TROPICUM.

Synonyms.—Yemen ulcer, Aden ulcer, Annam ulceration, Cochin sore, Mozambique sore, Sarnes (Congo). *French :* Ulcère Phagédénique des Pays Chauds. Ulcère Phagédénique Endémique. *Italian :* Ulcera Tropicale, Phagedæna Tropica. *German :* Tropische Phagedenismus.

Definition.—Ulcus tropicum is a tropical chronic sloughing ulcer, which may take a phagedænic character, and spread down to the muscles and bones, and which, left to itself, shows hardly any tendency to heal.

History.—Phagedænic ulceration is mentioned in many of the early works on tropical medicine. Thus, Hunter in 1792 refers to it in Jamaica in the following terms:—

'Sores . . . spread quickly, and form large ulcerated surfaces. . . . The granulations turn flaccid, and even mortify in parts. The portion skinned over ulcerates afresh, and the sore becomes larger than ever. Ulcers of some standing . . . could not be healed in that country. . . . Opportunity was taken to send home men with ulcers.'

After this date there are numerous references to the complaint, which is generally described under the name of the locality in which it was found, which accounts for many of the above synonyms. In 1862, Rochard took a broader view of the disease, and in 1864 Le Roy de Méricourt introduced the term 'Phagedænic ulcer of warm countries.'

In 1874, Treille suggested that the disease was likely to prove to be of a parasitic origin, but he failed to demonstrate any parasite. Bacteria have since been described by many observers, and more recently spirochætes have been considered to be the cause of the disease, as will be described in the section on Ætiology.

Climatology.—Ulcus tropicum is found in all tropical and subtropical regions of Africa, Asia, and America. There are localities, however, such as the hinterland of Aden, the low, marshy plains of Cochin China and Tonkin, and some islands of the Red Sea, where the affection is particularly common. It may be found also, though rarely, in temperate zones, cases having been reported from Greece, Macedonia, and South Italy.

Ætiology.—Numerous bacteria have been described by Petit, Boniet, Blaise, Crendiropoulo, as being the cause of the disease. Le Dantec described in the lesions the fusiform bacillus, and considered it to be the cause of the affection. Vincent found in addition to the fusiform bacillus numerous spirochætes, and considered that the affection was due to the association of the two germs. Vincent's observations have been confirmed by Smith and Peil in Sierra Leone, Patton in Aden, and many other observers in various parts of the tropics. Prowazek has fully described the spirochæte which he named *Spirochæta schaudinni* Prowazek, 1907. This term, however, is a synonym for *S. vincenti* Blanchard, 1906.

The important researches of Keysselitz and Mayer, and the more recent ones of Wolbach and Todd, confirm Prowazek's work.

Spiroschaudinnia vincenti Blanchard, 1906 (synonym, *Spiroschaudinnia schaudinni* Prowazek, 1907).—This is a spiral-shaped organism, very actively motile, its length varying between 10 μ and 22 μ, though much shorter or longer individuals may be met with. The coils are few in number, and elongated. The organism possesses a well-marked undulating membrane, which is best brought into evidence by using Löffler's flagellar stain. A delicate, rather short flagellum is occasionally seen at one of the extremities. Forms undergoing longitudinal division are frequently observed. Prowazek distinguishes, also, male and female forms. Variously shaped regressive and rest forms may be seen. According to Prowazek, *Spiroschaudinnia vincenti*, apart from being more slender, has the greatest resemblance to the spirochæte which Prowazek himself and Hofman have described in a form of balanoposthitis.

The *S. vincenti* is often found mixed with other types of spirochætes, some slender, some thick.

According to Le Dantec, Brault, Vincent, and others, ulcus tropicum is identical with the so-called 'hospital phagedæna' which used to rage in hospitals of all countries before the antiseptic era. In our opinion ulcus tropicum is a separate disease, though occasionally, owing to secondary infections, it may take phagedænic characters similar to those found in hospital gangrene.

Inoculation Experiments—Communicability.—Experiments to inoculate the disease in men and in the lower animals have been made by several authors. Blaise inoculated himself with the secretion of a case of ulcus tropicum, but no ulcer was produced—only a slight superficial, purulent lesion, probably due to pyogenic cocci present as secondary infectious agents in the secretion which had been used for the inoculation. Blaise tried to inoculate the disease, also, in guinea-pigs, but without any definite result. Similar experiments on the lower animals by Jourdeuil and Gayer failed. Halberstädter tried to reproduce the affection in monkeys (orang-outang and *Macacus cynomolgus*), but without success.

It would seem, therefore, that, to a certain extent, the disease is not directly contagious. It is probable that some insects or other blood-sucking vermin may play an important rôle in the transmission of the disease. In Ceylon, patients often state that the ulcer developed at the site of a leech-bite. Leeches are extremely common in Ceylon and other tropical countries. Prowazek in Java has examined many leeches, but he never found any spirochætes except once. The spirochæte observed, however, was quite different from *Spiroschaudinnia vincenti*. Prowazek examined, also, on many occasions the mud of rice-fields, but of spirochætes he found only *S. plicatilis*, and once a very thin, short, very actively mobile spirochæte.

Predisposing Causes.—A hot, damp climate is said to have a predisposing influence, as cases of ulcus tropicum occur more frequently in the hot rainy season and marshy lowland localities rather than in dry or higher regions. It may be that it is in hot, marshy places that the carriers of the infection thrive.

The disease is very common among the poorer classes of the population, who go barefooted and wear but scanty clothes. We have observed it very often in beggars and in scabies patients. The disease is much more common in adults than in children, in men than in women.

Histopathology.—This has been thoroughly studied by Keysselitz and Mayer, and by Wolbach and Todd. The surface of the ulcer is covered often by a tenacious membrane composed almost solely of coarse-meshed hyaline fibrin, with detritus and masses of spirochætes and various bacteria. The fundus and walls consist of granulation tissue, which does not present any characteristic feature. The deeper tissues and corium surrounding the ulcer present a heavy lymphoid and plasma cell infiltration, and, as noted by Wolbach and Todd, numerous eosinophiles are found in the vicinity of small vessels. On microscopical examination of vertical sections of the ulcer, it will be seen that the superficial layers of the fundus show a large amount of granular detritus and numerous foci of leucocytic infiltration, while the

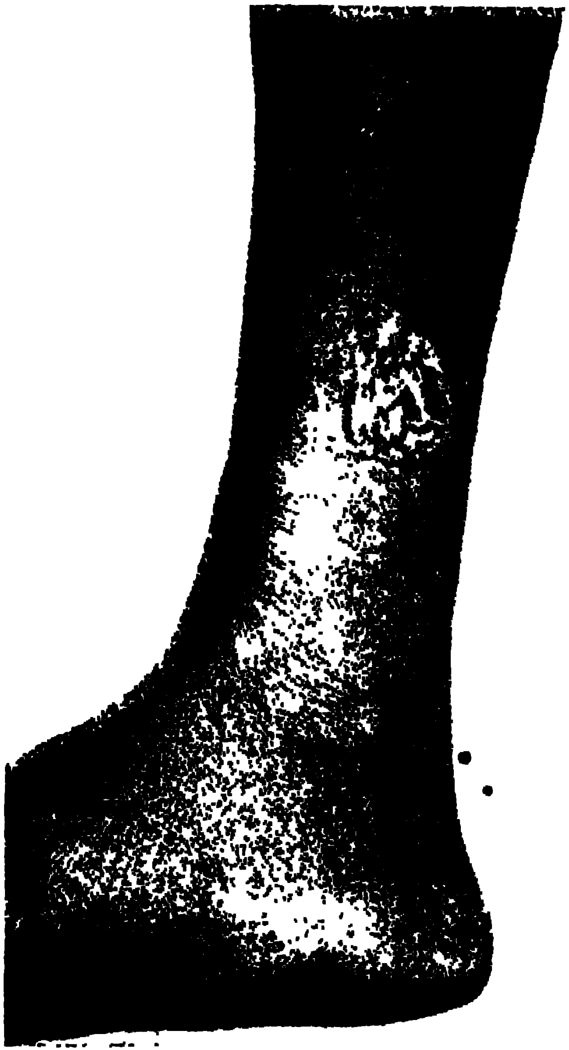

FIG. 858.—ULCUS TROPICUM: TYPICAL.

deeper layers consist of fairly dense fibrous tissue. Hæmorrhagic foci are to be seen in various parts, and, as observed by Keysselitz and Mayer, fusiform bacilli and spirochætes are found in the superficial layers, while in the deeper strata only spirochætes are present.

Symptomatology.—The affection is generally found on the lower limbs, especially the lower third of the leg, the ankle and dorsum of the foot. Occasionally it may develop on other uncovered parts of the body. It is single in most cases, but two or more ulcers may be found in some patients.

Ulcus tropicum begins with the appearance of a small, painful occasionally pruriginous papule or papulo-pustule, surrounded by a deeply infiltrated dusky red areola. The initial lesion soon undergoes purulent and degenerative changes, which rapidly extend to the infiltrated area. A sloughing process sets in, and an ulcer is formed, which gradually extends in depth and surface. The margins are not sensibly raised, nor thickened, unless the case be very old. They are not perpendicularly cut, nor undermined, as a rule, the whole ulceration having generally a roundish or oval outline, and, when the secretion is removed, a concave fundus. The parts surrounding the ulcers are often œdematous, and somewhat painful on pressure. It is remarkable, however, how comparatively little pain there is in many cases.

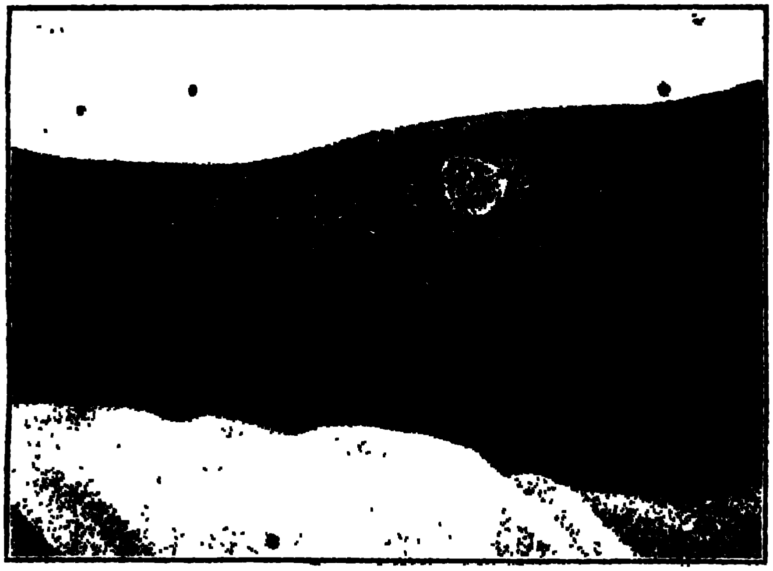

FIG. 859.—ULCUS TROPICUM: EARLY STAGE.

When the patients are first seen, the whole ulcer is generally covered with a thickish, dirty greyish secretion, exhaling a highly offensive odour. On removing the secretion the fundus will be found to be of a red colour, or in chronic cases pale pinkish, and feebly granulating.

The fundus is often somewhat infundibular in its central area, and not rarely may present a circular raised ridge, which divides the ulcer into two portions—an external more superficial one, and an internal infundibuliform one.

Occasionally, if left untreated, the ulcer may take a real phagedænic character, involving a large surface, and deepening till the deeper structures—muscles, tendons, and periosteum—are affected.

The course is always chronic, lasting for months—in fact, the ulcer has hardly any tendency to spontaneous healing if untreated. Healing takes place by a very slow process of granulation, and begins from the periphery. A thick, whitish, often disfiguring scar is left at the place of the ulcerations. At times, however, the cicatrix is at first very delicate, and the ulcer may break out again after the least irritation or traumatism.

The microscopical examination of the greyish, bad-smelling secretion shows leucocytes undergoing various degenerations, some red-blood cells, threads of connective tissue, and very often spirochætes and fusiform bacteria of various types, sometimes accompanied by the usual pyogenic cocci. In old untreated cases larvæ of flies may be found, small acarids, and ants.

Diagnosis.—According to Le Dantec, Vincent, and several other observers, ulcus tropicum is identical with 'hospital phagedæna.' The fact, however, that, in contrast to 'hospital phagedæna,' ulcus tropicum shows very little or no direct contagiousness, and in most cases is self-limited, clearly shows, in our opinion, that the two are separate diseases.

FIG. 800.—ULCUS TROPICUM.

Differential Diagnosis—*Frambœsia.*—The lesions in frambœsia are generally multiple—either granulomatous or ulcerative. Scrapings from frambœsia lesions—after the superficial strata have been removed—will often reveal the *Treponema pertenue* Castellani, which is much more slender than any of the spirochætes found in ulcus tropicum. Occasionally an ulcerative frambœsia lesion may become infected with the virus of ulcus tropicum. In our experience, however, the reverse is much more common—viz., an ulcus tropicum becomes infected with frambœsia virus, takes a papillomatous appearance, and is followed by a general eruption of frambœsia granulomata.

Syphilis.—Ulcus tropicum does not show usually the clean-cut margins and the punched-out circular or reniform appearance, with the frequent wash-leather slough on the surface, of a tertiary ulcer. The mercury and potassium iodide treatment has no influence on it.

Oriental Sore.—An old-standing Oriental sore may present some characters of a chronic ulcus tropicum, though generally a tropical ulcer is much larger. The process of ulceration and breaking down is very slow in Oriental sore, while it is very rapid in ulcus tropicum. In difficult cases the search for *Leishmania tropica*, which is present in Oriental sore, will clear the diagnosis.

Ulcus Cruris Varicosum.—There are often varicose veins visible, the parts surrounding the ulcer are congested and frequently eczematous, the ulcer is often shallow and irregular.

Ulcers of Tubercular Origin.—They are rare on the lower extremities, and their development is long and insidious. In ulcus tropicum the tubercular cuti and ophthalmic reactions are negative unless the ulcer develops in a tubercular patient.

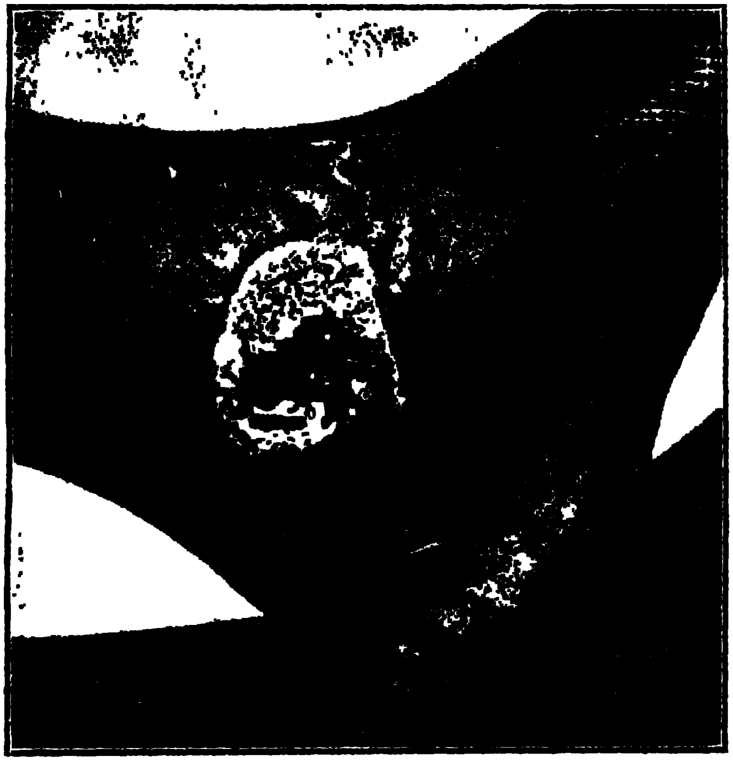

FIG. 861.—ULCUS TROPICUM.

Blastomycosis—Sporotrichosis.—In blastomycosis there are generally warty patches with minute abscesses; while the lesions of sporotrichosis often show at first the characters of gummata. The bacteriological examination will reveal the presence of the fungi.

Acladiosis.—The ulcerative lesions are multiple and of smaller dimensions. The bacteriological examination will reveal the presence of *Acladium castellanii* Pinoy.

Mycosis Fungoides.—Is generally preceded by a general pruriginous dermatitis of various character, lichen-planus-like, psoriasis-like, eczematous-like. The ulcerative lesions are multiple, and have the characters of granulomata.

Prognosis.—If untreated, tropical ulcer has very little or no tendency to spontaneous recovery, and in some cases may extend, damaging the deeper structures, tendons, muscles, nerves, and vessels. Occasionally a general septicæmia and pyæmia may supervene. In countries where frambœsia is endemic the ulcer often gets infected with its virus, and the patient develops a general eruption of frambœsia.

Treatment.—Salvarsan, neosalvarsan, and their substitutes have been administered by intravenous or intramuscular injection by Werner, Hillenberger, and others, with success in certain cases.

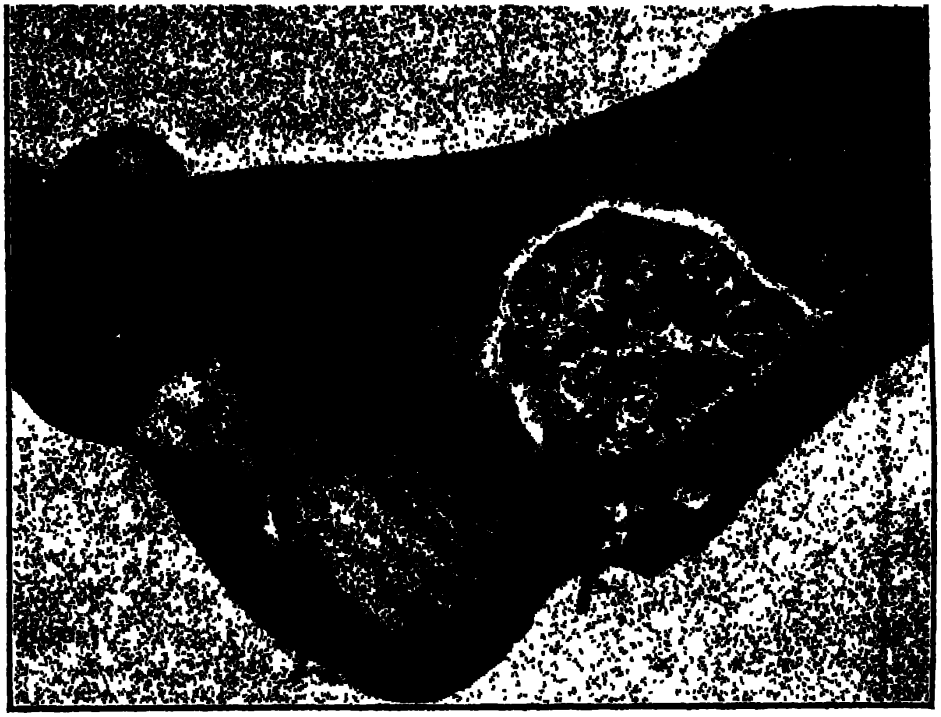

FIG. 862.—ULCUS TROPICUM, WITH CORNU CUTANEUM.

The details of the treatment are found in the chapter on Frambœsia (p. 1550). Mercury and potassium and sodium iodides are useless, but calcium iodide (gr. iii.), well diluted, three times daily, seems occasionally to be of some slight benefit. As regards local treatment, the patient, whenever possible, being kept at rest, the dirty greyish, foul-smelling secretion is removed by using a disinfecting solution, such as mercury perchloride, 1 in 1,000; cyllin, 1 in 300; hydrogen peroxide, 10 per cent.; permanganate of potash, 1 in 2,000.

For the first few days it is better not to apply any so-called disinfectant ointments or powders: simply keep the ulcer covered with gauze, moistened as often as possible with one of the disinfecting solutions already mentioned. This generally stops the formation of the greyish, dirty secretion. The ulcer will then appear clean and of a pinkish colour; but whatever be the further treatment used, whether powders (iodoform, boracic acid) or disinfecting ointments (white, red precipitate, or iodoform ointments), the improvement will be very slow, and several weeks, and often months, will elapse before a firm cicatrix is formed. Much quicker results will be obtained by using a protargol ointment. The ulcer is cleaned every morning with a perchloride lotion (1 in 1,000); then a protargol ointment (5 to 10 or 20 per cent.) is thickly spread on a piece of lint or gauze and applied to the ulcer, which is then fairly firmly bandaged.

The superiority of the protargol treatment over other kinds of local treatment is patent in many cases. Castellani, who introduced it for ulcus tropicum, made the following experiment: in a patient presenting two ulcers of little difference in size and deepness, one on the right leg, one on the left, he treated the one on the right leg, which was slightly larger and deeper, with protargol, and the one on the left leg with iodoform. The ulcer treated with protargol healed in three weeks, the one treated with iodoform in two months.

A silver nitrate ointment (½ per cent.), or a silver nitrate (½ per cent.), balsam of Peru (2 per cent.), ointment may also be used.

To accelerate cicatrization allantoin preparations have been used, and also scharlachroth powder. Salvarsan has been used locally as a powder, but this method is not advisable, as it induces a very severe, painful inflammation. Bougey and Vincent recommend a powder consisting of 10 parts of fresh hypochlorite of soda and 90 parts of boric acid.

ULCUS INTERDIGITALE.

This affection is not rare among natives. It was described in 1909 by Castellani, whose work has been recently confirmed by Breinl, Martinez and Lopez. The patient complains of some itching between the toes, though no papules or vesicles are seen. After a few days a fissure appears, which rapidly deepens, and enlarges into a large oval ulcer with a dull, dark red fundus and sodden-looking margins. There is practically no discharge whatever. The ulcer is generally very painful. The skin surrounding the ulcers does not show signs of inflammation. Under proper treatment the ulcer heals in a few days. The patient must remain at rest, washing the ulcer twice daily with a 1 per cent. carbolic lotion, followed by dressing with a bismuth-boric acid ointment:—

Bismuthi subnitratis	gr xxx.
Acidi borici	gr. xv.
Vaseline	℥i.

ULCUS INFANTUM.

Historical and Geographical.—Under this name Castellani described a rather rare ulcerative condition of the legs met with in Ceylon among children, both native and European. His researches have been confirmed by various observers, among whom Gabbi and Sabella in Tripoli. The condition is found in Ceylon, India, and North Africa.

Ætiology.—This is unknown. A bacillus which cannot be grown is the only germ present in most cases; but as to its ætiological rôle nothing can be said definitely.

Symptomatology.—A reddish spot appears on some part of the leg. The spot becomes slightly elevated, and shows a yellowish central point. The yellowish point breaks down, and a small ulcer appears, generally of circular shape, and with a red fundus. The ulcer secretes a yellowish, thickish secretion, which dries into a yellow crust. If after some days the crust is removed, the ulcer will be found much larger and deeper—the size of a shilling to a half-crown piece. The ulcer is generally indolent, except on pressure. There may be a little pruritus. The ulcer may be single or multiple. The inguinal lymphatic glands may become enlarged, and occasionally the child has fever. The duration is between four to six weeks and three or four months. On healing, a permanent whitish scar is left.

FIG. 863.—ULCUS INFANTUM.

Diagnosis.—The ulcus infantum is differentiated from ulcus tropicum by the less severe symptoms, by being almost always multiple, by the smaller dimensions of the sore, by the absence of spirochætes, and by the absence of any tendency to phagedæna. In contrast to veldt sore the ulcers are deep, and the crust very thick. No streptococcus is found.

Treatment.—Touch the ulcers with pure hydrogen peroxide once every other day, and dress them with simple boric acid lotion (2 per cent.).

REMARKS ON ULCERS.

Ulcerative conditions of the skin are extremely common in the tropics. They may be classified as follows:—

1. Cutaneous leishmaniasis.
2. Ulcus tropicum.
3. Ulcus infantum.
4. Veldt sore.
5. Ulcus interdigitale.
6. Gangosa ulcers.
7. Leprotic ulcers.
8. Ulcers of frambœsial origin.
9. Elephantoid ulcers.
10. Blastomycetic, sporotrichitic, acladiotic, and, generally, hyphomycetic ulcers.
11. Cancerous and sarcomatous ulcers.
12. Tubercular ulcers.
13. Syphilitic ulcers.
14. Glanders ulcerations.
15. Ulcers of pyogenic origin (pyosis tropica).
16. Ulcers due to varicose veins.
17. Undetermined chronic or subchronic ulcerations.

The ulcerative conditions which may be considered as strictly tropical and well defined, such as Oriental sore, ulcus tropicum, etc., have already been described. The *cosmopolitan ulcerations*, such as the syphilitic ones and those due to varicose veins, show the same characters in the tropics as in temperate zones, except that very often, owing to their being neglected for a long time, they may present enormous dimensions, and may show secondary infections and become phagedænic. Ulcers due to varicose veins are very common among rickshaw coolies, who have to run and stand for hours at a time. It is remarkable how quickly they heal in most cases in these coolies, if the patient is kept at rest for some time; whereas in temperate zones the healing of varicose veins ulcers is of very long duration.

Undetermined Subchronic and Chronic Ulcers.

Knowledge of this group of ulcers is scanty, but the investigations of Strong, Stitt, Rho, Wherry, and Clegg, and others have thrown some light on this subject. Our experience tallies with that of Stitt, and we therefore consider that such ulcers may be roughly divided into three groups:—

1. Septic Ulcers—Ulcerations following on Neglected Wounds.
2. Painless Chronic Ulcers.
3. Diphtheroid Ulcers.

Septic Ulcers—Ulcerations following on Neglected Wounds.—These are of pyogenic origin and often very large dimensions. They are generally of roundish or irregular shape, and may be very deep. The secretion is abundant, purulent, and contains the various staphylococci. If the pus is removed, and a scraping taken from the fundus, the preparation will show numerous polymorphonuclear leucocytes and various cocci. These ulcers do not show tendency to spontaneous cure, but heal quickly under an antiseptic treatment. We generally treat them with hydrargyrum perchloride (1 in 2,000). The opsonic treatment also gives good results.

Nichols has called attention to discharging sores in the Philippine Islands, called 'puente,' which are produced by the natives applying some lime to the skin, and afterwards betel powder, with the object of counter-irritation.

Painless Chronic Ulcers.—A small red scaly, slightly itching spot appears, generally on the legs, and gradually enlarges for about four to eight weeks, when the affected area begins to exude a serum which quickly dries into crusts. Under the crust ulceration slowly takes place. At first the ulcers are shallow, and may have undermined edges: later they are often punched out, and may become indurated. There is no pain, except slight pain on pressure, and the general health is not affected. Healing takes place under the crust, and lasts between two and twelve months. A pale cicatrix, with hyperpigmented margins, is left.

As noted by Stitt, scrapings from the fungus show a prevalence of mononuclear cells, polymorphonuclears being practically absent. No pyogenic organisms are found.

Treatment.—The treatment is difficult. Cauterization does very little. In some cases the application of bismuth subnitrate, xeroform, novoform, dermatol, and firm bandaging is useful. In others a protargol ointment (5 to 10 per cent.), or a nitrate of silver (½ per cent.) balsam of Peru (1 per cent.) ointment is of advantage. Allantoin preparations may also be used. When the ulcers are very large and atonic, skin transplantation may be necessary.

Diphtheroid Ulcers.—An angry red, painful spot, often surrounded by vesicles, appears on the legs. Within a few hours—twelve to forty-eight—the affected area is turned into a dark greyish or blackish membrane. If this membrane be removed, an ulcer will be found covered with greenish pus. The membrane reforms rapidly, and, apart from the dark colour, it closely resembles a diphtheria membrane. These ulcers extend rapidly, but do not take, as a rule, a true phagedænic character. The margins after some time may become indurated, but do not show a punched-out appearance. Scrapings taken from the fundus show numerous polymorphonuclears. The course is very long. These ulcers are with difficulty distinguishable from true ulcus tropicum except by the absence of *Spiroschaudinnia vincenti* Blanchard.

Treatment.—Excision is not to be advised, as in Stitt's and our own experience, when this has been done, additional lesions have appeared. Bier's passive congestion method is painful, and does not improve the condition. On the whole, the best treatment is to keep the ulcers well disinfected with a perchloride lotion (1 in 2,000), occasionally touching them with pure hydrogen peroxide. Should the ulcers become phagedænic, the application of pure carbolic is advisable.

GRANULOMA INGUINALE.

Synonyms.—Ulcerating granuloma of the pudenda, Granuloma Venereum (Brooke), Esthiomène de la vulve.

Definition.—Granuloma inguinale is a chronic granulomatous affection of probable protozoal origin attacking the generative organs, from which it spreads to the inguinal regions and the perineum.

History.—In 1896 Conyers and Daniels described a disease of the generative organs in both men and women in British Guiana which was very painful, disfiguring, and contagious. Daniels thinks that it was previously described by Macleod and Maitland in India. Since then papers have appeared on the subject by Ozzard, Galloway, Wise, Donovan, Siebert, Flu, Martini, Gabbi, Sabella, Torres, Rabello, Pijper, Mayer, Newham and Low, and many others.

Climatology.—It occurs in British Guiana, the West Indian Islands, West Africa, South Africa, India, South China, and Northern Australia; but is rare in Ceylon, Malaya, Sudan, and Central Africa. It has been reported from Northern Africa (Tripoli) by Gabbi and Sabella. A similar or identical condition has rarely been met with in Europe and North America.

Ætiology.—It appears in the genitalia of both sexes after puberty, but is rare after forty-five years of age.

Donovan, in 1905, described certain peculiar rod-like bodies 2 μ by 1 μ, lying singly or in groups in mononuclear cells, obtained by scraping the sores. Donovan stated that the bodies looked 'like gigantic bacilli with rounded ends,' but left the nature of them undecided. Siebert, in 1907, carried out an investigation on material originating from various countries, demonstrating the same or similar bodies in all instances, but referring to them as *diplococci*.

Markham Carter, in [illegible] described the parasites as 'bean-shaped bodies resembling the gregariniform stage of a herpetomonas or a crithidium,' and came to the conclusion that the affection was due to either a herpetomonas or a crithidium.

Flu, in 1911, in South America confirmed Siebert's work, but considered the bodies to be bacilli, with capsules, and not cocci. At the same time, however, he called attention to the possibility of the bodies being a stage of a chlamydozoal infection. Martini, in 1913, announced that he had succeeded in cultivating the germs described by Siebert and Flu on blood agar. He described them as anaerobic, capsulated, Gram-negative diplococci, and stated that he had succeeded in producing granulomata in mice by inoculation of cultures, though he failed with guinea-pigs and rabbits. In the same year Aragão and Vianna also stated that they had succeeded in growing the bodies, which they considered to be of bacterial nature, using the term 'calimmato-bacterium granulomatis.' Their work was confirmed by De Souza Araujo.

It is very doubtful whether the cultures obtained by all these observers are in reality cultures of Donovan's bodies. The inoculation of vaccines made from such cultures do not induce any improvement.

Wise, in 1907, found in the eruption spirochætes resembling *Treponema pallidum* and *Spiroschaudinnia refringens*, together with small bodies consisting of a thin capsule surrounding a clear unstained space, in the middle of which was a curved chromatic rod, which was thinner in the centre and club-shaped at either end. He found from two to twenty five of these in the leucocytes. Cleland confirmed Wise's observations, and called the spirochæte *S. aboriginalis* Cleland, 1909.

Bosanquet confirmed the presence of spirochætes in sections, associated with numerous bacteria, but did not consider the spirochætes to be the ætiological agents of the affection. De Souza Araujo observed that after the injection of salvarsan the spirochætes disappeared, but the condition did not get better; hence he came to the conclusion that the spirochætes had nothing to do with the ætiology of the disease.

Cleland and Hickinbotham, in 1909, published further observations on granuloma inguinale, and stated that spirochætes were present only in a certain number of cases, while they constantly found large numbers of diplobacillary bodies. Le Dantec, in 1911, was still of opinion that the malady was of tubercular origin. Torres and Rabello believed it to be a form of sporotrichosis, and Greco a blastomycosis. Pijper, in a recent interesting publication, has definitely brought forward a chlamydozoon theory, and considers that the variously shaped bodies described by so many observers are stages of the same organism, a stage of which, in Pijper's opinion, closely resembles the initial or elementary bodies described by Prowazek in the development of the Guarnieri bodies.

Communicability.– The disease is generally transmitted by sexual intercourse.

Cleland states that in West Australia the malady is especially common among 'gins' (native women), and there is an idea prevalent among the white settlers that the girls become infected by connection with dogs, in which animals a condition similar or identical with granuloma venereum is said to be found. Ernest Black, who has made a thorough investigation, states that Cleland's hypothesis is untenable.

Pathology.—According to Galloway, the microscopical changes begin some distance from the lesion, and consist of a round-celled infiltration into the upper regions of the corium. This induces the papillæ to increase in length, thus producing the typical papule, and at the same time causes an elongation of the interpapillary processes of the epidermis, until they are some eight or ten times their original length.

The connective tissue of the corium swells and disappears, and its place is taken by a round-celled infiltration, which consists of leucocytes, Unna's plasma cells, mast cells, and connective-tissue cells. Giant cells are not found. The leucocytes are the ordinary polymorphonuclear leucocytes, while Unna's cells are characterized by possessing a rounded nucleus, with a certain amount of surrounding protoplasm containing basophile granules. The connective-tissue cells are spindle-shaped. The cells of the epidermis are modified over the papule by becoming swollen, hyaline, and showing mitosis. The stratum granulosum fails to develop its kerato-hyalin granules, and eventually disappears halfway up the papule, as does the stratum corneum, so that on the summit the different layers of the epidermis cannot be differentiated.*

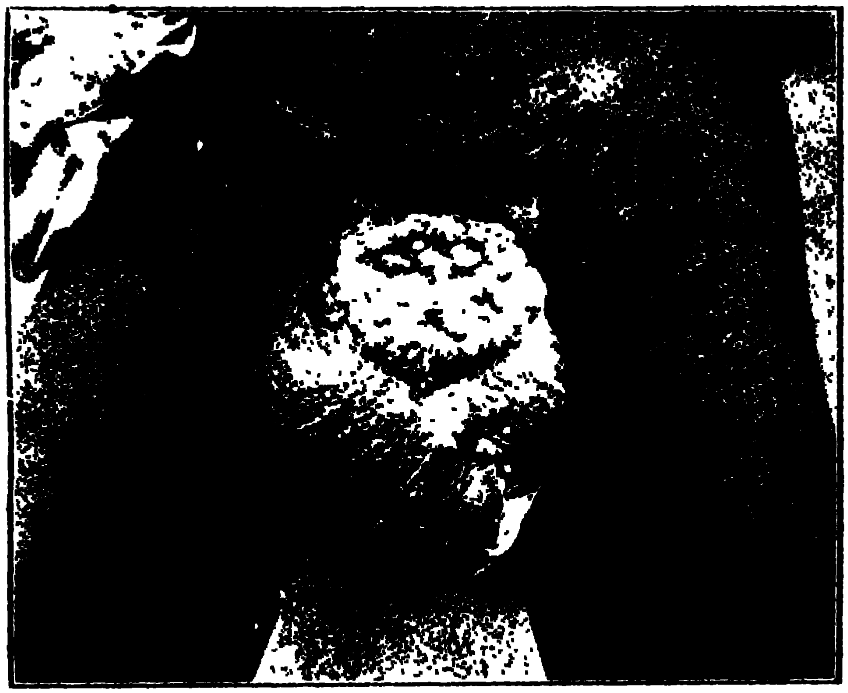

FIG. 804.—GRANULOMA INGUINALE.
(From a photograph by Sambon.)

There is neither caseation nor suppuration, but in the older parts of the specimen the cells of the infiltration become swollen and disappear, and in their place there appears cicatricial connective tissue, which causes the papule to shrink and the whole area to assume a scar-like appearance.

Symptomatology.—The disease in the male begins on the penis, as a rule, as a papule or small nodule, which extends over skin and mucosa by peripheral growth, which is aided by the formation of new papules and nodules at the growing margin and in the healthy skin. It grows into the groins, causing the hair to fall out, and between the scrotum and the thighs, and from thence backwards into the perineum and around the anus, into which it may pass.

When fully developed, it appears as a mass of nodules or papules, without deep ulceration as a rule, but with a thin, offensive discharge. In the older regions it shows some attempt at healing in the formation of dense scar tissue. There is very little pain or pruritus.

In the female the process begins as a papule on the labium minus, and then extends into the vagina, along the perineum, around the anus, and up the rectum, and into the groins. The growth extends into the tissue between the rectum and the vagina, and may give rise to rectovaginal fistulæ. The whole growth is also much more liable to ulcerate in the female than in the male.

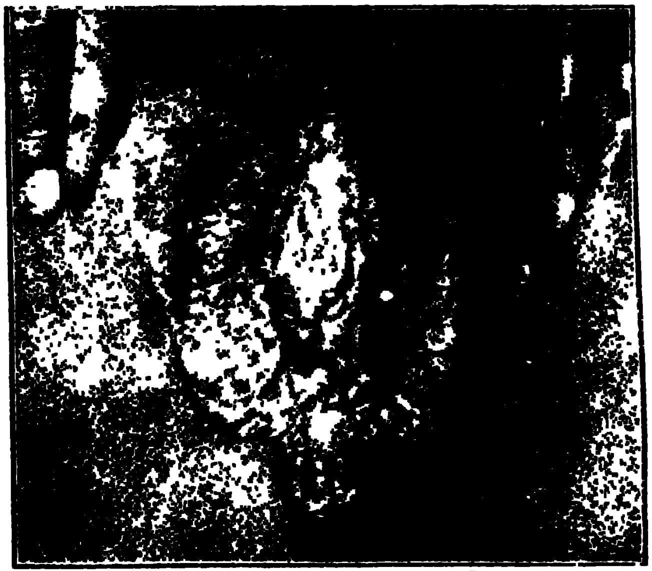

FIG. 865.—GRANULOMA INGUINALE.
(From a photograph by Sambon.)

The lesions may become œdematous, and present an appearance analogous to elephantiasis.

Bonne and Verhagen have described a case in which the disease after a time attacked the upper lip and alæ nasi.

Varieties.—Daniels lays stress upon the fact that the disease varies much in different races. In negroes it is more granular, and spreads farther; in Indians it is less marked; in Fijians it is softer, and separate areas more common.

Diagnosis.—It is most likely to be confused with syphilis, lupus, and epithelioma. From syphilis it can be differentiated by the absence of the secondary eruption and the inefficacy of mercurial treatment. Lupus is very rare in such situations, and in epithelioma the lymphatic glands would be early infected. In doubtful cases microscopical examination of a piece of the diseased tissue will enable the diagnosis to be made from lupus as well as from epithelioma.

Prognosis.—The disease as a rule does not affect the general health, but is extremely chronic, lasting for years.

Treatment.—Tartar emetic, though not efficacious in every case, should always be given a thorough trial. The treatment is carried out in the same way as for cutaneous leishmaniasis (see p. 2173).

Tartar emetic was first used in granuloma inguinale in 1913 by Arago, Vianna, and De Souza Araujo. Breinl and Priestley confirmed the work of these observers in a case in Australia, and very shortly after Newham and Low in a case in Europe. Low, however, reported later on a complete failure of the tartar emetic treatment in another case.

Greig and Cujel consider that tartar emetic benefits the condition only when given in very large doses; according to them the drug acts, not as a true specific, but as a general protoplasmic poison.

The best local treatment is radiotherapy with X rays which has been found quite successful in Madras. If these are not available, antiseptic lotions should be applied, and then portions excised, or the diseased areas may be scraped and then cauterized. Convers and Daniels recommend the application of an ointment of salicylic acid (gr. xxx.), unguentum creosoti (℥i.).

Certain observers claim to have had good results with salvarsan and neosalvarsan. The technique of the treatment has been described in the chapter on Frambœsia (p. 1500). Large doses of potassium iodide are said to be useful.

PAPILLOMA INGUINALE TROPICUM.

Synonym. Acanthoma Inguinale (Castellani).

A peculiar papillomatous affection of the inguinal regions is not rare among Tamils. Further experience will probably show that other races are also affected. Women are apparently more liable to the disease than men, inasmuch as, although the number of male patients in the Colombo Clinic and hospitals is much larger than the number of female patients, not a single case has been detected among men.

Symptomatology.—One or both inguinal regions are occupied by extremely numerous tall filiform vegetations of a pinkish or darkish colour. No ulcerative lesions are present. There is neither pain nor pruritus. The general health does not seem to be affected. The affection is very chronic, and is probably contagious, but nothing is known of the ætiology. In the cases so far observed the genital organs of the patient were normal, and there was no history of gonorrhœa or any other venereal disease.

Treatment.—The treatment is surgical—removal of the vegetation by the knife and cauterization. The patient, as a rule, however, will not consent to the operation.

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CHAPTER XCVI

THE DERMATOZOIASES

Classification—Hexapode dermatites—Creeping eruption—Circinate creeping eruption—Dermatitis macrogyrata—Chilopode dermatites—Acarine dermatites—Copra itch—Grain itch—Scabies—Nematode dermatites—Cestode dermatites—References.

CLASSIFICATION.

THE term 'dermatozoiasis,' in the widest sense of the word, means any skin disease of animal origin, but it is usually restricted to indicate those skin lesions which are caused by metazoan parasites. Used in this restricted sense, dermatozoiasis includes:—

I. Hexapode dermatites.
II. Chilopode dermatites.
III. Acarine dermatites.
IV. Nematode dermatites.
V. Cestode dermatites.

I. HEXAPODE DERMATITES.

The Hexapode Dermatites include the lesions of the skin caused by either the bites, the stings, or the presence of the larvæ or the pregnant female of various species of the *Hexapoda*.

These hexapode dermatites may be divided into four classes.—

1. Dermatites caused by bites of the adult.
2. Dermatites caused by blistering fluids excreted by the adult.
3. Dermatites caused by stings of the adult.
4. Dermatites caused by the presence and bites of the larvæ.
5. Dermatites caused by the presence of the imago.

||1. Dermatites caused by Bites of the Adult.

These lesions are most commonly due to bites of species of the families Pediculidæ (p. 753); Clinocoridæ (p. 762); Anthocoridæ (p. 766); Reduviidæ (p. 767); Aradidæ (p. 770); Culicidæ (p. 774); Psychodidæ (p. 806); Simuliidæ (p. 810). Tabanidæ (p. 817); Muscidæ (p. 831), and by species of the orders Siphonaptera (p. 837) and Hymenoptera in which comes the family Formicidæ, or ants (p. 222).

The bites of these insects are either considered in pp. 223-226, or in the references given above, and need not be further considered except with regard to the Pediculidæ. which cause the dermatosis called Pediculosis.

Pediculosis.

Synonyms.—Phthiriasis, Vagabond's disease.

Definition.—Pediculosis is a term applied to the various lesions primary and secondary, induced by the bites of *Pediculus humanus* Linnæus, 1758, *Pediculus corporis* de Geer, 1778, and *Phthirius pubis* Linnæus, 1758 (pp. 755-757).

Remarks.—Pediculosis is extremely common in the tropics, where it is an everyday sight to see the lower-class natives busily employed in killing the lice in their friends' heads. It is also commonly present in all armies on active service, and as lice are carriers of such diseases as typhus, relapsing fever, and trench fever, etc., they have assumed a very important position in the recent war.

Ætiology. Pediculosis is due to the irritation caused by the venom injected during the bites of the three species of lice mentioned in the definition.

Pathology. -The mouth parts of a louse consist of two tubes one inside the other: the outer chitinous tube, called the *proboscis*, is composed of the fused labrum and labium, and is armed with a collar of minute curved hooklets, while the inner membranous tube is composed of the maxillæ and mandibles, and is called the *suctorial tube*. When about to bite, the louse inserts its hard proboscis into a sweat duct, everts its small hooklets, and thus obtains a hold upon the skin. It then protrudes the suctorial tube, which it drives deep into the skin of the host until it reaches the blood. It is during this process that it probably injects the venom from its salivary glands, but the nature of this poison is quite unknown, although its presence is with reason suspected owing to the pruritus caused by the bites of the lice.

Having reached the blood, it proceeds to fill itself to repletion, pumping the blood into its alimentary canal by means of the chitinous pharyngeal pump. After feeding, it withdraws its proboscis, and the blood fills up the orifice and coagulates, forming a minute red papule. Considerable pruritus is now felt, and the victim scratches vigorously to relieve this sensation, and often produces marked excoriations, which may become secondarily infected with the common pyogenic cocci, causing purulent lesions. Repeated biting, associated with injection of the venom, and constant scratching, leads to pigmentation of the skin, causing the so-called pityriasis nigra of Willan, or melanoderma pediculis. If this process is continued, the skin becomes thickened and deeply pigmented, and forms the so-called 'vagabond's disease.' The pigmentation is naturally not observable in very dark skins, and may not be so entirely dependent upon the scratching as is usually stated, but may be, in part at least, caused by the venom.

Symptomatology.—The essential symptom is pruritus, which need not be localized, but may be general, accompanied by the presence of the minute papules with bright red centres, but this simple picture is generally complicated by the erythema or excoriations set up by the scratching induced by the pruritus, and this again may be complicated by the appearance of pustules, due to secondary pyogenic infections, which dry and leave scabs. In these cases the neighbouring lymph glands are usually enlarged. Very rarely may pediculosis give rise to general symptoms, such as fever.

Varieties.—Three clinical varieties of pediculosis are described—viz., pediculosis capitis, pediculosis corporis, and pediculosis pubis.

Pediculosis capitis is caused by *Pediculus humanus* Linnæus, 1758, which, though usually confined to the hairy regions of the head, may rarely be found in other parts of the body. They are grey on Europeans, and brownish or even black in colour upon dark-skinned natives, and are said to be yellow on Chinese, and orange-coloured on Hottentots. They often infect European ladies, probably coming from the native ayahs, and thus a very dark pediculus may be found on a fair European. They cause intense irritation of the head, and may give rise to secondary impetiginous lesions and enlargement of the lymphatic glands, especially those of the back of the head, and in very dirty people with long hair they may cause the peculiar condition of matted hair called 'plica polonica.'

Pediculosis corporis.—This is caused by *Pediculus corporis* de Geer, 1778. These pediculi live in the clothing, especially in thick seams, and are therefore to be found on natives in the region of the waist, where the clothing is twisted into a thickish roll. In Europeans the most common site for their attacks is the back of the shoulders, where the small papules with the bright red centres and the linear scratches may be seen.

Pediculosis pubis.—*Phthirius pubis* lives wherever there are large thick hairs—viz., on the hairs of the pubis, or the eyelids or eyebrows, and of the beard and armpits. Here again it is accompanied by the characteristic signs. In addition, Morrison's spots or maculæ ceruleæ may be seen in the form of small, roundish or oval greyish-blue maculæ, which are thought by some authorities to arise from the pigment on the thorax of the louse opposite the anterior pair of legs, but which more probably arise from the action of the venom. The reddish deposits seen on the hairs are said to be the fæces of the parasite. The eggs may be seen as small, oval bodies attached to the hairs.

Diagnosis.—The diagnosis depends upon the history of pruritus of a more or less severe type, usually worse in some given region, and by the appearance of scratches associated with the little papules and the discovery of the lice on the body or in the clothing, which must be that usually worn by the patient. The rare diffuse pigmented forms of pediculosis may be mistaken for Addison's disease or the suprarenal form of malaria, but may be recognized by the finding of the lice, the non-diminution of the muscular power, and by the presence of the pruritus. From scabies it may be distinguished by the lack of lesions on the hands and wrists, and the absence of the sarcoptes.

Treatment.—*Pediculosis capitis* may be treated by soaking the hair with petroleum (care being taken not to approach a light), followed by a good wash with soap and water, the whole process being repeated in twenty-four hours. Another method is to sponge the hair little by little with carbolic acid (1 in 40), or soak long hair in carbolic lotion (1 in 80) followed by a good wash with soap and water, and later by a lotion of acetic acid (25 per cent.), used to loosen the eggs, which are then removed by the use of a small-toothed comb.

Another method of killing the parasites is by dabbing the hair with xylol, remembering, however, the danger of fire with this inflammable substance.

Impetigo contagiosa may be treated by an ointment composed of ammoniated mercury (5 grains) and lard (1 ounce), and in children the hair may be cut and this ointment may be applied.

Pediculosis corporis.—The clothing and the bedding must be disinfected by steaming or boiling, and the patient must have several large baths, with free use of soap and water, as well as a soothing calamine lotion (40 grains calamine to 1 ounce of water) for application to the irritated skin. Lice destruction is more fully detailed on pp. 1338, 1339.

It is important to remember that the eggs of *P. corporis* are often attached to the lanugo hairs. Merely cleaning the clothing is often useless. Rub or spray the whole body with paraffin and take a warm bath.

Martini recommends a depilatory consisting of strontium sulphate 2 parts, zinc oxide 1 part, talc 1 part. This is mixed with a little water and applied as a paste for ten minutes, when it is removed and some olive oil used to soothe the irritation.

Pediculosis pubis.—A white precipitate ointment (5 to 10 per cent.) or an ointment of oleate of mercury (5 per cent., 6 drachms) with ether (2 drachms) will kill parasites and ova, after which calamine lotion may be applied to allay the irritation.

Clinocorosis.

Bugs produce wheals, with central red spots surrounded by zones of hyperæmia. A solution of menthol (5 grains in 1 ounce of rectified spirits) will relieve the irritation; or, if the area has been scratched, the application of a lotion of carbolic acid (1 in 40) is preferable. As regards prophylaxis, see p. 765.

Siphonapteriasis.

Flea-bites are characterized by small red papules with dark red centres, and are to be distinguished from the maculo-papules of enteric fever, which disappear on pressure. The linen of a person probably suffering from flea-bites should be inspected for the brown fæcal marks made by the fleas. For further details, see pp. 857 and 908. To keep these pests away, some powdered camphor may be used.

Formiciasis.

Ant-bites usually only produce local pain, inflammation, and swelling; but the larger tropical ants may cause faintness, shivering, and even temporary paralysis by their bites. In Ceylon the very small ants, which infest the beds, produce urticarial pomphi. These bites are best treated by applying a solution of carbolic acid (1 in 20), and as a preventative against ants infecting beds some powdered camphor may be dusted in the sheets (see p. 222).

2. Dermatites caused by Blistering Fluids excreted by the Adult.

The insects which act in this manner are the well-known '*blister beetles*' (*vide* p. 226), which cause the eruption called 'Seasonal bullous dermatitis' (synonym, Seasonal vesicular dermatitis), which we will now describe.

SEASONAL BULLOUS DERMATITIS.

Definition.—Seasonal bullous dermatitis is characterized by an epidemic of bullæ of varying size and shape in healthy people at a definite season of the year. The bullæ or blisters are followed by sensations of itching, burning, or pain, and are caused by blister beetles.

Historical.—Beetles have been known to cause blisters and eschars on the skin since the days of Archigenes, a contemporary of Celsus, or, according to other authors, since the time of Aretæus the Cappadocian. Pliny says that authorities differ as to the origin of the blistering fluid, some thinking that it comes from the mouth and others from the feet. Moffat, in 1634, wrote a long chapter on these insects, and Linnæus, Fabricius, and Latreille gathered together quite an amount of information on these beetles and their varieties.

In 1890 Beauregard wrote a large book on 'Les Insectes Vésicants,' but notwithstanding all this ancient and modern knowledge works on tropical medicine were singularly silent on the subject.

In 1912 P. Da Silva drew attention to an outbreak of this eruption among cultivators on the banks of the rivers São Francisco, Itapicurû, and Jacuricy, in the interior of Bahia, which was traced to a vesicant beetle, *Pæderus columbinus*. In 1913 Adolf Eysell mentioned *P. peregrinus* as the cause of the same eruption in the island of Sunda, in the Malay Archipelago. In 1915 Rodhain and Houssiau saw the disease in Léopoldville, in the Belgian Congo, and Bequaert at Boma. In 1916 P. A. Ross noted it at Nairobi, in British East Africa, and in 1917 Chalmers and King gave an account of its occurrence in Khartoum, Anglo-Egyptian Sudan.

Ætiology.—The blisters are caused by the fluid which exudes from the joints of the legs, especially the so-called knee-joint of certain species of insects belonging to the order *Coleoptera* Linnæus, 1735, and to the families *Staphylinidæ* Leach, 1817, and *Cantharidæ* Leach, 1817. The following is a list of those known to cause the complaint, though doubtless many more insects can do so equally well:—

Staphylinidæ :—

Pæderus columbinus de Laporte, 1832.
Pæderus peregrinus Fabricius, 1801.
Pæderus cerebripunctatus Epp (?).

Canthuridæ :—

Epicauta sapphirina Macklin, 1845.
Epicauta tomentosa Macklin, 1845.

The seasonal occurrence is due to the fact that the adult insects are only present for a limited period in the year, the remainder of which is occupied by the long and complicated development.

Symptomatology.- So long as the insect merely walks over the skin, and is not irritated, it does no harm. If, however, it starts to crawl up the arm, down the neck, or up the trousers, it is soon annoyed by the clothing and excretes the blistering liquid.

If only a small quantity of this fluid is ejected, then only a single small bulla may form, but if the insect moves a series of these may be produced. If, however, the blistering fluid is well rubbed into an area, then an eschar forms, with considerable surrounding irritation. Occasionally, instead of a series of blisters, one long blister may extend a considerable distance along the forearm or down the back.

Usually there are no immediate symptoms, and it is only after an interval of twelve to twenty-four hours that an itching or burning sensation, or even severe pain, invites attention to the affected area, when the blister or blisters, varying in size and number, as already stated, are to be found full of yellowish serum and situated on an erythematous areola.

As a rule the victim does not see the insect and may not remember one crawling on him, and he may be entirely at a loss to account for the blisters. It is here that the difficulty of diagnosis arises in that the practitioner may see only one or two cases, and at the moment may not think about these insects.

If pricked and carefully treated, they quickly vanish and cause no further trouble: but if they burst, and are allowed to be rubbed by the clothing, they become raw, very tender, and painful a condition which may last for days.

More rarely a considerable portion of the blistering liquid appears to get well rubbed into one spot, and then a small white eschar is formed which may be surrounded by an extensive inflammatory areola, with its surface raised above the central necrotic area and covered with numerous small red papules. The whole region becomes very painful and tender, and some couple of weeks elapse before healing is completed, which generally takes place without any cicatrization. Secondary septic infections are rare. After being *en evidence* for some three to four weeks, the beetles disappear and the epidemic ceases for the year.

Diagnosis.—The characteristic features of seasonal bullous dermatitis are as follows:—

1. The sudden appearance of bullæ, varying in size and number, surrounded by a certain amount of inflammatory redness.

2. The persons in whom the bullæ are found are usually in good health, and as a rule they are unable to assign a cause for the eruption.

3. The bullæ are single or grouped together, often in a row.

4. There is no tendency to bilateral symmetry.

5. In a given individual usually only one region of the body is affected.

6. A number of healthy people living in the same place may be similarly affected at the same time.

7. The bullæ only appear during a certain season of the year.

The differential diagnosis requires to be made from the following accidents and diseases causing bullæ:—

1. Seasonal bullous dermatitis may be readily separated from the bullæ caused by burns and scalds, and by chemicals, by the history of the case.

2. It has also to be differentiated from the various forms of Hydroa as follows:—

(*a*) It can be separated from the milder forms of dermatitis herpetiformis by the absence of severe itching and of circinate and papular erythematous lesions, and by the absence of the tendency of the bullæ to be grouped like herpes.

(*b*) From the rare form of dermatitis herpetiformis called hydroa pruriginosa it can be diagnosed by the larger size of its bullæ, which do not appear in successive crops.

(*c*) From dermatitis recurrens it can be distinguished from the hiemal variety by only appearing in warm weather, and from the æstival in not being papulo-vesicular in character.

3. It may be differentiated from herpes zoster by the absence of severe pain, lasting for three to four days before the appearance of the eruption, and by the non-distribution of the bullæ in Head's areas.

4. From Acute Pemphigus it is easily separated by the absence of the severe constitutional symptoms.

5. It can be recognized as distinct from dermatitis venenata, due to plants, by the absence of the marked œdema and erythema, which generally attack the face, hands, and genitalia, and by the presence of bullæ.

6. It is easily separable from Dermatitis caused by mites, as these give rise to small wheals and vesicles, and not to bullæ.

7. Ant and tick bites, stings of wasps, bees, scorpions, centipedes, etc., are at once differentiated because the eruption in the present instance is bullous.

As the eruptions described by Rodhain and Houssiau and by Ross are stated to be vesicular, it is possible that these may be differentiated clinically from this bullous type, while it certainly is not so severe as the eruption described by P. Da Silva, in that ulceration and cicatrization are absent, but perhaps these may be only differences in details and not in essentials.

Prognosis.—This is good. Cases recover fairly rapidly and as a rule without cicatrization, hence the outlook as regards rapidity of cure and the absence of scarring is good.

It will, however, be remembered that P. Da Silva describes a much severer form of dermatitis than that mentioned here, and that this was followed by cicatrization.

Treatment.—The best treatment is to prick the blister and apply a dressing of 1 in 80 carbolic acid, but the majority of the victims just let the lesions alone, and they heal up rather more slowly than when treated and are more painful. If they become rubbed, they are often very painful.

3. Dermatites caused by Stings of Adults.

Stings are mainly caused by species belonging to the family Apidæ of the Hymenoptera, which includes the bees and wasps. A description of these stings will be found on pp. 219-222.

4. Dermatites caused by Larvæ.

The larvæ of various species of the Œstridæ and Muscidæ are compelled to undergo their development in the skin of some warm-blooded animal, and as these are plentiful, as a rule the flies do not attack man, who only occasionally suffers from their effects, and when he does the pathological condition is usually named dermal myiasis (p. 1631). Other larvæ—as, for example, that of *Auchmeromyia luteola* Fabricius, 1805—are blood-suckers.

Blood-sucking Dipterous Larvæ.

Only a very few blood-sucking dipterous larvæ are known, and these belong to two genera, which may be distinguished from one another as follows:—

A. Abdomen long and narrow, with unequal segments and distinctly longer than the thorax—*Auchmeromyia* Schiner and Bergenstamm, 1819.

B. Abdomen short and broad, with equal segments and but little longer than thorax—*Chœromyia*, Roubaud, 1911.

There are two species belonging to the last-named genus—viz.:—

Chœromyia chœrophaga Roubaud, 1911.
Chœromyia boneti Roubaud, 1911.

Neither are known to attack man. They live in the burrows of the wart-hog and the ant-bear in the Sudan. There are also two species belonging to *Auchmeromyia*—viz.:—

Auchmeromyia luteola (Fabricius, 1805).
Auchmeromyia prægrandis Austen, 1910.

Both these may attack man.

Auchmeromyia luteola (Fabricius, 1805) lays its eggs in soil contaminated with fæcal matter or urine around or inside native huts in the Congo (hence its name *Congo floor maggot*), Central and Northern Mozambique, Eastern Transvaal, East Africa, Nyassaland, and Kordofan. The larva, escaping from the egg, seeks the cracks and crevices in the mud floors of these huts or pass into dirty native mats. When hungry, these larvæ are thermotoxically drawn to a temperature of 38° C., and hence they attack man, both biting and sucking blood. When replete, the researches of Roul and show that they are no longer thermophilus. Under favourable conditions the larvæ become pupæ in some fifteen days, but under unfavourable circumstances larval existence may be prolonged for seventy-six days. Only the larvæ are blood-suckers, and they may be killed by sprinkling the floor with Jeyes' fluid.

Auchmeromyia prægrandis Austen, 1910, is found in South Africa.

IRRITATING LEPIDOPTEROUS LARVÆ.

The larvæ or caterpillars of many genera of Lepidoptera are well known to possess tegumentary glands, which secrete an irritating fluid, which passes from the gland to hollow hairs. These are the instruments by which the caterpillar injects this fluid into the skin, causing erythema and irritation.

White gives long lists for Europe and America, while Wellman has studied the subject in Angola, where he mentions larvæ belonging to the Arctiidæ, Limacodidæ, and Liparidæ, and gives details concerning one—viz.:—

Ochipia is a native name signifying 'that which burns,' and is applied to the larvæ of the tiger-moth, which is very irritating.

IRRITATING COLEOPTEROUS LARVÆ.

Wellman says that in Angola there is a coleopterous larva called *Ochisia* (*Noli me tangere*), which possesses bristles which can penetrate into the sole of the foot and cause pain, inflammation, and sloughing. It is related to the genus *Drilus*, of the Malacodermata.

DERMAL MYIASIS.

This subject has been discussed in Chapter LXVII., p. 1631, and need not be further mentioned, except to invite attention to Baier's work, published in 1740, entitled 'De generatione insectorum in corpore humano,' and Clarke's paper in 1797 to the Linnæan Society of London, establishing the relationship between the larvæ and the adult insects in the Œstridæ. Smith's paper at the 1881 International Medical Congress is also of interest.

Creeping Eruption.

Synonyms.—Larva migrans. *Bulgarian :* Nova Bolest, Pulziasta Bolest. *German :* Hautmaulwarf. *Northern Nigeria :* Larbish or Œrbiss.

History.—This disease was first described by A. Lee in 1875. Later on, Procke, Blanchard, Topsent, Füllebørn, Macfie and others have recorded several cases. It is not rare in some parts of Europe, Africa, and Asia, and in South America. We have seen numerous cases in Ceylon. It is extremely rare in North America.

Ætiology and Pathology.—Larvæ of the genera *Gastrophilus*. *G. hæmorroidalis* and *G. nasalis*, *Œstromya satyrus*, *Hypoderma* *bovis*, and *H. lineata* have been found in several cases. In others no larva whatever was found. Looss states that the same clinical picture may be caused occasionally by ancylostoma and strongyloides (*Anguillula*) larvæ, or even by an inanimate object like a piece of horsehair.

Fig. 866.—Larva Migrans.

Symptomatology.—The eruption is characterized by the presence of a narrow raised red line, $\frac{1}{8}$ to 1 inch broad. This line extends daily one or several inches, and is generally sinuous, but may be straight. While the advancing end progresses, the opposite end slowly fades away. The duration of the malady is long—generally several months, but occasionally two or three years. There is much pruritus.

Treatment.—Hypodermic injections of various disinfectants have been tried with little success. Hutchins recommends a cocaine injection, followed by the injection of 1 or 2 drops of chloroform.

Circinate Creeping Disease.

In Ceylon cases are met with of a peculiar eruption, which is possibly of the same nature as the creeping disease previously described, though larvæ were not found.

The condition is characterized by the presence on the back of the hands of a ringed eruption, with markedly elevated, thick, angry, red borders. In all the cases the eruption started suddenly after the patient had been gardening and handling turf. There may be one ring or several. The skin inside the rings is normal. The rings expand excentrically. The patients complain of the extreme irritation, and in all the cases stated that they felt something creeping along the red circles, as though a worm had got inside in handling the turf. The duration varies, but it generally does not exceed two or three weeks.

Ætiology.—The eruption does not appear to be a form of dermatitis venenata, due to touching certain plants and vegetables. Possibly it is due to some larva entering the skin, but so far the search for larvæ has been fruitless. No trichophyton-like fungus is present.

Treatment.—Liq. plumbi and other soothing applications are generally useless. The best results are obtained by continuously applying on lint a diluted alcoholic solution of resorcin:—

Resorcin	ʒi.
Sp. rect...	℥ii.
Aq. dest.	ad ℥xii

Dermatitis Macrogyrata.

Dermatitis macrogyrata is a rare condition found in Ceylon and South India, of unknown causation, and characterized by the presence on the palms of the hands of one or two very large gyrations formed by scaly and crusty lesions. On removing the crusts and scales a broad shallow furrow can be seen situate in the epidermis. The eruption is associated with pain, sometimes severe, but there is seldom any pruritus. The condition is most persistent, and in our cases neither fly larvæ could be found nor fungi isolated. In none of our cases was there history of syphilis, and potassium iodide and mercury had no effect. The treatment is most unsatisfactory. Antimycotic substances, such as chrysarobin and tincture of iodine, have no effect. The application of a lotion of liquor plumbi (ʒii.), tincture of opium (ʒi.) diluted with 8 ounces of water, or of dressing soaked in 0·5 per cent. of resorcin, may cause a slight improvement.

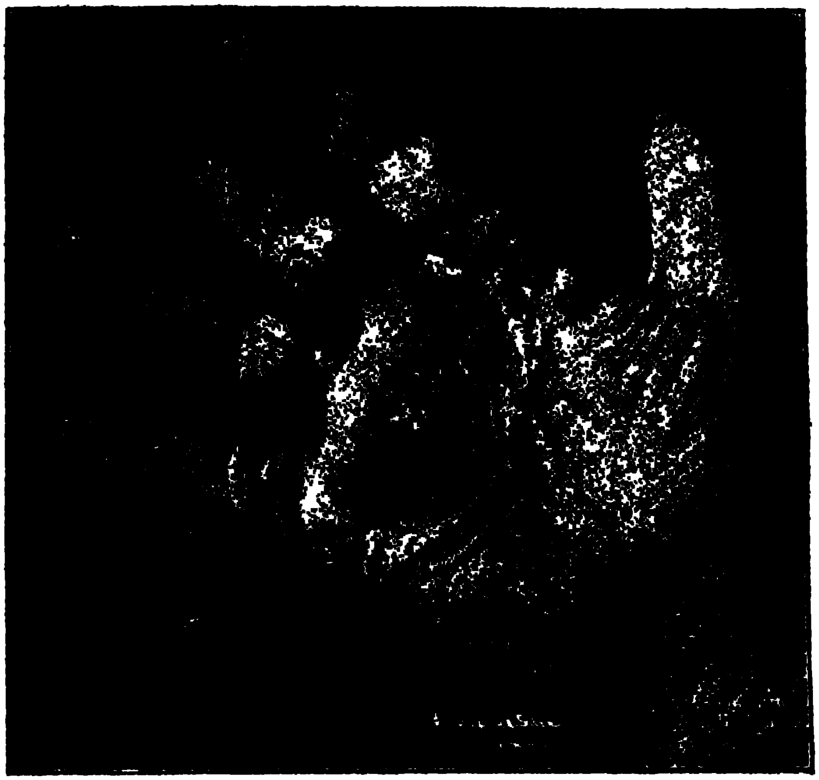

Fig. 867.—Dermatitis Macrogyrata.

5. Dermatites caused by the Presence of the Imago.

At times the impregnated female insect burrows into the skin while the eggs mature.

A good example of this is *Dermatophilus penetrans* Guérin, 1838.

Dermatophiliasis (Jigger).

Synonyms.—Nigua (Honduras), Chique (Salvador), Chica (Columbia), Bicho, Tunga (Brazil), Pique (Argentine), Chique (French Colonies).

Definition.—Dermatophiliasis is the invasion of the skin and subcutaneous tissue by the pregnant female jigger (*Dermatophilus penetrans*).

Remarks.—The home of the jigger is in tropical America, from 23° N. to 28° S., but it and its wanderings over the world have been sufficiently described on p. 862. At present it is found in South America, West and East Africa, Madagascar, Uganda, India, and, it is said, China.

Pathology.—The pregnant female jigger pierces the skin obliquely near the nails and between the toes, but it may occur in any part of the foot, and even on the arms, scrotum, and face. All but the last two segments are embedded in the skin. These last segments plug the orifice and discharge the eggs.

Symptomatology.—The symptoms begin with itching and irritation, generally in some part of the foot, especially the toes, and often under the toe-nail. On inspection, a small dark dot (the last two abdominal segments of the parasite) is noticed in the skin. If left alone, painful inflammation and suppuration develops around the distended abdomen of the parasite, giving rise to a swelling which may attain the size of a small pea, in the centre of which is seen a depression containing the black dot, and, finally, ulceration takes place, and the body of the parasite is thrown off, but not until all the eggs are laid.

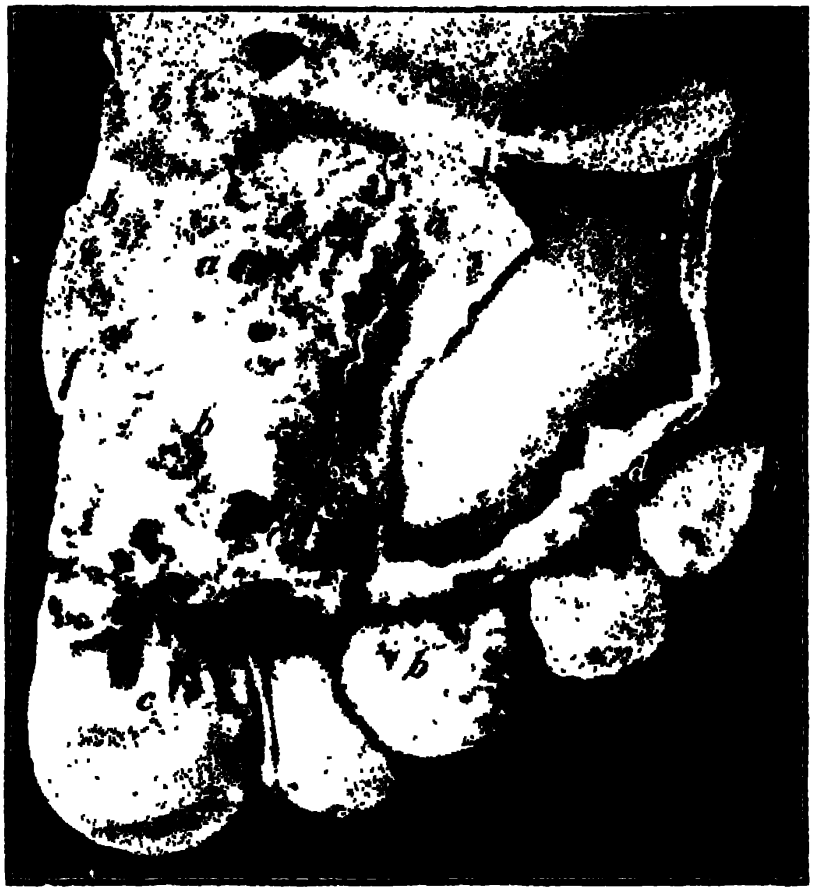

FIG. 868.—DERMATOPHILIASIS. (After Newstead.)

a, Group of jiggers; *b*, isolated jiggers; *c*, pits left by jiggers; *d*, lateral view of jiggers deep in the skin.

When the parasite has been dislodged by treatment or suppuration, a small ulcer is left, which is very liable to septic or other bacterial infections. These infections may lead to phagedæna, gangrene, and tetanus. When the feet are badly affected, walking is impossible, which is of especial importance in carriers and native troops.

Treatment.—The treatment is the careful removal of the little insect with a clean needle, after rubbing weak carbolic ointment (1 per cent.) or lotion (1 to 2 per cent.) into the foot, and cleansing and dressing the little wound antiseptically with a lotion of perchloride of mercury.

In cases of heavy infection, Quirós recommends the use of petroleum, or of an ointment consisting of salicylic acid 1 part, ichthyol 4 parts, vaselin 4 parts.

Prophylaxis.—Prophylaxis consists in keeping the house clean, and pigs, poultry, and cattle kept away therefrom. High boots should be used, and especial care should be taken not to go to a ground-floor bathroom with bare feet. The feet, especially the toes and under the nails, should be carefully examined every morning to see if any black dot can be discovered, when the jigger should be at once removed, and in this way suppuration will be prevented. It is advisable, also, to sprinkle the floors with carbolic lotion, Jeyes' fluid, or with pyrethrum powder, or with a strong infusion of native tobacco, as recommended by Low and Castellani.

II. CHILOPODE DERMATITES.

Centipedes, when they bite, cause local itching followed by intense pain, which spreads over the whole limb when the bite is on an extremity. A red spot appears at the site of the bite, and this enlarges and becomes black, and is sometimes associated with lymphangitis, adenitis, headache, vomiting, dizziness, irregular pulse, and mental anxiety.

The treatment is to bathe the parts with a solution of ammonia (1 in 5 or 1 in 10), and to apply a dressing of the same solution, and if there is much swelling an ice-bag, while if the pain is severe, an injection of morphia may be necessary; while later, fomentations are required for the local inflammation (see also pp. 217-218).

III. ACARINE DERMATITES.

The *Acarine Dermatoses* include the skin lesions caused by the ticks and mites. The tick bites are described on pp. 215 and 217. The mites (pp. 690-693 and 724-732) which most commonly attack man are:—

DERMANYSSINÆ.

Dermanyssus gallinæ de Geer, 1778.

Dermanyssus hirudinis Hermann, 1804.—These mites produce a papular eczematous dermatitis in poultrymen.

Holothyrus coccinella Gervais, 1842, cause a swelling in the part attacked.

TROMBIDIDÆ.

Microtrombidium akamushi Brumpt, 1910, is the cause of Tsutsugamushi disease.

Microtrombidium holosericeum Linnaus, 1746, has a larva (*Leptus autumnalis*) which causes irritation in England in the autumn, and is called the harvest mite. As a fairly effective preservative for this pest the following may be used:—Oil of lavender ♏viii., spirit of camphor ♏xxx., oil of eucalyptus ʒi., soap liniment ad ℥i.

Trombidium tlalsahuate Lemaire, 1867, is the tlalsahuate of Mexico, which, with the allied species called the balata mite of the Guianas, are well-known plagues, burrowing into the skin, and causing intolerable itching and painful little blisters; but the zoological names of these, as well as of the 'pou d'agonte' of Guiana, the 'niaibi' of New Granada, the 'colorado' of Cuba, the 'mouqui' of Para, and the 'bête rouge' of Martinique and Honduras, are not known.

Trombidium wichmanni Oudemans, 1905, is the gonone of Celebes, whose larvæ attack man, burrowing into the skin as just described above.

Trombidium vandersandei Oudemans, 1905, is the gonone of New Guinea, which acts like *T. wichmanni*.

The *Leptus* stage of an unknown *Trombidium* is reported in North Queensland.

TETRANYCHIDÆ.

Tetranychus molestissimus Weyenbergh, 1886, causes severe itching in the Argentine and Uruguay during the months December to February, by thrusting its hypostome into the skin, and thus causes 'Bicho-colorado itch.'

EUPOPIDÆ.

Tydeus molestus Moniez, 1889, is the cause of 'Guano itch.'

TARSONEMIDÆ.

Pediculoides ventricosus Neuport, 1850, is the cause of 'grain itch,' and being a parasite of the pink bollworm of cotton, is found in cotton infested with this pest, and from this source has attacked persons handling the infected cotton in Egypt and England.

Tarsonemus uncinatus and *T. intectus* are also known to attack man.

TYROGLYPHIDÆ.

Tyroglyphus longior Gervais var. *castellanii* Hirst, 1912, is the cause of 'copra itch.'

Tyroglyphus siro Linnæus, 1758, and *Aleurobis farinæ* de Geer are believed to be the cause of vanillismus.

Glyciphagus prunorum Hermann is the cause of 'grocer's itch.'

Rhizoglyphus parasiticus Dalgetty, 1901, is the cause of a type of so-called 'coolie itch' of the feet. Bell states that it causes a large circular superficial sore on the sole of the foot. 'This is produced by numbers of the parasite invading the skin.

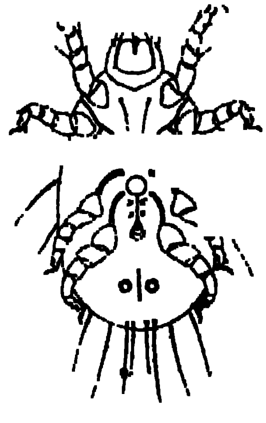

FIG. 869.—*Rhizoglyphus parasiticus*: MALE. (After Dalgetty.)

SARCOPTIDÆ.

Sarcoptes scabiei var. *hominis* Linnæus, 1758, is the cause of scabies in man.

In addition to this common parasite, there are several varieties, usually occurring in the domestic animals, which may at times attack man—*e.g.*, *Sarcoptes scabiei* var. *canis*, found in the dog; *S. scabiei* var. *ovis* in the sheep;

S. scabiei var. *equi* in the horse; *S. scabiei* var. *suis* in the pig; *S. scabiei* var. *auchenia* in the lama; *S. scabiei* var. *cameli* in the camel.

Notœdres cati var. *cati* Hering, 1838, found in cats, may occur in man.

DEMODICIDÆ.

Demodex folliculorum Simon, 1842, is said to be the cause of certain inflammations in seborrhœa. Some authors consider them to be of importance in the carriage of certain diseases, such as leprosy and cancer.

Rarer Acarinæ, which attack man occasionally, are *Trombidium striaticeps* Heim and Oudemans, 1904, on fowls and dogs; *T. americanum* Riley and *T. irritan* ; *Metatrombidium poriceps* Heim and Oudemans, 1904, on fowls and dogs; *Microtrombidium meridionale* and *M. pusillum* Hermann.

Copra Itch.

Definition.—A very pruriginous dermatitis, found in people handling copra, and caused by *Tyroglyphus longior* Gervais var. *castellanii* Hirst (p. 729).

Historical and Geographical.—This dermatitis was described by Castellani in 1911, who observed it in Ceylon in people handling copra, and considered it to be due to an acarus-like parasite, swarming in many samples of copra. He sent the specimens of the parasite to Hirst, who described it as a new variety of *Tyroglyphus*—*Tyroglyphus longior* Gervais var. *castellanii* Hirst.

Castellani's researches have been recently confirmed by Graham Little, Whitfield and Ditlevsen.

Ætiology. — The mite is present in huge numbers in certain samples of copra, and may occasionally be found on the skin of the patients, but remains on the skin only temporarily, as it does not bury itself. It apparently induces the dermatitis in the same manner as *Pediculoides ventricosus* Neuport, which lives in diseased cereals, produces an eruption in persons handling such cereals.

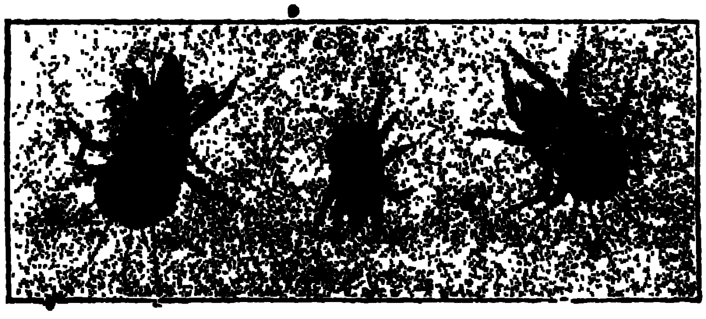

FIG. 870.—MICROPHOTOGRAPH OF THE TYROGLYPHUS OF COPRA ITCH. (×40.)

Experimental Reproduction.—When copra dust containing the mite is rubbed into the skin, itching frequently begins very shortly after, and twenty-four to forty-eight hours later an extremely pruriginous urticarial or papuloid eruption often develops. The same result is obtained by picking the mites out of copra dust and placing them (alone, without any dust) on the skin under a covering, such as a piece of lint kept in place by a bandage. The pustular stage did not occur, but this being due to scratching and secondary pyogenic infections, there was no time for it to develop, all the people refusing to go on with the experiment after the second day. Some individuals seem to be unaffected by the presence of the mite or the copra dust containing it.

Symptomatology.—The hands, arms, legs, and sometimes the whole body except the face, present fairly numerous, very pruriginous papules, often covered by small, bloody crusts due to scratching; papulo-pustules and pustules are also generally present. The eruption has no tendency to spontaneous cure while the patient goes on working in the infected mills.

Diagnosis.—On superficial examination the condition may be easily mistaken for scabies, but burrows are not present and the two parasites are very different.

Treatment.—The best treatment is the daily application of β-naphthol ointment (5 to 10 per cent.). The action in these cases cannot be compared to what takes place in scabies, because in copra itch the acarus-like parasite remains for only a short time on the body, and in most cases when the ointment is applied at night the mites are no longer there. It may act as an antipruritic antiseptic, and in this way diminish scratching and secondary pyogenic infections. It is probable also that a small amount of the ointment may remain on the skin after the morning bath and be repellent to the mite, in this way preventing the daily reinfection which otherwise takes place.

Grain Itch.

Synonyms.—Straw itch, Barley itch, Dermatitis Schambergi, Urticarioid Dermatitis, Dermatitis Ditropenotus, Aureoveridis, Acara Dermatitis urticarioides, Schamberg's disease, Straw-mattress disease, Cotton-seed Dermatitis.

Definition.—Grain itch is a dermatosis caused by *Pediculoides ventricosus* Neuport, 1850 (*vide* Figs. 343-345, p. 728).

History.—During the last fifty to sixty years this disease has been recognized in Europe, but only since 1901 in America, when Schamberg described it. In 1909, Goldberger and Schamberg found that it was caused by the same mite as in Europe. Since 1914, when Willcock drew attention to the matter, it has been well known to be present in cotton seed infested with the pink bollworm, of which it is a parasite, and from which it has passed to man to Egypt and England.

Climatology.—It is found in Algeria, where it is common, and in other parts of Northern Africa, in Italy, and it is said to occur in India. Cases have also been recorded from France, England, Austria, and Germany. In France there was an epidemic as long ago as 1850 in Bordeaux. In 1867 some cases were found in the department of Indre and in 1872 in the Canton of Creon.

Ætiology.—The disease is caused by *Pediculoides ventricosus* Neuport, which usually feeds upon the wheat-straw worm (*Isosoma grande* Riley), the joint worm (*Issoma tritici* Fitch), the Angoumois grain moth (*Sitotropa cerealella*) and the caterpillars of the cotton moth (*Gelechia gossypiella*). The mite attacks people; it attaches itself to the skin by its sucking discs and claws, and probably injects some irritaing substance into the skin while attempting to obtain nourishment.

Symptomatology.—The mite causes an urticarial and papuloid eruption on the breast, arms, face, neck, and shoulders of persons handling corn and barley, or cotton seed, which has no tendency to spontaneous cure while the people continue to handle the infected grain. The symptoms begin after an incubation of twelve to sixteen hours with itching and the appearance of wheals surmounted by vesicles, which are usually about the size of a pin's head. These vesicles may at times pustules in a few hours. Severe cases show febrile symptoms, vomiting, and albuminuria.

Diagnosis.—The presence of an eruption somewhat resembling lichen urticatus in people handling grain or straw or cotton seed, or sleeping on new straw mattresses, should always arouse suspicion of the presence of this mite, and search for it should be made in the grain or straw or cotton seed.

Treatment.—The treatment consists in removal of the cause—*i.e.*, of handling the infected grain—and the application of soothing lotions, such as calamine lotion, or a dilute carbolic acid or acetic acid lotion.

Scabies.

Synonyms.—Scabrities, Psora (term wrongly applied), Itch, Courap (=itch Bontius), Scabies indica (Sauvages), La gale (French), Kraetze (German), Sarna (Madeira), Scabbia (Italian).

Definition.—Scabies is an infection of the superficial layers of the skin by the female of *Sarcoptes scabiei* var. *hominis* (Linnæus, 1758), which, making a minute opening into the horny layer, forms a burrow more or less parallel to the surface, and in so doing causing itching. Secondary lesions are vesicles (of which the most typical is at the far end of the burrow, immediately beyond which lies the acarus), scratches, scabs, pustules, and a superficial dermatitis.

History.—Aristotle appears to have known the itch insect, but if this is true the knowledge was lost, and certainly Avenzoor in the twelfth century deserves the credit for discovering or rediscovering it. Scaliger, in 1557, described it as being globular in form and so minute as to be scarcely perceptible. He says that the people of Turin called it *scirro*, while in Gascony it was known as *brigant*. He also described the burrows, and in 'Exercitatio 194, de Subtilibus,' numero 7, he states that when extracted it shows a certain amount of movement, and when crushed between the nails causes a slight noise and emits a little fluid. After this it was described by Ingrassius of Naples, by Gabucinus, by Jobertus, by Aldrovandus, but more especially by Mouffet in his 'Insectorum,' completed in 1589. In 1654 Hauptmann, who called the acari 'Reitleisen,' published the first figure of the mite in 1654 and again in 1657. He was followed by Haffenreffer in 1660, by Heintke in 1675, who gave extraordinary illustrations of the arachnid, and by Ettmuller in 1682, whose illustrations are recognizable. In 1683 Bonomo and Cestoni published their letter to Redi on the subject, and in 1702 this communication was read by Mead before the Royal Society, and published in the Philosophical Transactions. Bonomo described and figured the egg. He was followed by Morgagni in his fifty-fifth letter, Book IV., by Bonanni in 1691; by Linnæus in 1767, who named it *Acarus* in his 'Systema Naturæ,' calling it *Acarus exulcerans*, but earlier in 'Entomologia Faunæ Suecicæ' he termed it *Acarus humanus subcutaneus*, and in the thirteenth edition of the 'Systema,' 1788, *Acarus siro* is separated from *Acarus scabiei*. It was described by Schaeffer in 1766, by De Geer in 1778, by Fabricius in 1780, by O. F. Müller in 1776, and by Latreille as *Sarcoptes hominis*; by Baker in 1744, by Casal in 1762, by Wichman in 1786, and by Adams in 1905. Adams says that in Madeira there is a disease due to ouçoes which is not itch, being associated with fever, but is due to a small animalcule. Excluding the observations (*sic*) of Galés we next come to Gras' pamphlet which appeared in 1834, and to Raspail's work which was also published in the same year, and which established firmly the belief in the arachnid.

In 1861 Fuerstenberg wrote a monumental work on the subject entitled 'De Kratzmilben der Menschen und Thiere.' Finally, in 1915, Charles Singer wrote an interesting history of the small animalcule. Notwithstanding all this scientific work, the dermatologists were for long sceptical as to the causal action of the small parasite—*e.g.*, Bateman—but Erasmus Wilson, in 1842, was quite clear on this point.

Climatology.—Scabies is known all over the world, and has local names in all localities. It is very common in the tropics, and is more frequently met with in the low country than in the hills.

Ætiology.—The causal agent is the mite *Sarcoptes scabiei* var. *hominis* (Linnæus, 1758), which lives on the surface of the skin, but after impregnation the female burrows into the epidermis, making a little orifice marked by slight fraying of the horny layer. From this orifice it slowly works its way more or less parallel to the skin, but penetrating deeper and deeper. In so doing it deposits fæces and eggs along the burrow, while the mite itself lies buried in the horny layer at the far end of the burrow and just beyond a small vesicle, which often marks its position. It may be obtained by opening the burrow by means of a fine needle until it reaches the grey speck which marks the mite, which can then be extracted. The female finally dies in the burrow, and the males are believed to expire after copulation, but the species is kept in existence by the eggs, which produce six-legged larvæ in some four to eight days. These moult several times, and then become the eight-legged nymph, without fully developed sexual organs, which finally becomes the sexually mature mite. The adult female is 330-450 microns in length, but the male is smaller.

More rarely 'scabies' may be caused by the mite belonging to an animal, but the infection in this instance does not last long.

The vesicles and the irritation are thought to be caused by excretions from the mite.

Infection generally takes place by contact, and hence is more common among the poor, who are crowded together, whereas in the better classes it usually begins about the generative organs, and is usually thought to be spread by sexual intercourse.

Symptomatology.—The primary symptom is itching, especially when warm and when in bed, while the first clinical sign is a small line on the surface of the skin, and which may be reddish. If this line is carefully examined with a lens the orifice of entry may be found as well as a minute vesicle at the farther end, but this may be absent. Just beyond the end of the burrow a small body of greyish glittering appearance may be seen in the depth of the epidermis if examined by means of a lens. This body is the mite.

In addition to these primary lesions secondary signs may be visible in the form of scratches, papules, pustules, and even eczematous patches.

The primary sites are between the fingers, the wrists, the ulnar side of the hands, the elbows, the front of the armpits, the nipples, the umbilicus, the penis, the gluteal regions, and between the toes.

In the tropics in cleanly people it is often confined to the scrotum.

Diagnosis.—The characteristic signs are the burrows and the distribution of the eruption, while the basis of the diagnosis is the discovery of the mite.

Treatment.—Order the patient to take a hot bath and to scrub himself all over with soap and water, and then to rub all over the body sulphur ointment of the British Pharmacopœia from the margin of the hairy scalp to the soles of the feet. Next day only the face is washed, and that night more ointment is rubbed in, and the same treatment is applied another night. Then on the fourth a hot bath is taken and all the clothing and bed linen changed, the old underclothing and bed linen being disinfected by being placed in boiling water.

This usually cures the eruption, but a recurrence may occur in about a week if any ova have survived, and may require a repetition of the treatment.

The sulphur ointment may cause a slight dermatitis with itching, which may be mistaken for a recurrence of the affection. In order to cover the odour of the sulphur a few drops of oil of lavender may be added.

Prophylaxis.—Every person suffering from itch should be carefully and promptly treated in order to avoid epidemics.

The horse, sheep, dog, cat, wolf, fox, pig, poultry, and many other animals, suffer from scabietic conditions due to mites more or less closely allied to the *Sarcoptes scabiei* of man. These mites may occasionally be transferred to man, and induce a dermatitis which clinically may resemble scabies, though as a rule much less severe.

IV. NEMATODE DERMATOSES.

Several species of the Nematode cause dermatoses—*e.g.*, *Rhabditis niellyi* Blanchard, 1885 (p. 627), *Strongyloides stercoralis* Bavay, 1876 (p. 628), *Filaria bancrofti* Cobbold, 1877 (p. 633), *Onchocerca volvulus* Leuckart, 1893 (p. 649), *Loa loa* Guyot, 1778 (p. 645), *Agamofilaria georgiana* Stiles, 1906 (p. 642), *Ancylostoma duodenale* Dubini, 1843 (p. 666), and *Necator americanus* Stiles, 1902 (p. 673).

The most important of these is the dermatitis caused by the two last-named worms. This dermatosis is described under the heading Ankylostomiasis on p. 1764.

V. CESTODE DERMATOSES.

The cestode dermatoses are usually due to *Sparganum prolifer* Ijima, 1905 (p. 606), which produces nodules in the skin, which are associated with considerable swelling, thus giving rise to an appearance not unlike elephantiasis. In addition, there may be an acne-like eruption all over the body, which is very irritable and causes pruritus. On scratching the papules and producing excoriations the worms may escape, while on incising a nodule a cyst, with one or two worms embedded in slimy jelly, or a watery fluid, may be found.

After lasting for some weeks or months the cyst walls become firm and thick, and so encapsulate the worms. The condition may last for years. There is no known treatment.

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CHAPTER XCVII

DYSIDROSES AND DYSTROPHIES

Hyperidrosis—Bromidrosis—Chromidrosis, etc.—Dysidroses: Prickly heat—Cheiropompholyx—Dysidrosis exfoliativa—Dystrophies: Leucoderma—Albinism—Melung—Chloasma bronzinum—Dermatosis festonata frontalis—Dermatosis nigro-circinata—Ochrodermatosis—Melanonychia—Xanthoderma areatum—Mongolian spots—Tattooing—Ainhum—Symmetrical palmar erythema—Acrodermatitis vesiculosa—References.

HYPERIDROSIS.

Remarks.—This condition, as well as bromidrosis, is a cosmopolitan one, but for climatic reasons both are so common and important in the tropics that a short account of them is given in this chapter.

Synonyms.—Idiopathic hyperidrosis, Idrosis, Polyidrosis. Ephidrosis Sudatoria.

Symptomatology.—Excessive perspiration may be generalized or localized. In the latter case it is generally symmetrical, the regions most frequently affected being the axillary regions, hands, feet, and genital regions. Other regions may be affected. In one of our native assistants during the hot season there is an extremely severe localized hyperidrosis of the anterior region of the neck, the sweat falling down continually in large drops.

Symptomatic Hyperidrosis.—This occurs in many tropical diseases, especially in malaria, Malta fever, etc. Localized one-sided hyperidrosis has been observed by us in some cases of framboesia.

Prognosis.—In the idiopathic type the prognosis is good, the condition disappearing when the hot season is over, but it is often associated with prickly heat.

Treatment.—For the general hyperidrosis common during the hot season we are not in favour of any drastic internal treatment such as the administration of belladonna. In fact, we think it may be dangerous to stop suddenly this hyperidrosis, which is in reality merely a physiological fact. For such cases we simply recommend using some potassium permanganate, or cyllin, or a little menthol alcoholic solution in the daily bath, and dusting of the body with any simple antiseptic powder, such as zinc oxide, starch, and boric acid in equal parts (see Prickly Heat, p. 2224).

In really severe cases of generalized hyperidrosis, belladonna or atropin may be administered; but they stop the secretion only for a time, and must be pushed till unpleasant symptoms appear. Sulphur and acid drinks have little effect, but they are harmless. Sulphur is occasionally given by us in cachets (3 grains) three times daily after meals.

In localized hyperidrosis the treatment varies according to the parts being non-excoriated or excoriated. In patients not presenting excoriations, naphthol or salicylic or formalin-alcoholic lotions (1 per cent.), followed by a salicylic, boric, or tannoform powder, are very useful. If there are excoriations or inflammatory signs, no alcoholic lotions should be used, but merely water solutions of boric acid (2 per cent.), carbolic (1 per cent.), permanganate of potassium (1 in 4,000), and occasionally hydrogen perchloride (1 in 2,000 to 1 in 4,000), after which a salicylic or boric powder is applied. It should be always remembered to sprinkle with the same powder the socks, shoes, and undergarments.

BROMIDROSIS.

This term is used to denote offensive sweating.

Ætiology.—The bad odour seems to be due to the growth of various bacteria, as observed by Thin, and is due not only to the sweat, but also, and probably in a higher degree, to the sebaceous secretion. The condition is very common in native races—negroes, Indians, and Chinamen; most natives seem to have it to some extent, in fact. On the other hand, however, it is to be noted that certain natives state that they can detect in almost every European a special, disagreeable odour. Certain authorities are of opinion that each race has a recognizable different odour.

Symptomatology.—As a rule, when the sweat has an offensive odour, there is also hyperidrosis, but in certain cases the quantity of sweat is not more than usual. The condition is usually localized, occasionally general. The situation of bromidrosis is, in order of frequency, the feet, the axillary regions, the perineum, and genital organs. When the condition affects the feet—the commonest localization—the odour is most offensive, and has been compared to that of putrid cheese. When it affects the axillary regions, the odour is offensive, but as a rule is of a different character.

Symptomatic bromidrosis has been described in pinta, in certain cases of Madura foot, in acanthosis nigricans, after eating certain foods, etc.

In contrast to bromidrosis, cases have been described of certain individuals having a pleasing smelling sweat, with the odour of violets or musk. There is a tradition that certain saints exhaled a pleasant odour.

Prognosis.—Except in those cases when the bad smell is due to accumulated dirt—when a thorough washing with carbolic soap will cure the condition—bromidrosis is not of easy cure, but the bad smell may be hidden in various ways.

Treatment.—This is the same as for hyperidrosis, but formalin lotions (½ to 3 per cent.), alcoholic or watery, are especially useful, Lysoform (2 to 5 per cent.) is efficacious. Afterwards a powder such as ac. salicyl. gr. x., talci ℥i., or ac. borici ʒi., talci ℥i., should be used, and some boric acid should be sprinkled in the socks and also in the boots. If there are excoriations, formalin should not be used, but instead hydrogen peroxide (10 per cent.) or potassium permanganate (1 in 4,000), followed by boric powder or a dermatol, xeroform, or tannoform powder (ʒi. of any of these drugs to ℥i. of talci). Internal treatment is not of much use, but sulphur (gr. iii.) three times daily may be tried. One of us had good results in a case by the administration of urotropin, gr. x., thrice daily.

Chromidrosis.

The term is applied to coloured excretion of sweat or sebum. The condition affects in most cases the armpits, but cases have been described affecting the face, chest, abdomen, inguinal regions, hands, and feet. The colour has been described as black, blue, red, green, yellow, and violet. We have personally observed only two cases of chromidrosis. In both the axillary regions were affected, the colour was brick-red, and the sweat stained the clothes red. In one of the cases it was due to *B. prodigiosus*, in the other to a red pigment-producing coccus.

Phosphoridrosis.

Synonym.—Phosphorescent sweat.

This condition has been described by Kostor and others, but is very rare. In one case it was stated that it appeared after eating phosphorescent fish. According to Beyerink the phosphorescence is due to photo-bacteria.

Uridrosis.

Small white crystals, forming a sort of hoar-frost, are present on the skin, due to excretion by the skin of urinary constituents, especially urea and chlorides. Nash records several cases of a whitish deposit on the skin in native children and natives, which, according to some authorities, may have been the same condition.

Hæmatidrosis.

Several cases of hyperidrosis with red blood cells and leucocytes in the sweat have been placed on record.

Anidrosis.

Idiopathic total anidrosis, or absence of sweat, is exceedingly rare, but a diminution in the secretion of sweat is often observed. There are people in whom the bringing about of perspiration by hot-air baths and drugs is very difficult.

Symptomatic anidrosis is present in leprotic patches, and may be of diagnostic value. It is seen also in scleroderma, general or circumscribed (morphœa), and in xeroderma. The secretion of sweat may be much decreased in diabetes and certain nervous conditions.

DYSIDROSES.

Prickly Heat.

Synonyms.—Lichen Tropicus, Sudamina Papulosa, Miliaria Rubra, Miliaria Papulosa, Salpullido (Cuba), Calor Picante (Minorca), Humon El-Nil (Arabic).

Definition.—Prickly heat is a papular or papulo-vesicular eruption, with marked pruritus, and associated with profuse sweating.

Geographical Distribution.—The condition is found all over the tropics and subtropics. It may be observed also in temperate zones during the hot season, especially at sea-bathing places.

History.—Bontius described the affection in his work, 'De Medicina Indorum'; Cleghorn in his book, 'Diseases of Minorca,' identifies it with sudamina; he states that the term used in Minorca to indicate the eruption was *calor picante*. Willan, Johnson (1821) and other English observers described it in India and other tropical countries with the term *Lichen tropicus*. Armand in 1854 describes it in his book, 'L'Algérie Médicale,' using the name *Lichen miliar pruriginosus;* he mentions that sea-bathing often increases the severity of the eruption. Mestre, in Cuba in 1862, wrote a very complete paper on the condition; he uses the term 'salpullido.' In more recent times the eruption has been studied by Robinson, Török, Durham, and many others.

Ætiology and Pathology.—Politzer considers the disease to be due to the obstruction of the flow of sweat brought about by the cells of the epidermis swelling by imbibition from the excessive sweat. Pearse considers it to be due to an acute distension of the sebaceous glands by their own secretion. Robinson states that the inflammation is about the sweat-pore, while, according to Török, it has nothing to do with it. In our experience, the inflammation is not always about the sweat-pore.

Durham believes prickly heat to be an infective disease, caused by a minute actively motile amœba; his results, however, have not been confirmed.

Symptomatology.—This affection is extremely common in tropical countries, especially in new arrivals. The eruption consists of small pin-head papules, which may enlarge to the size of a millet-seed, and even larger. The papules are generally conical, angry red, and often occupy the orifices of the sudoriferous follicles; they are occasionally topped by a small vesicle, the contents of which may later, occasionally, become purulent. Besides the papules, roseola-like spots are often seen; these in some cases may coalesce and form large erythematous patches. Occasionally minute glass-like vesicles of sudamina crystallina are also present. The eruption is found on the parts of the body where the patient perspires most. It is very commonly observed round the waist, the back, chest, arms, and forehead; it may extend to the whole surface of the body, except, it is generally stated, the palms and soles. In our experience, when the eruption is general, the palms and soles also may be affected; in such situations, however, no papules are found, but only roseola-like spots. We would also call attention to another feature found in cases of acute severe general prickly heat eruption: in several such cases the oral mucosa and the fauces will appear acutely congested. The congestion subsides on the disappearance of the cutaneous lesions.

Diagnosis.—This is generally easy; from eczema it is distinguished by the greatly increased flow of perspiration, and by the absence of any moist lesions during the whole course of the malady. Our experience is, however, that in some cases true eczema—especially of the papular type—develops on prickly heat lesions. In cases of generalized prickly heat, with roseola-like spots on the palms and soles, acute patchy congestion in the oral mucosa and pharynx, a syphilide must be excluded, for several of our patients believed themselves to be affected with syphilis; but the extreme pruritus is generally sufficient to exclude it.

Prognosis.—As a rule, the prognosis is good, the eruption disappearing quickly under proper treatment. The patient, however, complains of the severe itching, which often keeps him awake at night. In some few cases no treatment is of any avail, and the patient must be sent up to the hills; in others, crops of boils develop, or pyosis mansoni or impetigo contagiosa may supervene, especially in children.

Treatment.—The patient must be kept cool; he should not take much to drink, and should abstain from drinking hot tea. Too warm clothing should be avoided; flannel and woollen things often make prickly heat worse. In such cases silk underclothing may be recommended, but not in people liable to abdominal chills. All underclothing must be changed at least once daily and after taking any violent exercise. Sea-bathing is injurious. The treatment which in our experience has answered best is the free use, several times daily, of a salicylic alcoholic lotion (ac. salicyl. ʒi., spir. rect. ℥viii.), followed by the general application of a salicylic or boracic or camphor powder, such as ac. salicyl. gr. x., talci ℥i., or ac. borici ʒi, talci ven. ℥i., or camphor gr. xxxv., zinci ox. amyli āā ℥ss. It is better, as a rule, to avoid greasy preparations.

After the eruption is cured the patient should be directed to use some Condy's fluid, cyllin, or other disinfectant in the bath, and afterwards to apply one of the powders mentioned above.

The so-called 'Castellani's lotion' much used in the East, consists of menthol gr. x., ac. salicyl gr. ii., zinci ox ʒvi., calaminae ʒiii., spirit. rect. ℥ii., glycerin. ʒi., aq. rosae ad ℥vi. It should be diluted with the same amount of water when applied to the face or when used for children.

Cheiropompholyx.

Synonyms.—Dysidrosis, Pompholyx.

This affection is seen in the tropics, and is also met with in temperate zones during the hot season. To Tilbury Fox and J. Hutchinson belongs the merit of having separated this affection from eczema.

Ætiology and Histopathology.—Tilbury Fox believed the disease to be due to accumulation of sweat induced by the blocking of the pores of the sudoriparous glands. The more recent researches of Unna, Norman Walker, Williams, and others show that the lesions are of an inflammatory character; the vesicles are found in the prickly layer, and often press to one side of the sweat channel.

Unna described a bacillus as the cause of the disease. Some authorities consider the condition to be of neurotic origin.

Symptomatology.—The eruption is found in individuals who suffer from hyperidrosis. It is characterized by the presence of deeply seated translucent or opalescent, sago-like vesicles between the fingers and toes; the vesicles are not, as a rule, surrounded by an inflammatory halo; they very rarely coalesce, and usually do not break, but dry up gradually, being thrown off with the exfoliating epidermis. The vesicles in many cases are few in number; in others they may be numerous, and the eruption may extend to the palms, backs of the hands, and occasionally the arms. There is unbearable pruritus, and in some cases, owing to the scratching, an eczematous dermatitis may develop, especially between the toes.

Diagnosis.—Some authorities still maintain that cheiropompholyx is merely eczema. In our experience, the disease must be separated from eczema, the principal characters of differentiation being the deep situation of the vesicles, the fact that they very rarely rupture, and that, as a rule, they are not surrounded by an inflammatory zone; moreover, the parts affected are generally bathed in sweat.

Prognosis.—The disease is not a serious one, and, under proper treatment, the eruption heals; but the tendency to recur is great.

Treatment.—When the vesicles are few in number, pricking them with a sterile needle, washing them with a perchloride lotion (1 in 2,000), followed by the application of a 1 to 2 per cent. naphthol ointment, gives much relief. When the vesicles are numerous, and the eruption has spread to the backs of the hands and arms, calamine lotion, to which a little menthol and alcohol has been added, answers well, or a salicylic alcoholic lotion (ac. salicyl. ʒi., alcohol rect. ℥iv., aq. ad ℥viii.) may be used.

Dysidrosis exfoliativa.

This affection, described by Castellani, is closely related to cheiropompholyx. The affected parts—generally the palms of the hands—are bathed in continuous perspiration, and large flakes of epidermis exfoliate. In most cases no cheiropompholyx-like vesicles are found; in fact, no vesicles of any type can be detected. The affection becomes cured spontaneously on the patient going to the hills or during the cold season, but it is apt to recur.

Bathing the affected parts with a resorcin lotion (½ per cent.) at first, and later, when the desquamation has ceased, the application of calamine lotion, is useful.

Sweat Desquamation.

Schornberg has applied the term '*sweat desquamation*' to the minute whitish scales, often arranged in rings, and found on the palms of persons who perspire profusely. The condition may occasionally be confused with a syphilide, from which it is differentiated by the absence of other syphilitic signs, such as enlargement of the lymphatic glands, etc., and by the fact that it disappears on the patient going to the hills.

DYSTROPHIES.

Leucoderma.

Synonyms.—Leucopathia, Vitiligo, Acquired leucopathia, Acquired leukasmus, Acquired achromia, Acquired piebald skin, Maladie de dépigmentation (O'Zoux).

Leucoderma is much more common in tropical countries than in temperate zones. The natives of Ceylon and India have a dread of developing leucoderma, and look upon it as a loathsome disease.

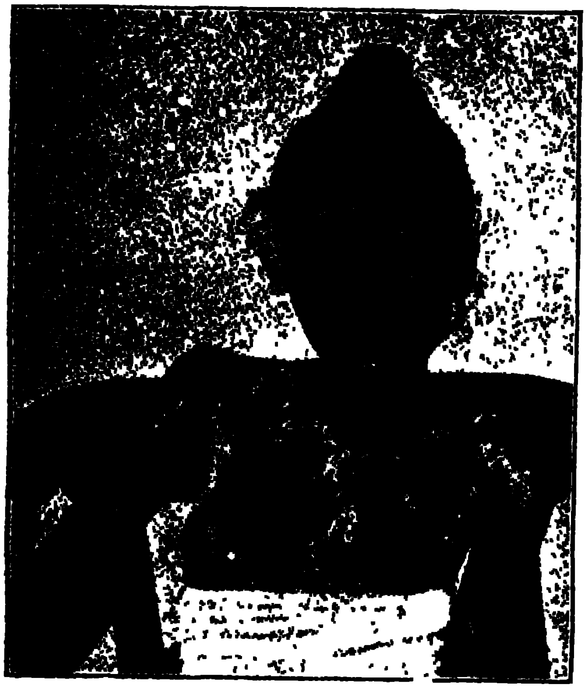


FIG. 871.—LEUCODERMA IN A SINHALESE WOMAN.

Ætiology and Pathology.—The ætiology is unknown. It is generally considered to be a trophoneurosis. Occasionally there is evidence of hereditary influences, several members of the same family being affected. The malady may start without any apparent cause, or in some cases may begin after an injury, after a burn, after too strong a caustication. In fact, the application of strong remedies should be used with care in natives. We have seen leucoderma patches appearing after the application of pure formalin. Patches of leucoderma may develop also in chronic epiphytic skin diseases, the fungi apparently having a deeply disturbing effect on the pigment formation.

FIG. 872.—LEUCODERMA OF THE HANDS AND ARMS.

Symptomatology.—Leucoderma is characterized by the presence of non-pigmented areas, white, ivory-like, or pinkish. The patches are roundish or oval, with a smooth surface; they slowly enlarge and coalesce, giving rise to large, irregularly outlined areas. Occasionally almost the whole body becomes affected; more often it is the face and hands which are affected, and there may be a certain symmetry. The initial patches are often surrounded by a zone of hyperpigmentation. Occasionally within the white areas small dot-like zones of pigmentation are left. The hairs of the affected parts frequently become white, but sometimes remain of normal colour. The white patches do not show any marked change in sensation; there is never anæsthesia; in many cases there is hyperæsthesia to heat and light stimulation. The texture of the skin remains normal; occasionally slight atrophic processes may be noted. It is usually stated that the general health is not impaired. In our experience, however, when the patches are large and situated on uncovered parts of the body, especially the face, symptoms of severe asthenia have been noticed. Moreover, the patients complain that they cannot do any work in the sun, as they experience a burning sensation in the white patches, and they suffer from giddiness.

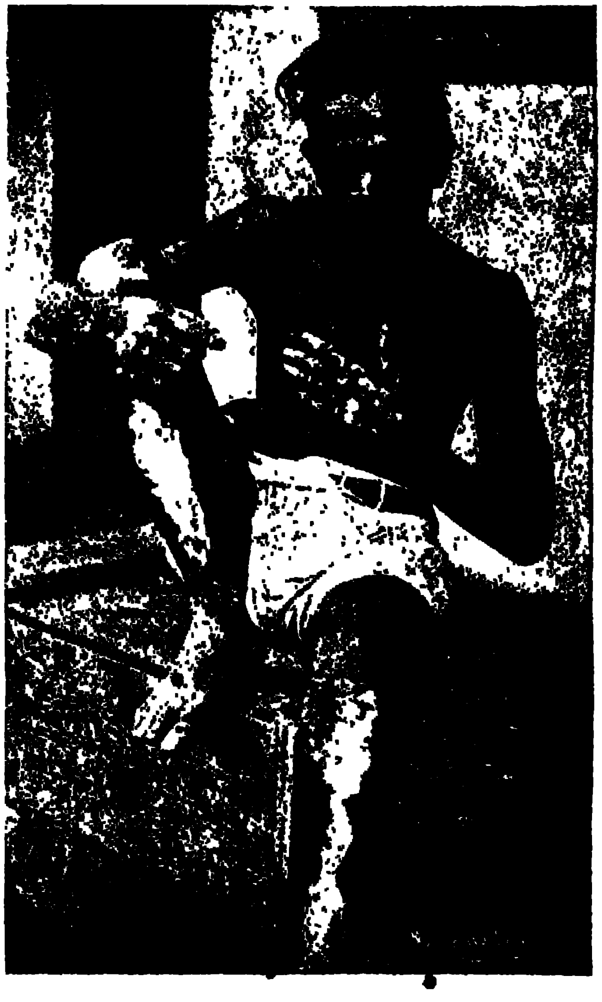


FIG. 873.—LEUCODERMA IN A SINHALESE.

Clinical Varieties—*Melung* (*Beta*).—This type of leucoderma was first described by Ziemann, and is fairly common among West African negroes. It is found also in Ceylon, India, and Burma, in the last-mentioned country having been described by Castor. The affection is always symmetric, and attacks only the palms or the soles, or both palms and soles. Small areas of the skin undergo a slow process of depigmentation, becoming whitish or yellowish; there is no alteration of sensibility. The depigmented areas, which are generally of various shape, are intermixed with patches of normally pigmented skin, so that the palms and soles present a marmoriform appearance.

The disease is chronic and incurable. It often develops in childhood, and several members of the same family may be affected.[1]

A variety of leucoderma in the shape of two small, often triangular spots, one at each angle of the mouth, has been observed by Pusey in a Burmese girl and by one of us in Ceylon. The mucosa of the lips may also show leucodermic patches.

Diagnosis.—The diagnosis is generally easy. The patches, in contrast to leprosy, do not show anæsthesia; from *morphœa* it is distinguished by the absence of any abnormality in the texture of the skin; from tinea flava, tinea alba, and pinta, by the absence of any fungus.

Prognosis.—The disease may be said to be incurable. When large patches are present, the patient complains often of asthenia, and may become unfit for work, especially work in the open air and sun.

Treatment.—The disease is generally incurable, but the spreading of the patches may be prevented, and occasionally a slight improvement may be brought about, in our experience, by an energetic arsenical treatment. We generally give arsenious acid in a pill (gr. $\frac{1}{50}$) three to six times a day, or atoxyl injections (5 grains every other day). Gillmore has tried soamin with fairly good results. We have seen no benefit from the administration of suprarenal extract, as recommended by several authors. The white colour may be partially hidden by applying a lotion of nitrate of silver or potassium permanganate, or by tattooing.

Heidingsfelt has devised an instrument consisting of a group of ten needles, which are put in movement by electrical power. In this way tattooing may be performed much more rapidly than by hand.

Sommer claims to have cured several cases of leucoderma by injections of adrenalin.

Albinism.

Synonyms.—Congenital leucoderma, Congenital leukopathia, Congenital achromia, Congenital leukasmus.

The affection is found in the tropics more frequently than in temperate zones. It is characterized by congenital absence of pigment in the skin, hair, iris, and choroid. There are cases, however, of partial albinism in which only the skin is affected. The skin has a milky-white or pinkish appearance; the iris is rose-coloured, and the pupil red. There is intolerance to light; hence the pupils will be generally found to be contracted, and the patient, to avoid the strong light stimulus, may go about with the head downwards. Nystagmus is observed in several cases. The hair is generally white or yellowish-white, fine and silky. We have seen albinos with red hair. Albinos are generally poorly built, weak and feeble individuals.

Ætiology and Pathology.—The ætiology is unknown. The affection is more often observed among coloured races than in the white races. It shows a certain family tendency. It is said that cases occur more frequently in the offsprings of consanguineous marriages. The histological examination of the skin shows absence of pigment as the only abnormality.

Treatment.—The affection is incurable.

Erythema Solare.

The effects of sunlight on the skin, including the histology of the lesions, have already been discussed in Chapter III., pp. 83–85. They are caused by the active effects of the rays at the violet end of the spectrum. The skin of the parts exposed becomes erythematous, swollen, and vesicles and bullæ may appear. Desquamation follows, and the skin is often left pigmented (sunburn).

The treatment consists in applying calamine lotion, and later any bland ointment such as simple cold cream.

Dermatitis Solaris.

After repeated attacks of erythema solare—or at times without any history of such—the skin of the hands and exposed parts in planters and other people living an outdoor life in the tropics becomes slowly reddened, and may be slightly rough to the touch. Freckles and hyperpigmented spots are generally present, and not rarely small telangiectasia. In a later stage warty patches often appear, and the dermatitis, as noted by McLeod, may somewhat resemble the dermatitis produced by X rays. Atrophic changes may also develop. The condition, which is also known by the term *tropical skin*, is somewhat similar to what Unna called 'seaman's skin' and to senile atrophoderma or biotripsis (see p. 2282).

Diagnosis.—The diagnosis from pellagra has already been discussed (see p. 1730).

Prognosis.—The dermatitis is very obstinate, but generally becomes cured spontaneously in a cold climate.

Treatment.—A change to a temperate climate is the only efficacious treatment. Exposure to the sun is to be avoided as much as possible.

Chloasma.

Chloasma, which, as is well known, is characterized by the presence of dark brownish or dirty yellowish patches, situated commonly on the face, is of frequent occurrence in the tropics in Europeans as well as natives. The patches are plainly distinguishable in the skin of Indian and Sinhalese natives, though in African negroes they may be indistinguishable. The condition may be due to several causes, and the following types may be mentioned:—

1. **Chloasma solare (melasma solare)**, due to exposure to the sun. A similar condition may be due to exposure to a powerful light or glare of any kind, and may even occasionally develop in people who pass a long time on glaciers and fields of snow. Chloasma solare is found among Europeans, half-castes, and also in natives. In natives who wear clothes it is easy to see that the parts exposed to the sun are darker. The condition is generally found on the face, and it may be diffuse, or one or two small patches only may be present. The colour varies from a slight yellowish-brownish

to a deep black bronzine one (see Chloasma Bronzinum). On close examination it will be found that often patches of hyperpigmentation are seen side by side or alternate with patches of depigmentation of various degree, but generally slight. The patches of chloasma solare may appear quite suddenly without being preceded by erythema solare; in one of our cases they appeared on the forehead twenty-four hours after a motor-car drive in the midday sun without the hood on; in another, a European lady, who had a very delicate skin and was used to wearing gloves, very dark hyperpigmented patches appeared on the back of the hands and wrists twelve hours after exposing her hands without gloves to the midday sun. In addition to hyperpigmented spots, depigmented patches also developed.

2. **Chloasma caloricum,** from exposure to heat, or possibly the glare of fires. We have seen it several times in stokers.

3. **Chloasma traumaticum,** from mechanical irritation of any kind, scratching, etc.

4. **Chloasma toxicum,** due to irritating drugs, as, for instance, after a blister.

5. **Chloasma symptomaticum,** as, for instance, chloasma uterinum, found during pregnancy or during chronic diseases of the female genital organs. Chloasma uterinum is quite common in Sinhalese women, and is plainly distinguishable.

6. **Chloasma malaricum** and **kala-azar chloasma,** an important type of chloasma symptomaticum, is found in patients suffering from chronic malaria and kala-azar. A diffuse type of hyperpigmentation observed in chronic malaria and closely resembling Addison's disease has already been described (see p. 1180).

Hyperpigmentation may occur also in syphilis, leprosy, tuberculosis, diabetes, and many other chronic diseases.

In India a 'pigmentary fever' has been described of short duration, and said to be characterized by the appearance of hyperpigmented patches on the face (see p. 1461).

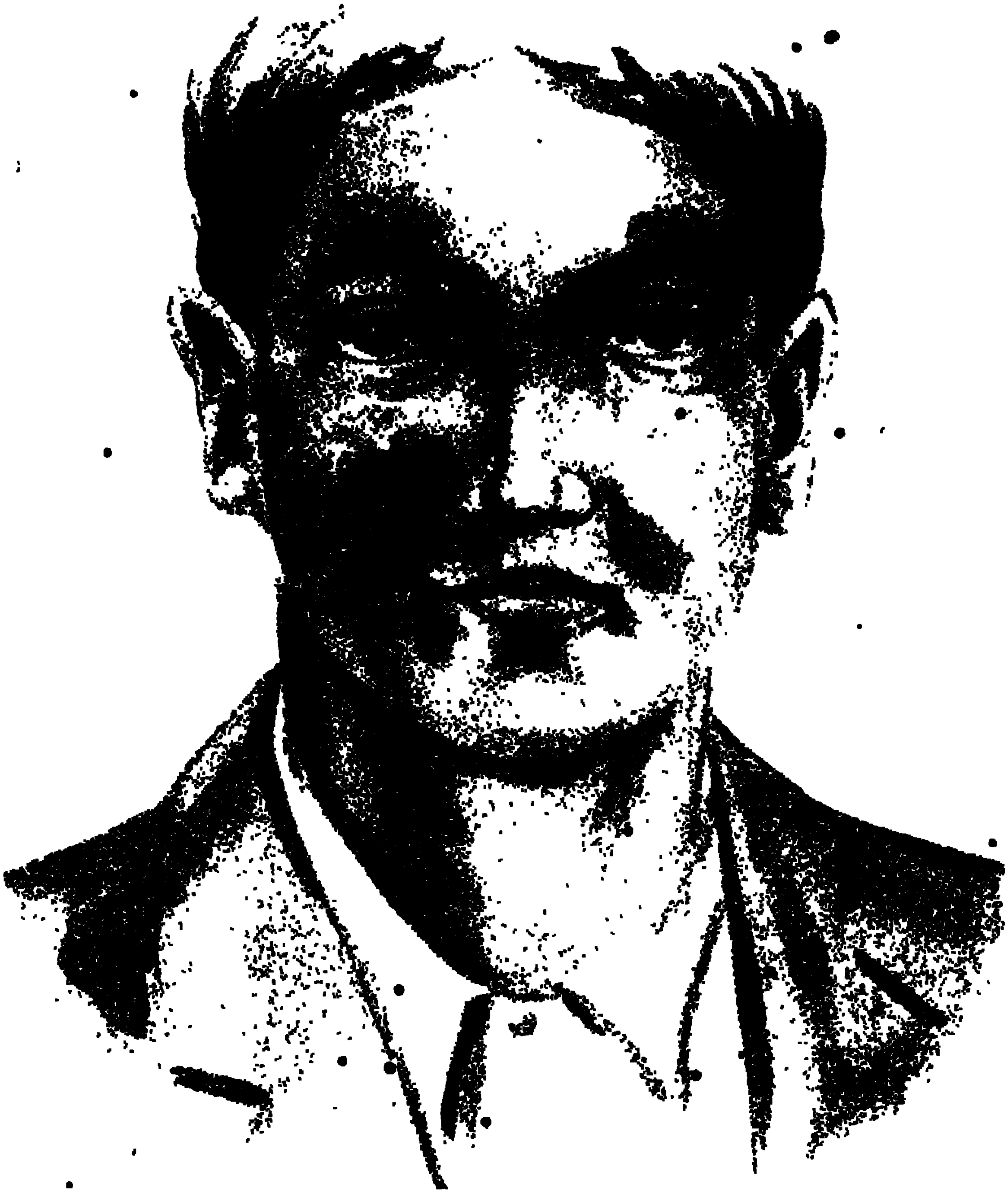
Chloasma Symmetricum.

This condition, which has been described Castellani, is often met with in Sinhalese, who greatly object to it. It is characterized by the presence of two dark brownish chloasma patches situated symmetrically one on each cheek, generally on the malar region. In some cases, in addition to these two patches, a third one is found on the nose. The colour of the patches is generally dark brownish, very rarely bronzine. The causation is unknown; it does not seem to be congenital. No treatment is of any avail.

Chloasma Bronzinum.

This somewhat rare affection is met with among natives as well as Europeans in India, Ceylon, the Malay States, China, and other

PLATE XIV.



CHLOASMA BRONZINUM.

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tropical countries. It was first observed by Cantlie, who called it 'tropical mask,' and was later described by one of us.

Ætiology.—This is unknown, but a life in the open air with daily long exposure to a tropical sun is apparently an important predisposing cause. All our patients were European planters, or native overseers or coolies.

Symptoms.—Part of the face or the neck, or occasionally the whole face, neck, and chest, presents a peculiar pigmentation, resembling a black bronzine mask; the pigmented areas slowly but steadily increase. The disease is very chronic and incurable if the patient remains in the tropics. The general health is not impaired. The examination of the various organs is negative. The blood and urine are normal.

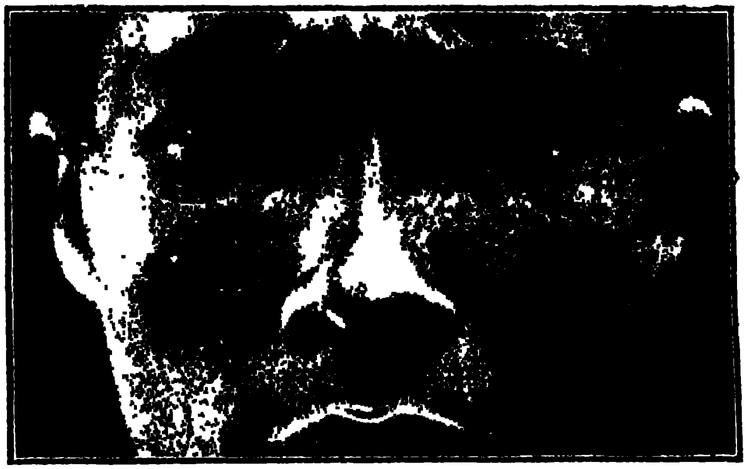

FIG. 874.—CHLOASMA SYMMETRICUM.

Diagnosis.—This is easy, even in very dark-skinned natives, the affected parts being completely black, and having a characteristic bronzine hue.

From ordinary *chloasma*, which is not rare—especially among women—the affection is easily distinguished by the bronzine tint. The absence of asthenia, loss of flesh, and diarrhœa, will suffice to distinguish chloasma bronzinum from *Addison's disease;* the history and the examination of the blood will differentiate it from malarial *pseudo-Addison's disease;* the examination of the urine will distinguish it from *diabetes bronzinum. Argyria* will be excluded by the history and by the fact that in chloasma bronzinum the mucosæ are not affected. In *ochronosis* the cartilages, ligaments, and fibrous structures become pigmented, and the discoloration is best seen about the knuckles and the tendons of the hands and feet; moreover, the urine often blackens on exposure to the air (alcaptonuria).

Prognosis and Treatment.—The disease seems to be incurable, but a long stay in a temperate zone generally improves it.

Dermatosis Festonata Frontalis.

Historical and Geographical.—This condition has been described by Castellani in Ceylon. It has recently been found also in Macedonia.

Ætiology.—This is unknown, but probably a continuous exposure to the sun and glare plays a certain rôle in the causation of the malady.

Symptomatology.—The affection, which in its severe type is rare, is found in Europeans who have resided for many years in the tropics, and who have lived an open-air life, such as planters and overseers, exposing themselves to the sun for long periods of time.

In a well-marked case (see Fig. 875) there is a festooned margin, at times slightly raised, often of a vivid bright red or coppery red colour, while the skin which it encircles has a peculiar whitish, occasionally leucoderma-like appearance, and may be slightly atrophied: at times small patches of hyperpigmentation may be present. There is very little or no pruritus, and sensation to the touch, pain, heat, and cold is not impaired.

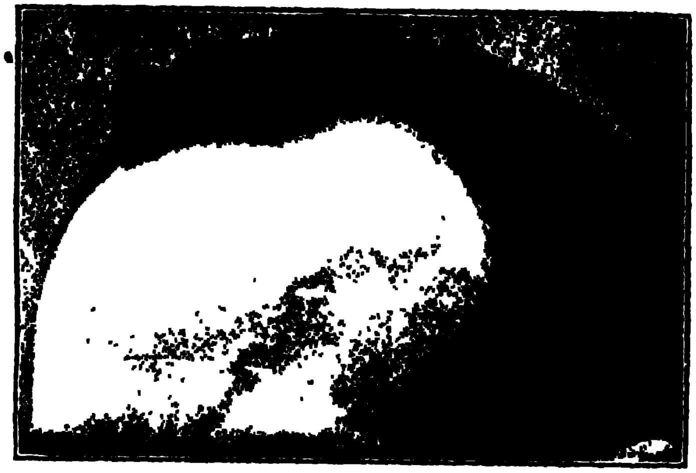

FIG. 875.—DERMATOSIS FESTONATA FRONTALIS.

The course is extremely long, the affection slowly expanding peripherally, and in a tropical climate has no tendency to spontaneous cure.

Diagnosis.—The affection is not rarely taken for a tricophytic condition, but the microscopical examination for fungi is always negative, and an antimycotic treatment does not induce any improvement. From a syphilide it is differentiated by the negative Wassermann and by the uselessness of salvarsan, potassium iodide, and mercury; from *leprosy* by the sensation being normal.

Prognosis.—The general health of the patient is not affected, but the affection runs an extremely long course, and has no tendency to spontaneous cure in the tropics. It gets much better if the patient goes to reside in a cold country.

Treatment.—The treatment is very unsatisfactory. The patient must be advised not to expose himself to the sun and glare, though it is doubtful whether the condition is directly due to such exposure. A wide-brimmed topee or sun-helmet lined with red cloth may be used.

Of the many drugs tried ichthyol seems to be the only one which at times keeps in check the condition, occasionally inducing a slight improvement. It is given internally in 5 grain doses three times daily before meals, and an ichthyol ointment or lotion (5 per cent.) may be applied to the affected skin at night, while during the day a calamine lotion may be used.

Mercury, potassium iodide, and arsenical preparations are useless.

Dermatosis Nigro-Anulata.

Historical and Geographical.—This condition has been described by Castellani in Ceylon natives and in a very dark-skinned gipsy in Macedonia.

Ætiology and Pathology.—This is unknown. It is not a frambœside, as the lesions are not influenced by salvarsan and potassium iodide; nor a syphilide, as they are not influenced by the same drugs nor by mercury; moreover, Wassermann is negative.

Symptomatology.—The condition is characterized by the presence of black, elevated, fairly hard, ring-like or elliptical multiple lesions, encircling apparently normal skin. There is no pruritus, sensation normal, Wassermann negative. The course is extremely long, lasting for years, with very little change in the aspect of the lesions

FIG. 876.—DERMATOSIS NIGRO-ANULATA.

Diagnosis.—The affection has to be distinguished from *tinea nigrocircinata* by the absence of fungi, and by the failure of any antimycotic treatment; from a circinate *frambœside* by the uselessness of potassium iodide and salvarsan; from a *syphilide* by the uselessness of the same drugs and of mercury; from *porokeratosis* by the multiplicity of the lesions.

Prognosis.—The general health is not affected, but the condition is most persistent.

Treatment.—This is very unsatisfactory. An exfoliative treatment by means of a salicylic acid ointment occasionally induces a temporary improvement.

Ochrodermatosis.

Synonym.—The yellow disease (Castellani).

Historical and Geographical.—This condition has been described by Castellani in Ceylon, in Europeans living in the low country.

Ætiology.—Unknown. The patients were not taking any drug and were not exposing themselves to the action of any toxic substance. On the strength that the condition gets much better or disappears on the patient going to the hills, a search for a possible causative organism was carried out, but with negative results.

Symptomatology.—The face, arms, hands, and at times the whole body, are of a bright yellow or saffron colour, quite different from the yellowish-greenish colour of jaundice. The scleroticæ remain completely white; the urine is of normal colour and composition; the sweat is not coloured; the stools are normally pigmented; the liver and spleen are not enlarged; and the general health is in no way affected; but naturally the patients greatly object to the disfigurement. The condition improves or disappears on the patient going to the hills or to Europe.

Diagnosis.—The bright yellow or saffron colour is different from the yellow colour generally seen in jaundice. Moreover, the scleroticæ remain white, and the urine and stools are of normal colour. The anamnesis and special analysis of urine for picric acid, etc., exclude the ordinary toxic pigmentations. The condition is distinguished from certain types of *chromidrosis*, as the sweat is not coloured and the clothes do not become stained.

In *ochronosis*, which is generally congenital, there is alcaptonuria, and the ligaments and cartilages become blackened.

In ***xanthoderma areatum*** the yellow patches remain localized to the legs, and are permanent.

Treatment.—The only successful measure seems to be to send the patients up-country. On the hypothesis that the condition might possibly be of parasitic origin, a formalin spirit lotion (1 per cent.) was prescribed is several cases, but the improvement, if any, was very slight, though certain patients stated that they thought the condition was affected in a beneficial manner by it.

Melanonychia.

Synonyms.—Black pigmentation of nails, Melanonychia falciformis.

Castellani has described in two European ladies a peculiar condition of the nails characterized by a band of black pigmentation along the free border of the nail. On superficial examination, it has the same appearance as though some dirt had accumulated beneath the free border of the nail, but on scraping this pigmentation does not disappear, and this shows that the condition is due to some pigmentation in the substance of the nail. The sufferers were in general good health, not using any internal or external

PLATE XV.

XANTHODERMA AREATUM.

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medicine which could account for the pigmentation, and the nails, apart from this line of pigmentation, appeared perfectly normal. We have, later, come across a case in a European gentleman and another case in Macedonia.

The condition slowly disappears spontaneously.

Xanthoderma Areatum.

This affection, which has been described by Castellani, is not infrequently met with among Europeans; it generally affects the lower parts of the legs; it starts very insidiously, with a yellowish or reddish-yellow spot, which is not elevated; the surface is smooth, not furfuraceous; there is no infiltration, and, apart from the colour, the affected skin is normal. There is no pruritus and no pain. The yellow spot slowly increases, and one or more other spots may appear near the first one or at a distance. Some of the spots may coalesce together, forming a large yellow-red patch of irregular or various outline. The larger patches also, apart from the colour, are normal, being of normal consistency and elasticity. The disease is very chronic. The general health is not impaired; the lymphatic glands are not enlarged, and the blood does not show any abnormality; urine normal. In all our cases syphilis could be excluded; in none was there any history of traumatism.

Diagnosis.—From chloasma, xanthoderma areatum is readily differentiated by the lighter yellow or yellowish-red, and by the different situation. The affection can be easily distinguished from xanthoma, as the texture of the skin is normal, and the patches are not elevated. In pseudo-xanthoma elasticum of Balzer there is an eruption consisting of mesh-like patches of buff-coloured infiltration, lumpy in some places, in others linear. It must be distinguished also from Schamberg's so-called 'cayenne-pepper' condition, characterized by the presence of brownish-yellowish patches on the legs, made up of small puncta, giving rise to a cayenne-like appearance of the skin, found at times on people suffering from varicose veins.

Treatment.—This is difficult; in some cases an energetic exfoliating treatment by resorcin pastes (resorcin, ʒii.; ac. salic., gr. xx.; Lassar's paste, ℥i.) improves the condition after the inflammation induced by the paste subsides.

Mongolian Spots.

Synonym.—Mongolian maculæ.

Definition.—A congenital condition characterized by the presence of dark bluish spots on the lower sacral region, not disappearing on pressure.

History.—The first complete description has been given by Baelz, who found them almost constantly in Chinese, Koreans, Japanese, and Malays. Later Adachi, Ashmead, Martinotti, Consiglio, and others have further investigated the subject. Castor and Fink have made a very complete study of it in Burma; where it is extremely common.

Geographical.—The condition was at one time considered to be limited to Mongolian races, but further investigations show that it is found in other races, including Europeans. Martinotti, and later Consiglio, have found it in Italy. The condition has recently been observed also in North and South America.

Ætiology.—The condition is of unknown origin; it is probably congenital.

Symptomatology.—'Mongolian spots' appear as blackish-bluish or mulberry-coloured, smooth, non-elevated areas. The colour does not disappear on pressure: it is, as already stated, blackish-blue. Some portions of the same spot may be darker than others The texture of the skin is normal; there is no pain and no pruritus. They are mostly roundish, but they may be oblong or almost square; they may be single, but are often multiple, five or six or more, each spot varying in size from ½ centimetre to 12 centimetres and even more. The patch may be sharply limited or the colour may fade gradually into that of the healthy skin. The commonest situation is on the lower spine, sacral region, and buttocks, but they may be found practically on any other part of the body. The patches appear at birth, and, as a rule, disappear between the third and fourth year.

In Burmese, Castor has found that Mongolian spots are extremely frequent, and are situated in order of frequency on the sacral region and buttocks, waist, arms, legs, shoulders, head, face, neck. Castor identifies with the Mongolian spots also the pigmented patches so often found in natives on the oral mucosa, tongue, and lips.

Diagnosis.—The condition is easily recognized, the roundish or variously shaped bluish patches, generally on the sacral region and buttocks, being characteristic; its being present from birth distinguishes it from patches of pigmentation of other origin. The complete smoothness and normal texture of the skin differentiates the condition easily from pigmented moles. In those rare cases in which confusion with some mycotic condition might arise the microscopical examination will clear the diagnosis, no fungi, of course, being present in Mongolian spots.

Course and Prognosis.—The patches generally fade or disappear completely about the third or fourth year.

Treatment.—The treatment is nil, nor is it generally asked for, the patches most frequently being on covered parts of the body.

Tattooing.

Nomenclature.—The word 'tattoo' is derived from 'tattow,' used by Cook and Banks in their journals in 1789. Tattow was derived from 'tau' or 'tatu,' a word which meant 'marking.' The Maori word is 'amoca' or 'moko,' which, however, refers to the furrowing of the skin—a more formidable operation than tattooing.

Definition.—Tattooing is the formation of more or less indelible marks in the skin by means of rubbing pigments or irritating substances into slight wounds made for the purpose.

General Account.—It appears to us that tattooing was originally preceded by face and body painting, which in the form of 'war paint' is well known to have been used in many savage tribes when about to enter into combat with their enemies. At first this painting was very simple, and consisted in merely smearing the face with some form of pigment, but eventually in certain peoples it became more and more elaborate. Painting, however, is only a temporary method of adornment, and many peoples have adopted in its place the permanent tattooing. The essential reason for tattooing is the ornamentation of the person, but taking its origin in the custom of painting the face before going to war, it is generally more elaborate in men than in women.

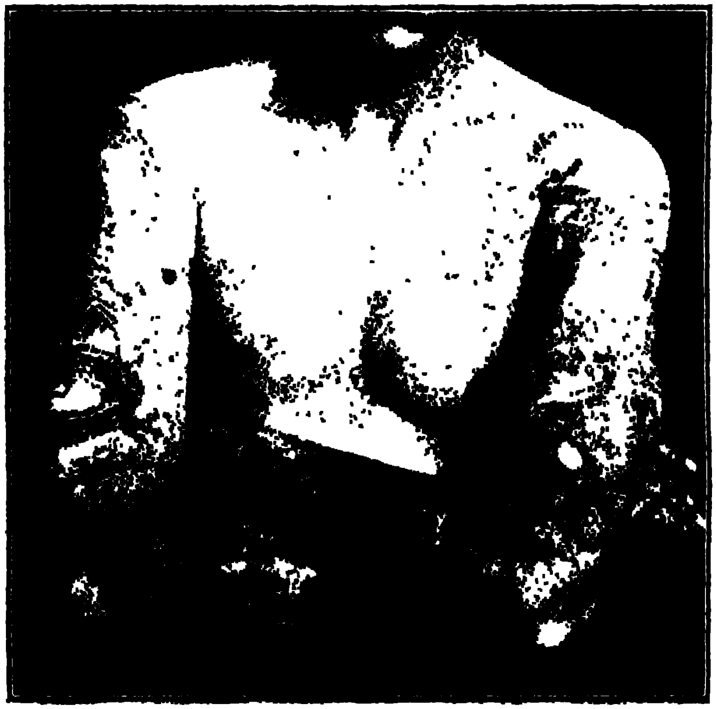

FIG. 877.—TATTOOING.

In Africa the marks have a most varied significance. Thus, according to Hobley, the Ja-Luo girls are tattooed because it is thought that unless this is done a woman will not bear children. Among the Ketosh, the warrior, after killing an enemy in warfare, has two rows of marks tattooed on his right chest and shoulder, to prevent the spirit of his dead enemy bewitching him.

In its simplest form it is seen in West Africa, where short straight skin-cuts are made by means of a sharp piece of iron, after which some pigment or irritating substance is rubbed into the wound, the idea being to produce a keloid. If this fails, another cut is made into the same place, and more pigment is rubbed in until the desired result is attained. These cuts, and hence the subsequent keloids, are arranged in some primitive form of pattern. More elaborate patterns, however, may be met with, being generally in the forms of curved lines or scrolls of keloids. Various types of tribal keloid tattooing have been recently studied by Miss Zaborowska.

In the Naga Hills of Assam the lines of the tattoo follow the contours of the face.

The most elaborate designs are found among the Maoris of New Zealand and the natives of the Pacific Islands. The Polynesians use lines and curves, but not spirals, the highest art being found among the Marquesans. The Maoris are, however, not content with mere tattooing, in which pigment is rubbed into slight cuts, for in their 'moko' they make deep furrows, which remain more or less permanently during life. According to Ling Roth, the Maoris use seven patterns: the first, *the linear*, composed of lines of dots or strokes; the second is *the mat* or *plait-work pattern*, composed of parallel lines, in groups of three, arranged more or less alternately; the third is *the ladder pattern*, in which the lines are arranged in horizontal groups separated by clear spaces; the fourth is *the chevron pattern*, being composed of coils with long tails or handles, the interspaces between which are filled in by slanting lines; the fifth pattern is *the circinate coil;* the sixth, *the anchor;* and the seventh, *the trilateral scroll.* This last pattern is said to imitate a flower—*Clianthus puniceus*. According to the same author, the Papuans are much addicted to the use of the spiral in tattooing. The Polynesians use simple pricking instruments, while the Maoris, in order to produce the deep furrows, use special instruments, shaped somewhat like a miniature garden-hoe, the cutting edge of which is toothed. These instruments were at first made of bone or hard wood, but later iron was introduced. They are made to cut the skin by means of blows from a hammer or a stick. As a result of the wound the blood flows freely, and is wiped away by the hand or a piece of stick, after which the pigment is rubbed into the wound. The nature of this pigment appears to vary, and may consist of charcoal, obtained by burning various animal or vegetal substances. The hair of the beard has to be pulled out by the roots, as it would spoil the effect of the tattoo or moko.

The pain of the operation of moko is naturally very great, especially when performed on the lips, and hence but little tattooing can be done at a time, and it takes years for an extensive moko to be produced. Inflammation often sets in, and it may be weeks before the wounds heal. The Maoris perform post-mortem tattooing and moko at times, but this is to be distinguished from tattooing made during life by the appearance of the cuts and the absence of subcutaneous colour.

In modern times the art of tattooing has been much developed by the Japanese, into whose country it was introduced about 300 years ago. The Japanese artists, by using special instruments, composed of fine and coarse needles, and by rubbing in various coloured pigments, produce the well-known designs so commonly seen on the arms and bodies of Europeans and Asiatics.

Varieties.—The different varieties of tattooing described above may be classified as follows:—

I. Simple tattooing.
  (*a*) Without furrows—tattooing of Japan and elsewhere.
  (*b*) With furrows—moko of New Zealand.
II. Keloid tattooing—tattooing of Africa.

Tattooing is not free from danger, for blood-poisoning, and even death, may result, while syphilis and tuberculosis of the skin may be acquired through the wounds.

Treatment.—When the marks are small, excision may be resorted to, but in general any attempt at removal fails. Nieurowsky removes the tattoo marks by blistering with Finsen light applied in the same way as for lupus. Carbide snow may also be used, but the application must be prolonged, and a scar results. When the tattooing is performed with gunpowder, it is said that the marks can be removed by painting with di-iodide of ammonium in solution, and afterwards with dilute hydrochloric acid.

Ainhum.

Synonyms.—Quigila (Brazil), Sukha Pakla (India), Faddidite (Madagascar), Gundurum, Affovi-burunkue (Gêgês tribes), Bankokerendé (Sudan), Excresis Spontanea (A. Collas), Dactylolysis essentialis (G. Beauregard), Silva Lima's disease (Egas Moniz de Aragao), Esola or Ombanja (Benguelo, West Africa).

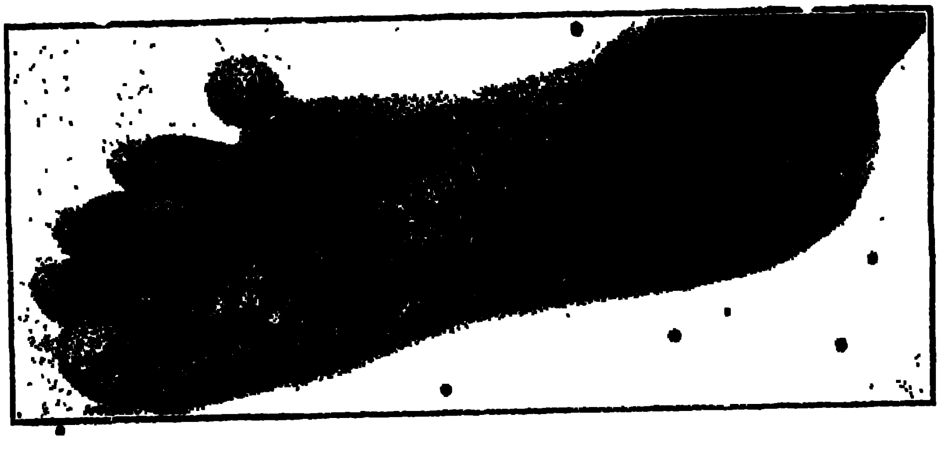

FIG. 878.—AINHUM.

'Anyum,' or 'ainhum,' is derived from a Yoruba word meaning to saw or to cut, and is used by the Nagôs.

Definition.—Ainhum is a chronic disease of the fifth, and more rarely of the fourth and other toes which occurs in native races, and is characterized by the formation of a furrow at the digito-plantar fold, which deepens and extends until it encircles the toe, which is finally severed from the foot.

History.—The disease was first described by Da Silva Lima in 1852. Clarke, in 1860, in his description of the Gold Coast, drew attention to a dry gangrene of the little toe found in negroes in that region, and considered it to be a manifestation of yaws. In 1867 Da Silva Lima further studied the disease, and with Wucherer described fifty cases of it in Brazil, and introduced the term 'ainhum'; in the same year Collas wrote an account of the disease. Da Silva Lima ventured no explanation of the disease. In 1873 Crombie described the disease as occurring in India; in 1876 Pirovano found it in Buenos Ayres; and in 1877 Corre mentions it in Réunion.

It is reported in the West Indies by Potoppidian in 1879; in North Carolina by Hornaday and Pitman in 1882; in Nossi-Bé by Deblenne in 1883; in Western Virginia by Duhring in 1884. This last observer, along with Wile, studied the disease microscopically, considering the essential pathological feature to be an inflammatory œdema of the hypodermis. In 1886 Eyles wrote an excellent account of the pathological histology of the disease as seen in the Gold Coast, concluding that irritation caused an internal proliferation of the epithelium, which, extending into the cutis, damaged the vasomotor nerves, leading to a spasm of the vessels, endarteritis obliterans, fibrosis of the cutis, and rarefying osteitis, whereby the digit is separated from the foot. After this date there are a number of papers, among which may be specially mentioned those by Moriera, Dalgetty, and Maxwell in 1900, Muir in 1903, Ashley-Emile in 1905, and Egas Moniz de Aragão in 1910.

Climatology.—The disease is known in South America, especially in Brazil and the Argentina, and also in British Guiana; in North America, especially in the Southern United States, but also, though rarely, in the Northern, and in Canada. It also occurs in the West Indies. In Africa it is especially well known on the West Coast, and particularly in the Gold Coast, but it also occurs in Algeria, Egypt, Sudan, East Africa, Madagascar, and the Transvaal. In Asia it is known in India, China (?), and Ceylon. It also occurs in Polynesia. We have seen a case in an Italian peasant.

Ætiology.—The causation of the disease is not known. The theories suggesting that the disease is due to leprosy, wearing rings, or other tight bands, self-mutilation, may be dismissed at once, as there is nothing to support them.

According to some authorities—Le Dantec, Da Silva Lima, etc. —the hereditary factor has a certain importance. Da Silva Lima quotes the example of a negro family all the members of which presented the condition.

The racial factor has also been given much prominence, for the condition practically occurs only among natives and mulattoes.

Zambaco Pasha, Eyles, and Moreira, are, in our opinion, correct in their view that the reason why the native races are attacked is because they walk barefoot, and that irritation or injury to the skin of the little toe is more likely to occur in negroes, who often are flat-footed. It is more common in males than in females, in adults than in children, and, though it can apparently be found at any age, is most common between thirty to thirty-five years.

We are inclined to believe that the condition is of parasitic origin, the infection taking place probably through the small superficial lesions or wounds which may be found in people going barefooted.

Pathology.—The constant irritation causes the epithelium to proliferate internally and depress the skin, and cause the fibrous tissue of the cutis to proliferate. There is also an endarteritis, by which the blood-supply is gradually cut off the distal portion of the toe, which therefore becomes œdematous and fatty, while the bone undergoes rarefying osteitis, so that the digit is gradually separated from the foot, a process which takes place through the bone of a phalanx. The histological examination at the line of the furrow shows proliferation of the epidermis, which projects downwards into the cutis, in which the connective tissue is increased in quantity. The vessels show endarteritis and periarteritis; the sweat-glands show proliferation and fatty degeneration of the cells. The bone is in a condition of rarefying osteitis.

Distally to the furrow the joints are effaced; the tissues show fatty degeneration and œdematous infiltration. No organisms can be found.

Symptomatology.—The disease is purely local, and is not, in our experience, attended by any general symptoms. It begins, as a rule, as a furrow on the inner side of the digito-plantar furrow, which slowly deepens and extends laterally and dorsally until the two wings meet on the dorsum of the toe. While this is proceeding the distal portion of the toe becomes swollen, and may appear as a small globule surrounded posteriorly by a deep groove, by which it is separated from the rest of the foot. Often an ulcer forms on the inner side of the groove, and may cause much pain.

Left to itself, the disease will last from two to ten years, though cases have been reported of fifteen to fifty years' duration: but eventually the toe drops off, or is knocked off, or is removed. The process may, however, begin again in the stump.

Usually the fifth toe is affected, but in about 10 per cent. of cases the fourth toe may be affected, and much more rarely the second or the hallux. There are reports of the affection occurring also in the fingers.

Diagnosis.—The diagnosis affords no difficulty, the presence of the constricting furrow being typical. It is easily differentiated from leprotic lesions of the toes by the sensibility being normal and by the absence of signs of leprosy in other parts of the body.

The history makes the diagnosis clear between true ainhum and a peculiar congenital ring-like constriction of the toes described by some authors. This condition is present at birth, and its course is not progressive.

Prognosis.—There is no danger to life in the disease.

Treatment.—The disease is best treated by making a longitudinal cut into the groove, when its progress may be stopped.

Prophylaxis.—The essentials of the prophylaxis are cleanliness, and the wearing of stockings and boots to protect the foot from injury.

Symmetrical Palmar Erythema.

Chalmers, in 1899, drew attention to a symmetrical non-pruriginous palmar erythema found in Europeans on the Gold Coast, and extending along the ulnar side of the palms of the hands. The affection was very persistent. We have seen similar cases in Ceylon.

Acrodermatitis Vesiculosa Tropica.

Historical and Geographical.—This skin disease was described by Castellani in Ceylon. It is of rare occurrence.

Ætiology.—This is unknown, but the affection may be of neuritic origin. It does not seem to be connected with leprosy, in all our cases the search for Hansen's bacillus being negative, and anæsthesia and other signs of leprosy being absent. No history of traumatism was elicited in our patients.

Fig. 879.—Acrodermatitis Vesiculosa Tropica.

Symptomatology.—In a well-marked case the skin of both hands, especially the fingers, appears glossy and tense, the fingers assuming often a tapering shape. Translucid vesicles the size of a millet seed or little more are seen deeply embedded in the skin of the fingers. They have clear contents, and the bacteriological examination reveals absence of any bacterium. They may apparently remain unchanged for a long time, then may slowly disappear; or a few may break, leaving very small superficial ulcers, which heal spontaneously and do not coalesce. The patient generally complains of very severe pains in the hands and fingers, which may be continuous, or may be of a neuralgic intermittent type. Pruritus is absent. There is often diffuse hyperæsthesia; anæsthesia is never present. No thickenings are found along the nerves of the arm. The general health is not affected.

Course and Prognosis.—The course of the disease extends to several months, and occasionally to two or three years, with periods of great improvement. Ultimately the condition may get cured spontaneously. The general health is not affected, but the patient is unable to work with his hands.

Diagnosis.—This is based on the patient complaining of severe pains in the hands and fingers, on the presence of deep-seated cheiropompholyx-like vesicles, on the glossy skin, and on the long course of the complaint.

The condition is differentiated from cheiropompholyx by the severe pains and absence of hyperidrosis; from a leprotic condition by the absence of anæsthetic patches, and absence of other signs of leprosy on other parts of the body. Moreover, though the course is long, the disease generally becomes cured spontaneously. From dermatitis repens of Crocker and acrodermatitis perstans of Hallopeau by there not being history of traumatism, by absence of exfoliative lesions, by the less severe objective signs, and by the absence of the large foci of disease with marked borders and fringed with sodden epidermis, which is thrown up by the undermining exudate.

Treatment.—The regular application of an ichthyol ointment (2 to 5 per cent.) to the hands and fingers, and the administration of the same drug (gr. iii.) three times daily by the mouth is beneficial.

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CHAPTER XCVIII

MISCELLANEOUS DISEASES

Craw-craw—Dermatitis nodosa rubra—Lichen convex—Symmetrical ear nodules—Ear lipomata—Porter's lipomata—Subcutaneous nodular lipomatosis—Multiple pruriginous tumours of the skin—Angiofibroma contagiosum tropicum—Multiple pruriginous tumours—West Indian nodules—Mossy foot—Botryomycosis—The hyperkeratoses—Juxta-articular nodules—Murmekiasmosis—References.

CRAW-CRAW.

Synonym.—Nodular dermatitis (A. Plehn).

Ætiology.—The cause of the malady is unknown. Pijper has described a diphtheroid bacillus.

In the Ceylon gaols, where the disease is common, the prisoners believe it is due to the diet and to the manner of cooking the rice.

O'Neil described in his case a *Microfilaria* which Manson is inclined to believe to be probably *Microfilaria perstans*. Nielly described, under the name of 'dermatose parasitaire' or 'craw-craw,' a papulo-vesicular eruption in which he found nematode embryos in the papulo-vesicles and blood of the general circulation. The conditions described by these authors are not the dermatosis we call craw-craw, and resemble more what Daniels and ourselves call cooly itch.

Symptomatology.—Under the term 'craw-craw' African natives denote practically any pruriginous skin disease. Our African experience has taught us that most of the so-called craw-craw cases are cases of neglected scabies or of tinea corporis, or what Daniels and ourselves call cooly itch. We apply the term 'craw-craw' to a dermatosis met with in Africa, in Ceylon, and in various parts of the tropics, characterized by the presence of numerous hard, *almost horny* papules, occasionally slightly exfoliating at the top, varying in size between a millet-seed and a small pea. Some of the papules may be follicular. They are not of constant shape; some may be roundish and flattened, and others acuminate. When disappearing, they may leave zones of hyperpigmentation. The eruption generally affects the legs and arms, but may spread to the whole body, excepting, as a rule, the face and scalp. Suppurative and ulcerative lesions are absent, except as secondary lesions due to scratching. The proximal lymphatic glands may be hard and enlarged. The disease, if not properly treated, may last many months, and even several years; some cases, however, become cured spontaneously.

Diagnosis.—The disease with which craw-craw presents the greatest resemblance is prurigo. It is distinguished from prurigo by the eruption appearing at any time of life, and not only in childhood; by most of the papules being larger, of horny consistency, and not covered by a small bloody crust, as is often the case in prurigo; and by the fact that it may be cured spontaneously.

The disease may be distinguished from tinea corporis by the absence of any fungus, and from scabies by absence of burrows, and, of course, the absence of the *Acarus*.

Treatment.—The regular application of a salicylic spirit lotion (2 per cent.), followed by β-naphthol ointment (5 to 10 per cent.) for long periods of time, often induces a marked improvement, and in many instances a cure. Internal treatment (arsenic, ichthyol, etc.) does not seem to influence the disease.

FIG. 880.—CRAW-CRAW

Dermatitis Pruriginosa Tropica (Cooly Itch).

The term 'cooly itch' is often applied to dermatoses of various nature, including scabies. We use it to denote an extremely pruriginous dermatitis affecting coolies and occasionally Europeans in certain parts of the tropics, especially in the low country. No acari or similar parasites are found.

Ætiology.—The ætiology is unknown; neither fungi nor animal parasites have been found. It may possibly be due to some parasitic agent which remains on the body only for a short time in analogy to Copra itch (p. 2215).

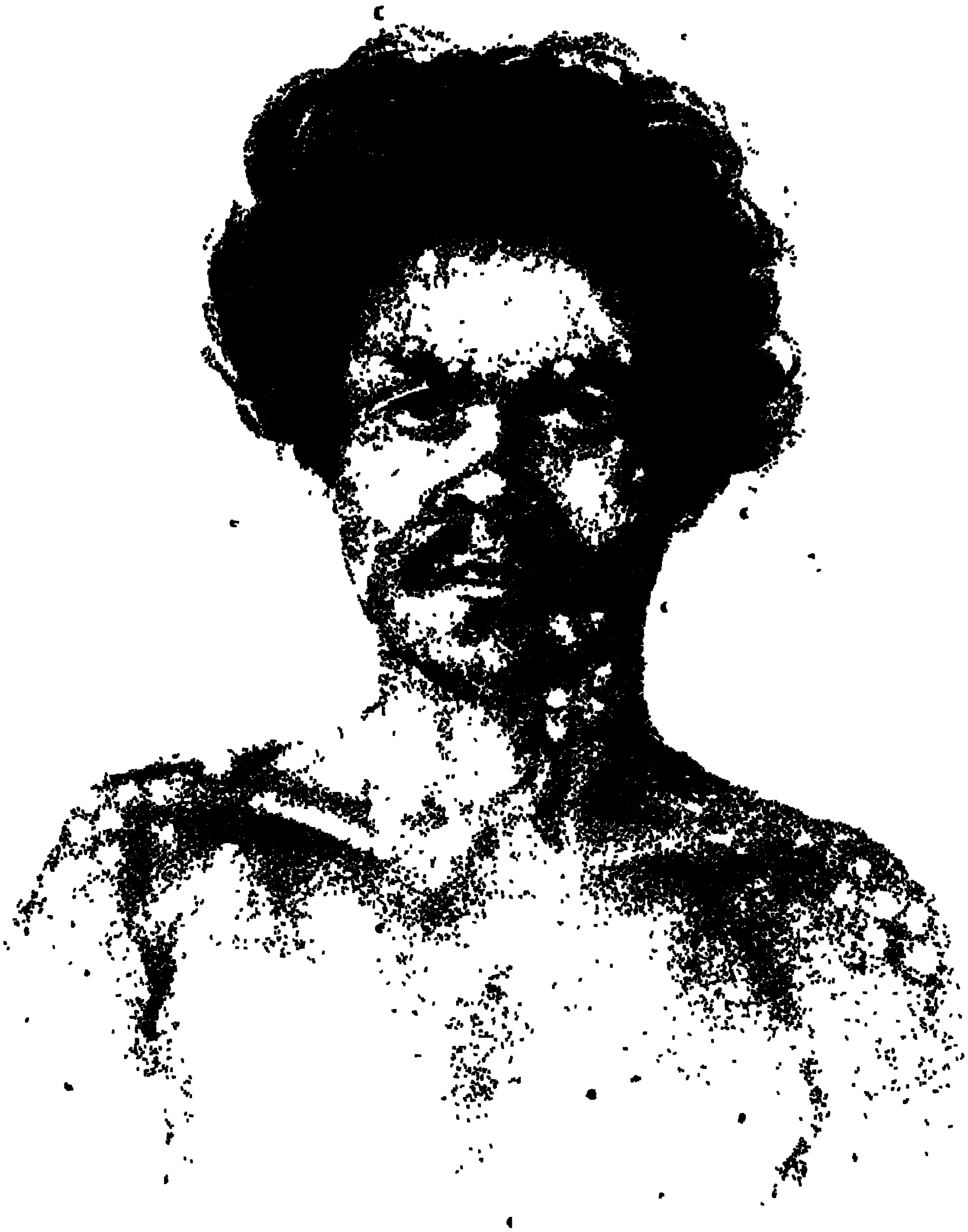
Symptomatology.—The eruption is generally found on the arms and legs, but may extend all over the body, even, though rarely, to the face. The patient complains of unbearable pruritus. The eruption is made up of small papules often covered by bloody crusts; vesicles, papulo-pustules, and pustules may be present, and the patient, on superficial examination, may be considered to be suffering from scabies, but no cunicula are found, and no acarus is observed.

Prognosis.—The eruption is very obstinate, and may last for months.

Diagnosis.—The absence of cunicula and of the sarcoptes differentiates it from scabies.

Treatment.—Sulphur (3 to 10 per cent.) and naphthol ointments (3 to 10 per cent.) are very useful, though their action, as remarked by Daniels, is much slower than in scabies.

PLATE XVI.



DERMATITIS NODOSA RUBRA.

IN REALITY THE PAPULES ARE OF A BRIGHTER ANGRY-RED COLOUR.

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DERMATITIS NODOSA RUBRA.

Historical and Geographical.—This condition has been described by Castellani in Ceylon.

Ætiology.—This is unknown.

Symptomatology.—The first impression received on seeing a patient suffering from this peculiar disease is that he is suffering from smallpox in the papular stage of the eruption, but the absence of fever and the closer inspection of the eruption will exclude smallpox at once. In a well-marked case the patient presents on his face, arms, chest, back, and practically on the whole body, numerous large papules and nodules. The colour of the eruptive elements is an angry red; the shape, hemispherical or roundish; the size, from a small split-pea to a large pea. The surface of the papules and nodules is smooth, does not show umbilication, nor scales; their consistency is hard; most of the papules are not follicular. There is unbearable pruritus, but the malady has no urticarial element whatever. Several of the superficial lymphatic glands are enlarged and hard. In several cases a well-marked enlargement of the parotid gland is present. The blood shows a certain degree of eosinophilia. The course of the disease is long—six months to a year, and sometimes much longer; the nodules become gradually smaller, and may disappear completely; they leave no scar or zones of hyperpigmentation, but occasionally the skin may take a slightly scaly or eczematoid appearance. Recurrences may be observed.

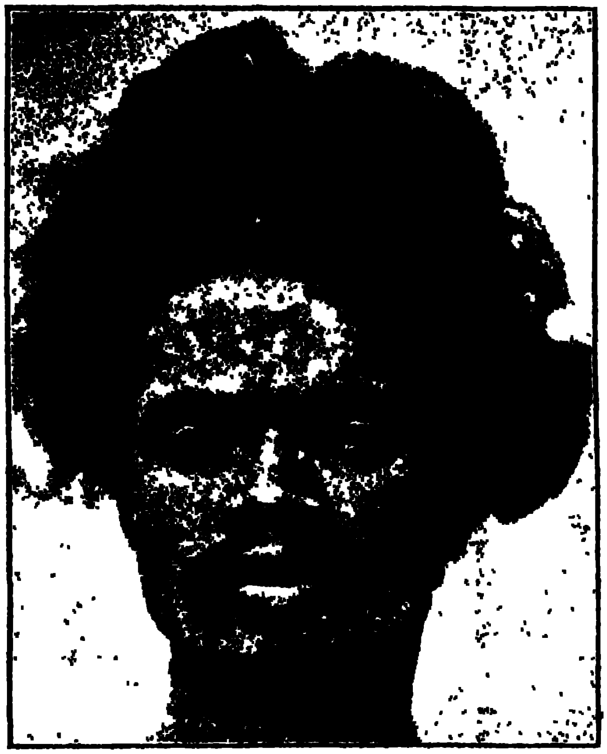

FIG. 881.—DERMATITIS NODOSA RUBRA.

Diagnosis.—From a *syphilide* by the extreme pruritus and the inefficacy of mercury and potassium iodide.

From *smallpox*, the papular stage of which it closely resembles, by the absence of fever, by the chronic course, and by the fact that the papules never undergo a purulent change nor leave scars on healing.

From *lichen planus* by the papules being very large, and by their not being flattened, umbilicated, nor polyhedric.

From *pityriasis rubra pilaris* by the papules being very large, and most of them not follicular, and by the absence of plugs and scaling.

From *acnitis* by the unbearable pruritus and by the eruption not being chiefly limited to the face, as well as by the absence of subsequent necrosis.

From *folliclis* by the condition not being limited to the extremities, and by the absence of central crusts.

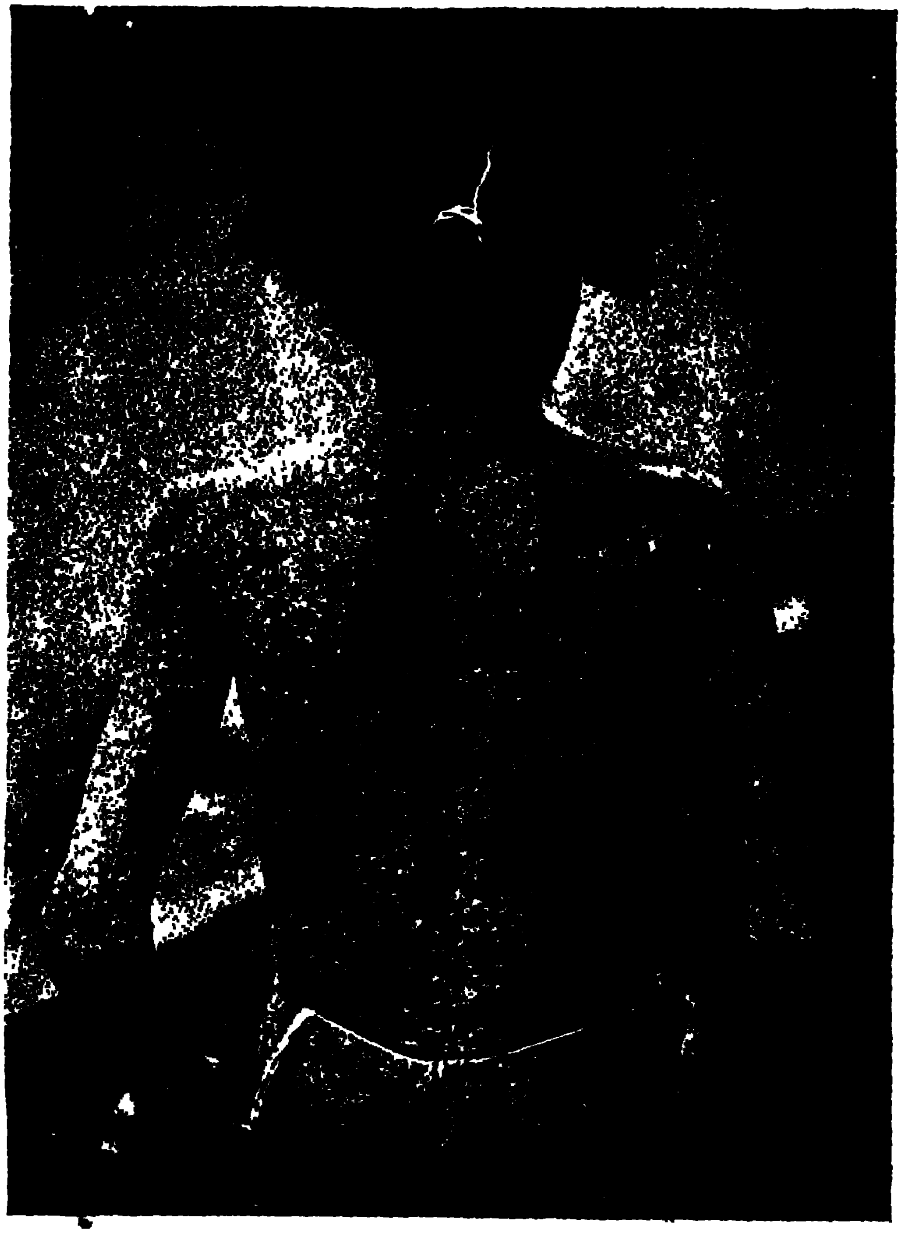

FIG. 882.—DERMATITIS NODOSA RUBRA.

From *erythema multiforme* by the eruptive elements being well-defined, persistent, solid papules and nodules.

Prognosis.—In most cases the general health is not much affected, but the patient complains of the disfigurement and the severe pruritus, and the course of the disease is a long one. Occasionally, after many recurrences, death ensues.

Treatment.—Arsenic, potassium iodide, mercury, do not influence the disease. To allay the pruritus salicylic alcoholic lotions (2 per cent.) and ointments may be used.

LICHEN CONVEX.

Synonym.—Lichen Pilaris Convex (Castellani).

Historical and Geographical.—This affection—which has been described by Castellani—is very common in Ceylon, especially among natives.

Symptomatology.—The regions of the body mostly affected are the thorax, dorsum, and shoulders. The disease is characterized by the presence of numerous firm papules, all of which are follicular. The surface of the papules is smooth; no squamæ or plugs are found; they have always a convex surface, and may be almost hemispheric, $\frac{1}{12}$ to $\frac{1}{8}$ inch in diameter. The colour of the papules has a pinkish hue in natives, and red in Europeans; they have no inflammatory base, they are not surrounded by any halo of inflammation, nor is there hyperpigmentation, nor do they leave pigmented areas on healing. The eruption is very pruriginous. The regions affected may show hyperidrosis. The general health is not affected; the lymphatic glands are not enlarged; in a few cases the blood may show a slight degree of eosinophilia.

FIG. 883.—LICHEN CONVEX.

The course is long, the eruption lasting about three to nine

months, and often recurring. When the eruption heals, no hyperpigmentation is left.

Diagnosis.—From *pityriasis rubra pilaris* by the papules never showing plugs and by the absence of scaling; from *lichen planus* by the papules not being flattened, nor polyhedric, nor umbilicated; from *dermatitis nodosa rubra* by the papules being always follicular and not so large; from a *syphilide* by the intense pruritus; from *papular eczema* by the papules being always follicular and larger and dome-like, with absolutely no inflammatory base, and by the skin not presenting a diffuse inflammation, whatever the stage of the disease. Moreover, even when the eruption is of long standing, the appearance of the skin between the papular elements remains quite normal, and there is no sign of what the French call *lichenification.*

Prognosis.—The eruption lasts for several months, but generally heals spontaneously; recurrences are observed. The general health is not affected.

Treatment.—Potassium iodide, mercury, and arsenic have no effect. Externally, antipruriginous lotions and ointments may be used—as, for instance, a salicylic alcoholic lotion (2 per cent.), followed by a naphthol ointment (2 to 5 per cent.). Change to a cool climate is very beneficial. One of our cases improved on a vegetarian diet.

SYMMETRICAL EAR NODULES.

This condition has been described by one of us in Ceylon in 1910, but further experience will probably show that it is to be found also in other tropical countries. In the deep substance of the lobule of both ears generally the condition is symmetrical—on palpation, a spherical nodule, hardly visible, is felt. Now and then the nodule becomes much larger, very tense, and may then present a somewhat translucid appearance: after some days it becomes smaller again, and may be hardly visible. There is, as a rule, no subjective symptom during the periods of quiescence; a feeling of tension and slight pain during the periods of increase of size of the nodules.

The condition is not leprotic, there being no anæsthesia or other sign of leprosy: it may possibly be of parasitic origin, but nothing definite can be stated, as none of our patients would allow the removal of the nodule. Further investigation may show that it is allied to the peculiar condition called Nepaul tumour (see Chapter XC., p. 2010).

EAR LIPOMATA.

Symmetrical lipomata of the lobules are not rare (see Chapter XC., p. 2010).

PORTER'S LIPOMATA.

Porters and hammock carriers often show one large lipomatous mass on one or both shoulders, where they carry weights, or where the pole on which the weight is carried presses.

SUBCUTANEOUS NODULAR LIPOMATOSIS.

Synonym.—Polymicrolipomatosis.

This condition seems to be common in the tropics in Europeans and natives alike. It is characterized by the presence of subcutaneous nodules, found only on palpation, roundish or oval, painless, the size of a pea to a nut. These are generally situated in the subcutaneous tissue of the arms, legs, and abdomen, and in our experience are not rarely mistaken for enlarged lymphatic glands. On tapping them with a sterile syringe only a trace of fatty material is removed, which, when placed on a slide, promptly dissolves when heated or treated with ether. The microscopical examination of one of these nodules, surgically removed, showed it to be composed of fatty tissue. Occasionally the tumours become much larger and may be plainly visible.

ANGIOFIBROMA CONTAGIOSUM TROPICUM.

This disease was first described by Unna and von Bassowitz. So far, cases have been reported from the southern regions of Brazil only.

Symptomatology.—The incubation period varies from fifteen to twenty-five days. There are no prodromal symptoms. The eruption consists of vivid red papules, which soon enlarge into nodules the size of a large pea to an almond. The eruption may affect any part of the body, but more frequently the face, neck, axillæ, and genital organs. It is rarely found on the legs. It very frequently affects the various mucosæ—oral, nasal, rectal, and urethral. The nodules present a smooth surface, of a violaceous colour, and they are somewhat of soft consistency; they bleed severely after the slightest traumatism. They may disappear spontaneously without leaving any scar, or in other cases secondary infections may set in, and large ulcers develop. The eruption is not pruriginous, there is no fever, and the general health is not impaired.

Ætiology.—This is unknown, but the disease is considered to be infectious. According to Bassowitz, the infection takes place during sexual intercourse, or by the habit the people of Brazil have of taking their maté (national beverage), using the same cannule.

Histopathology.—According to Unna's investigation, the histopathology is quite different from what is observed in framboesia and syphilis. The nodules consist of fibrous tissue, with scanty cells intersected by extremely numerous bloodvessels.

Diagnosis.—The disease must be distinguished from verruga peruviana and framboesia. In verruga peruviana there are severe constitutional symptoms—fever, and often enlargement of the liver and spleen. The condition, however, is considered to be identical with verruga *sensû stricto* (p. 1576), by Strong, Tyzzer, Brues, Sellards and Gastiaburu. In framboesia the nodules have a moriform surface, and do not bleed so easily.

Treatment.—Mercury and potassium iodide are useless. Bassowitz recommends iron and arsenic internally, and externally the injection into the base of the nodules of a few drops of formalin, or their excision, using the galvano-cautery.

MULTIPLE PRURIGINOUS TUMOURS OF THE SKIN.

Schamberg and Hirschler reported in 1905 two cases of multiple tumours of the skin in negroes, associated with itching. The tumours were sharply circumscribed nodules, from the size of a small pea to a large hazel-nut, situated on the extremities. They were of a blackish colour—the smaller smooth, the larger covered with a horny epidermis. These tumours showed, on histological examination, dilated vessels, cellular infiltration, with numerous mast cells, and the formation of new collagenous fibres. The same eruption was previously described in 1880 by Hardway in a white woman.

WEST INDIAN NODULES.

This affection, which seems to be very similar to the preceding one, has been described by Numa Rat in natives of the West Indies, who often confuse it with Guinea-worm. The eruption may attack any part of the body, and consists of subcutaneous nodules varying from the size of a pea to that of a small nut. There is extremely severe pruritus, and the natives destroy the skin covering the nodules with caustics, and extract the nodules, which appear yellowish-white and have a cartilaginous consistency.

Histologically, according to Macleod, they consist mainly of hypertrophied connective tissue made up of thickened collagen bundles. The ætiology is unknown.

MOSSY FOOT.

Synonym.—Piemugoso.

This affection is fairly common, according to Thomas, in the region of the Amazon.

The foot is covered with dense, warty, very vascular, painful masses, as much as a half to three-quarters of an inch thick, which may spread to the leg.

The disease is very chronic, and probably of parasitic origin.

The suggestion has been made by Cranston Low that it may be a type of tuberculosis cutis verrucosa, and by Da Matta that it may be a form of leishmaniasis.

BOTRYOMYCOSIS.

Synonyms.—Botryomycosis Hominis, Granuloma Pyogenicum.

Definition.—A granulomatous condition characterized by the presence of coccal bodies of various size and collected in clusters.

Historical and Geographical Distribution.—The condition was first studied in horses, in which it occurs often in the testicular cord after castration; but it is common also in the pig, dog, and cattle. Later it was found in man by Dor and Poncet in Europe. In the tropics it has been observed in Ceylon by one of us.

Ætiology.—The condition is believed by some observers to be due to an organism (*Botryococcus ascoformans* Kitt, *Micrococcus botryogenes* Rabe), the botanical position of which is not defined. The organism appears in the lesions under the form of spherical bodies of very different size (0·8 to 12 μ), singly or collected in clumps, Gram-positive, and to a certain extent acid-fast. They seem to reproduce by a process of endosporulation. The cultures obtained by some authors have, however, all the characters of a staphylococcus.

Some authorities, in fact, consider the disease to be merely a type of pyosis due to the usual staphylococci. Magrou, using a special technique, has succeeded in experimentally reproducing the disease by inoculating a strain of *Staphylococcus aureus* isolated from an ordinary case of sepsis. M. Nicolle and Cesari have shown that the serum derived from horses affected with botryomycosis neutralizes staphylococcal toxins. Letulle considers the disease to be due to an amœba, and his results have been confirmed by Bureau and Labbé, but not by others.

Pathology.—The condition, as seen by us in the tropics, has all the characters of a granuloma. The microscopical examination of sections shows young connective tissue with large numbers of plasma cells. Peculiar claviform bodies have been described by Magrou, who believes them to originate from the staphylococci. The lesions are very vascular. Later, denser fibrous tissue is observed.

Symptomatology.—The condition generally develops on some suppurating wound, but may occur upon the site of any abrasion or wound. It appears as a small, generally cherry-red, granulomatous nodule or mass, often roundish, of various size—from a pea to a nut or larger. Occasionally the nodule may be pediculated. At first it is of rather soft elastic consistency; later may become fibrous and much harder. There is very little tendency to spontaneous cure. A very mild type of botryomycosis occasionally develops after vaccination. We have seen several such cases.

Prognosis.—The general health is not much affected, but the condition has little or no tendency to spontaneous cure.

Treatment.—Excision, followed by light cauterization with pure carbolic or chloride of zinc, is the only method of treatment. The pedunculated form may be cured by ligature. The disease may occur again after operation, but this is rare.

Prophylaxis.—Care should be taken to keep suppurating wounds thoroughly disinfected.

THE HYPERKERATOSES.

Definition.—A hyperkeratosis is any cutaneous condition in which the cells of the horny layer have a greater coherence than normal, as tested with pepsin and hydrochloric acid, and thus tend to pile themselves up in the form of horny scales.

Remarks.—As defined above, a hyperkeratosis is more a symptom than a disease, and most of the so-called *primary hyperkeratoses* are probably induced by some chemical change produced by an altered metabolic condition brought about by some infection.

Thus syphilis and framboesia tropica are often believed to be the disturbing element which lays the foundation of these changes, even though no sign of their specific germs can be found in the lesions, which may appear long after the disappearance of other features of the disease, while the specific treatment for these complaints has little or no influence on the hyperkeratosis.

Further, syphilis can certainly act upon the fœtus *in utero* and lay the bases of changes of metabolism, which may result in the so-called congenital hyperkeratosis, and the same remarks, to a certain extent, appear to apply also to tuberculosis.

Classification.—With the above provisos, the hyperkeratoses may be classified into:—

A. *Hyperkeratoses obviously associated with a causal disease*:—
  1. *Non-follicular*:
    Found in leprosy, arsenical poisoning, and hyperidrosis.
  2. *Follicular*:
    Found in various tubercular and syphilitic affections, and some forms of lichen and acne.

B. *Hyperkeratoses of unknown origin or remotely associated with syphilis, yaws, tuberculosis, etc.*:—
  (*a*) *Develops during intra-uterine life*:
    Hyperkeratosis universalis congenita.
  (*b*) *Develops during post-uterine life*:
    1. Generalized affections:—
      Of these, *ichthyosis* and *pityriasis rubra pilaris* are met with in the tropics.
    2. Localized affections:—
      (i.) *Non-follicular*:—
        (1) Without acanthosis or markedly dilated papillary vessels—*Keratodermia*.
        (2) Without acanthosis, but with markedly dilated papillary vessels—***Angiokeratodermia***.
        (3) With acanthosis, but without markedly dilated papillary vessels—***Acanthokeratodermia***.
      (ii.) Follicular—*Keratosis*.

In the tropics we have met with leprotic and syphilitic hyperkeratoses, as well as with those connected with lichen planus. We have also seen ichthyosis, pityriasis rubra pilaris, and keratosis palmaris et plantaris, and several other forms; but of all these, three forms must receive a little further notice—viz.:—

1. Keratodermia cribrata.
2. Acanthokeratodermia præcornufaciens.
3. Keratoma plantare sulcatum.

KERATODERMIA CRIBRATA.

Synonym.—Keratodermia punctata.

Definition.—It is a localized non-follicular hyperkeratosis of the hands and feet, appearing in post-uterine life, in which the hyperkeratosic area is riddled with little pits caused by the shedding of little corn-like projections.

Remarks. In the tropics it was first described by Castellani and then by Chalmers.

Ætiology.—It seems that it is in some way associated with yaws or syphilis (congenital or acquired), probably by changes effected in the metabolism, and not by the action of their parasites.

Pathological Histology. The essential points are a mild chronic inflammation of the dermis and a hyperkeratosis of the sweat orifices, leading to the formation of corn-like projections, which are freed laterally and finally all round, and then fall out, leaving a depression.

Symptomatology.—The palms of the hands or soles of the feet may show hyperkeratosis associated with slight itching. In the hyperkeratosic area there are many corn-like bodies, some of which have fallen out and left depressions. The condition is very chronic.

Diagnosis.—The bilaterally symmetrical hyperkeratosis of the palms or soles, with the pits in the thickened areas and the corn-like bodies, are characteristic.

Treatment.—Nothing is known to permanently benefit the condition.

ACANTHOKERATODERMIA PRÆCORNUFACIENS.

This is an acanthokeratodermia characterized by the formation of thickened patches of epidermis in the palms of the hands and soles of the feet, which may (in the latter situation) become cracked and fissured and break down, forming painful sores, which prevent the patient from walking. Sometimes they are associated with a thickening of the horny layer of the nail-bed, thus giving rise to a peculiar elevation of the nail called by Unna *hyperkeratosis subungualis*. Most patients have been affected with syphilis, but the specific organisms cannot be found in the lesions, and antisyphilitic treatment is generally useless. Pathologically the condition resembles that in the first stage of the production of a cutaneous horn, which, indeed, had formed in one case reported by Colcott Fox.

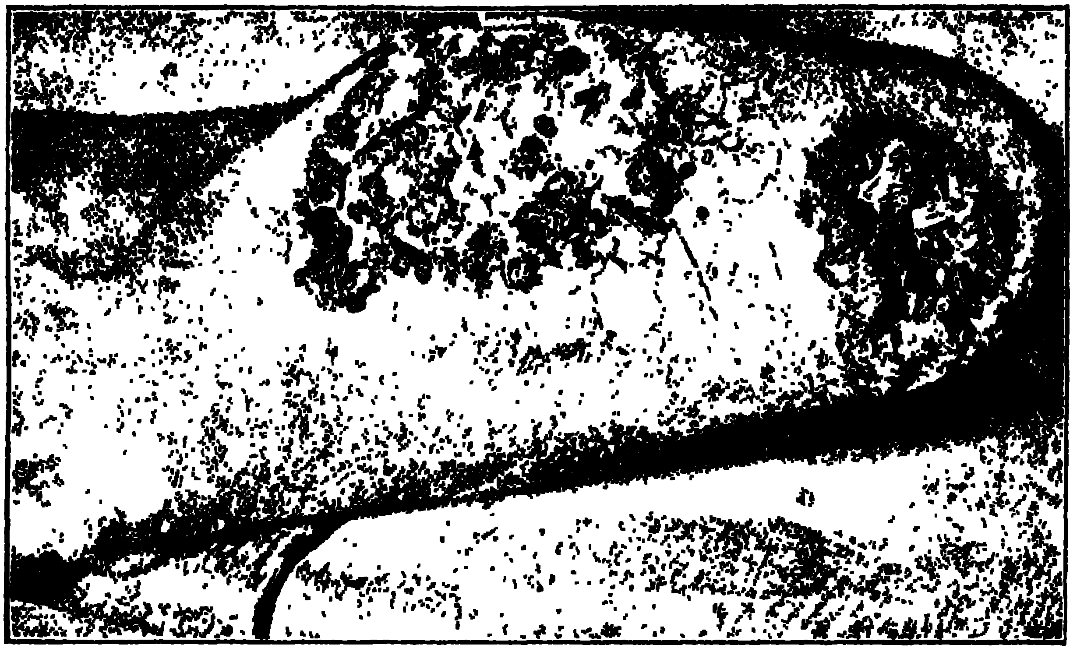

FIG. 884.—ACANTHOKERATODERMIA PRÆCORNUFACIENS.

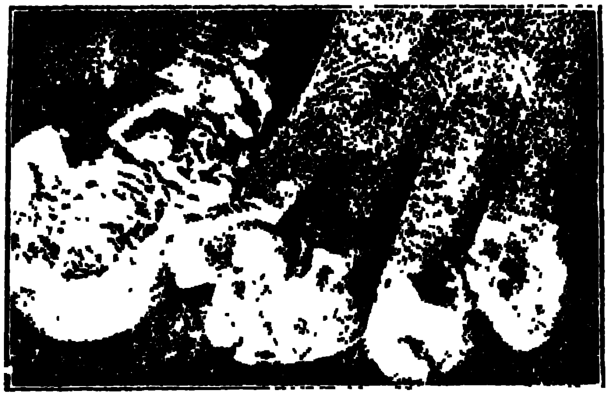

FIG. 885.—ACANTHOKERATODERMIA PRÆCORNUFACIENS.

KERATOMA PLANTARE SULCATUM.

Historical and Geographical.—This disease was first described by Castellani in Ceylon. It is found also in India and tropical Africa, and a case has been recorded in Macedonia.

Ætiology.—This is unknown, though in certain cases yaws may perhaps play a rôle in its causation. The affection is much more frequent during the rainy season, and occurs generally in natives who do not wear shoes or sandals; but we have seen a typical case in a European of good social standing. It improves or disappears completely during the dry season.

Symptomatology.—The epidermis of the soles—especially the anterior portion—and the heels is greatly thickened, and is generally of a dark yellowish colour, and presents numerous deep segmentary furrows, straight, semicircular, or ellipsoid; these furrows appear black, but if the dirt and dust accumulated in them is removed, the fundus of these sulci will be found to be whitish or pinkish. There is no sign of any local inflammation, though the patient generally complains of tenderness of the feet after much walking.

Diagnosis.—This is based on the presence of the characteristic deep sulci and punched-out holes in the thickened epidermis, which are absent in lesions of the soles of the feet of syphilitic origin.

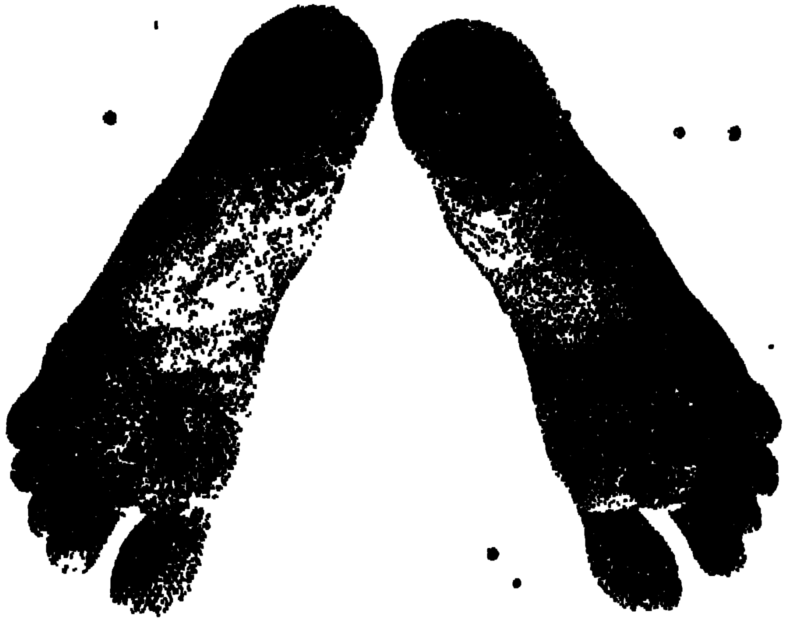

Fig. 886 Keratoma Plantare

Moreover, a mercury and potassium iodide treatment has no effect whatever on the malady. In yaws the lesions of the soles of the feet are, generally, either granulomatous, with large frambœsiform nodules piercing through the thick epidermis, or a diffuse scaly condition with thickened epidermis is observed. The rare pitted condition of the soles of the feet (p. 1550) found in yaws is distinguished by its lack of seasonal incidence and by the history. In the condition known as 'symmetrical keratodermia of the extremities' no deep sulci are found. The so-called 'mal de meleda,' which is very common in the Island of Meleda in the Adriatic, is, according to Neumann and others, identical with symmetrical keratodermia, and no deep sulci are present.

Prognosis.—The general health is not affected, but the condition may last for months, and if the patient has much walking to do, may become very painful.

Treatment.—Potassium iodide, mercury, and salvarsan are useless. Rest and local applications of salicylic ointment or salicylic collodion (ac. salicyl., ʒi.; collodion, ℥i.), or salicylic plasters induce a marked improvement.

JUXTA-ARTICULAR NODULES.

Synonyms.—'Enno,' Naridé, Macgregor's nodules, Steiner's tumours, Jeanselme's nodules.

Historical and Geographical.—This affection was first briefly described by Macgregor in 1901 in New Guinea, who also suggested a possible parasitic origin of it. It was later more fully studied by Steiner in natives of Java and by Jeanselme in natives of Siam, where it is known as 'enno.' Jeanselme introduced the very appropriate term of 'juxta articular nodules.' Fontoynont and Carougeau in Madagascar considered the cause of the affection to be a fungus, *Nocardia carougeaui* Brumpt, 1910. Cases have been observed in Northern Africa by Gros and in Ceylon by us, also by Chalmers and Archibald in the Sudan. The disease will probably be found to occur in many other tropical and subtropical countries.

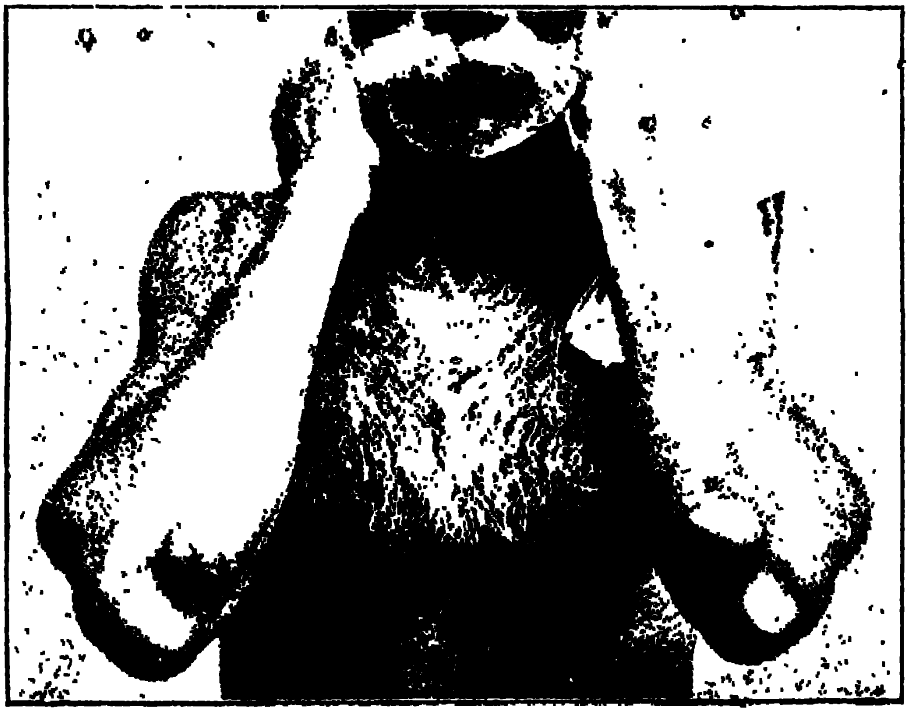

Fig. Juxta-Articular, N

Ætiology.—Macgregor, Steiner, and Jeanselme considered the nodules to be of parasitic origin, while Fontoynont and Carougeau found a fungus which they believed to be the ætiological agent of the condition. The description of this fungus—*Nocardia carougeaui*

Brumpt, 1910—is given in the chapters on fungi (see pp. 1065 and 1066). Recently the presence in the nodules and etiological rôle of this fungus has been doubted by many authorities. Several observers consider the condition [illegible] late manifestation of frambœsia.

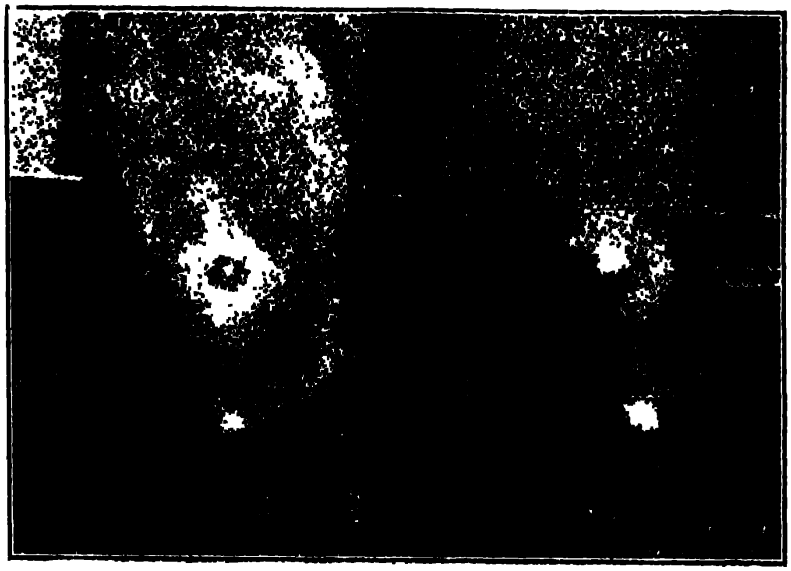

FIG. 888. JUXTA-ARTICULAR NODULES.

Symptomatology. In the legs and arms, especially in proximity to the articulations, several nodules are found, some of them the size of a walnut or more, of rather hard consistency, and covered by healthy skin. According to Macgregor, these tumours occur most frequently about the elbows or the parts of the body coming in contact with the ground when the native is sleeping. These nodules at first are rather soft, and are situated in the subcutaneous tissue, and the skin may be moved above them. Later they may, apparently, fuse together, forming hard, large tumours, and adhere to the skin, which generally does not present any alteration. The course is very chronic, but occasionally the nodules may disappear spontaneously.

FIG. 889. MURMEKIASMOSIS AMPHILAPHES.

Treatment.—The nodules may be excised. In the very first stage of the disease a potassium iodide treatment might be tried.

MURMEKIASMOSIS AMPHILAPHES.

Chalmers and Christopherson have described a case (Fig. 889) of spreading warts, associated with *Cryptococcus myrmeciæ,* which grew on the skin of the face and neck, destroyed an eye, and entered the mouth.

LYMPHO-FIBROMATOSIS.

This is a condition of elephantoid fibrosis (Fig. 890) met by us in Ceylon and Africa. It is sometimes associated with a secondary pyogenic eruption. Some cases may be associated with filariasis, but others are not. The skin is elevated into large, raised, flattened patches of fibrous consistency. The condition is chronic.

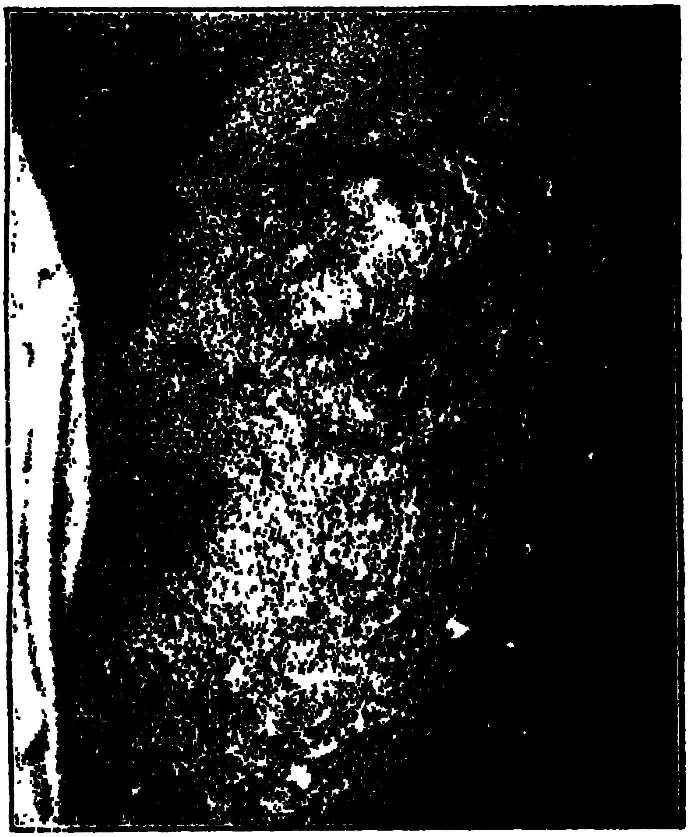

Fig. 890.—Lympho-Fibromatosis.

SEBORRHŒA SPINULOSA.

This condition has been seen by Castellani and Chalmers in various parts of the tropics and the Balkans. It is characterized by the presence of numerous yellow plugs, some of which are acuminate and hard. These plugs project from the orifices of the sebaceous ducts, and are often situate on an oily skin. Ordinary black comedones are absent. The term 'seborrhœa spinulosa' probably covers several varieties of seborrhœa.

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CHAPTER XCIX

COSMOPOLITAN SKIN DISEASES

General remarks—Pyogenic infections—The erythemata—The exanthemata—Urticaria—Dermatitis venenata—Parasitic diseases—Bullous eruptions—Herpes—Eczema, psoriasis, seborrhœa, and dermatitis exfoliativa—Acne—Hyperidrosis and bromidrosis—Lichen—Tumours—Tuberculosis—Syphilis—Ichthyosis—Kaposi's disease—Chloasma—Diseases of the hair and nails—Some cosmopolitan diseases of mucous membranes.

GENERAL REMARKS.

IN our experience, all the skin diseases met with in temperate zones are also found in the tropics, except those due to intense cold, such as erythema pernio and frost-bite, and even these may also be found in the high mountainous regions of the tropics.

The diagnosis of some of the cosmopolitan dermatoses may, owing to the colour of the skin of native races, be very difficult to the medical man newly arrived in the tropics. This is probably the cause of some of the statements that such common diseases as lichen planus and psoriasis are absent. There is no doubt, however, that some dermatoses which are frequently met with in temperate zones are less common in the tropics.

It is stated by some authorities that coloured races are, on the whole, less liable to skin diseases than the white races, but the reverse is more in accordance with our experience.

A few remarks as to the normal skin of native races may be useful before proceeding to review the various cosmopolitan diseases. In the African races and American negroes who descend from African negro stock (Guinea negroes, Yoloffs, Caffres) the whole skin, especially the derma, is thicker than in the white races. In Indian races the skin is about the same thickness as in Europeans, except in the Tamils, whose skin is somewhat thicker. As noted by Howard Fox, the glandular system—sweat glands and sebaceous glands—is much more highly developed in the native races, especially the African negroes. The sebaceous secretion is the cause of their peculiar odour and the shining appearance of the skin, and the large secretion of sweat, which, owing to the high temperature, quickly evaporates, is the probable cause of the skin feeling cooler when touched. In native races the hairy system is less developed, except on the scalp; in the African races the hair of the head is generally curly or woolly; in Indian races it is usually smooth.

The slight development of lanugo hair is the cause, as noted by Fox, of the peculiar velvety feeling of the negro skin.

The most important characteristic of the skin of tropical native races is the dark pigmentation. It is said that this pigmentation is not present at birth, but develops within a few hours to several days after birth. In our experience, it cannot be doubted that at the time of birth in many cases the babies present a much lighter colour than the adult people. The skin, however, is not whitish, but of a muddy brownish colour, and darkens greatly within a few days—in some cases is quite dark also at the time of birth. It is said that the pigmentation increases till puberty, and then, after remaining stationary during adult life, slowly decreases during old age. The maximum pigmentation is found on the loins, posterior portion of the trunk, shoulders, buttocks, and thighs; the least pigmentation is found on the prepuce, vulva, palms, and soles. In some races the oral mucosa is not pigmented; in others there is a patchy dark pigmentation which extends often to the tongue. The dark patches on the tongue have been considered by several writers to be a pathological condition, and a sign of ankylostomiasis. We have observed such patches, however, in numbers of normal natives. The hair is said to become white at a later date among negro races than in Europeans; we have not noted any distinct difference, either among them or the natives of Asia.

It is said by some writers that native races, and especially the negro African races, are less susceptible to pain than the white man. In our experience there is hardly any difference in the ordinary dolorific sensibility, but the thermic sensibility is probably less.

PYOGENIC INFECTIONS.

These are very common in tropical countries. **Impetigo** and **Ecthyma** lesions are frequently met with. The symptoms and course are identical with what one finds in temperate zones, and the treatment is the same—removal of the crusts, disinfection with a lotion, such as a perchloride of mercury (1 in 2,000), and dressing with a white precipitate ointment (1 per cent.).

Boils.—This is a common affection in the tropics, very stubborn, and difficult to cure. The quickest and most reliable method of cure in cases of multiple boils is, in our experience, Wright's vaccine treatment, the vaccine being prepared from staphylococci isolated from the patient. When this treatment cannot be carried out, the administration of yeast preparations internally will be found to be useful in some cases—*e.g.*, ceridin pills. Occasionally a small boil may be aborted by applying a droplet of pure carbolic acid by means of a pointed pencil of wood drilled into the centre of the papule. For old indurated boils the continuous application of a carbolic lotion (2 to 5 per cent.) on lint occasionally causes them to become absorbed.

As a preventive, a salicylic alcoholic lotion (1 to 2 per cent.) used after the daily bath is advantageous.

Sycosis coccogenica.—This is fairly common in both Europeans and natives. In the negroes Fox has often observed the formation of tiny cheloidal tumours after this affection. Depilation and the use of a vaccine is the best method of treatment. We have observed a case of *Dermatitis papillaris capillitii* (Kaposi).

Erysipelas.—Ordinary erysipelas due to streptococci, and to be distinguished from the filarial erysipelatoid attacks preceding the development of elephantiasis, is not rare. Ichthyol ointment or lotion (10 per cent.) answers well.

THE ERYTHEMATA.

Erythema solare is common in Europeans recently arrived, and in those who live an open-air life, such as planters. It is followed by pigmentation (sunburn, see pp. 82 and 2231). The application of calamine lotion, followed by the use of boric vaseline or rose-ointment, is beneficial.

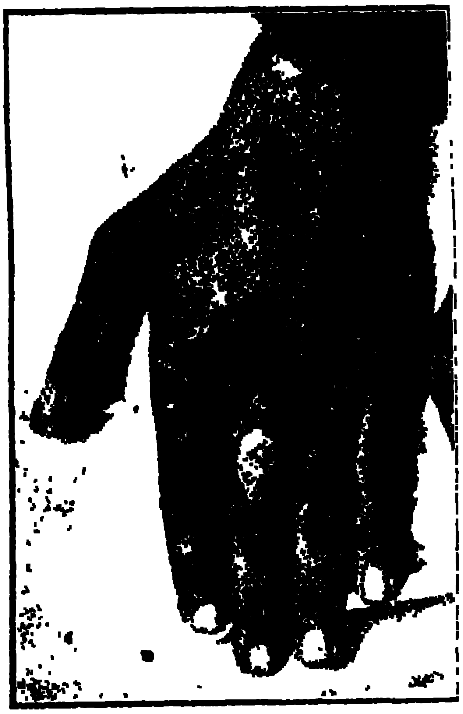

Fig. 89K—Herpes Iris.

Erythema intertrigo is very frequently observed in corpulent persons. Washing the parts with a potassium permanganate solution (1 in 5,000), followed by application of boric-talc or salicylic-talc powder (acid. boric. ʒi., talci ℥i., or ac. salicyl. gr. x., talci ℥i.), is useful. Persons suffering from intertrigo are very liable to become infected with tinea cruris.

Erythema nodosum — Erythema multiforme.—These affections are occasionally met with, but much more rarely than in temperate zones. We have seen two cases of the variety of erythema multiforme known as *herpes iris*.

Erythema annulatum and **Erythema gyratum,** in persons suffering from fever, and coming from tropical Africa, should always arouse the suspicion of trypanosomiasis.

Diffuse **Erythema scarlatiniforme** and **Erythema morbilliforme** may be seen in some malarial patients. They may occasionally be caused by quinine, but in most cases are of malarial origin. The diagnosis of erythemata in dark natives is difficult. The medical man of long experience, however, will be able to detect a peculiar shiny aspect of the skin, with a distinct pinkish tinge.

Purpura.—Schönlein's purpura, Henoch's purpura, and Werlhof's purpura are not common in the tropics, though we have seen cases. A symptomatic purpura eruption is occasionally seen in the last stage of kala-azar, in malaria and other maladies.

THE EXANTHEMATA.

Smallpox, chicken-pox, and measles are very common in the tropics, though scarlet fever is but rarely met with.

Smallpox, of which we have already given a description (p. 1486), is very common, and often spreads in extensive epidemics, and may present the confluent type and the hæmorrhagic type, which is rare in Europe. In colonies under European rule vaccination is extensively practised. The vaccine does not retain its immunizing properties for more than a few weeks in the tropics, and hence it is advisable for each colony to be provided with a central vaccine depot where the lymph can be prepared under careful supervision. Owing to the habits of the lower classes and to many of the vaccinators being non-medical men, serious infections with other diseases may occur.

Measles may be difficult to recognize, as the eruption in dark-skinned races is better felt than seen, but the coryza and other symptoms are generally sufficient to enable a correct diagnosis to be made.

URTICARIA—LICHEN URTICATUS—PRURIGO.

Urticarial eruptions are as frequent in the tropics as in temperate zones, though to the new-comer the diagnosis of urticaria in dark-skinned natives is far from easy. Of **lichen urticatus** we have seen several cases among European and half-caste children, and of **urticaria pigmentosa** we have seen one case—a European child. We have observed true **prurigo** of Hebra in two native girls.

DERMATITIS VENENATA.

Several tropical plants and grasses produce substances highly irritating to the skin, but the subject has already been treated in Chapter XCIV., p. 2151. The dermatitis so caused may be urticarial, erythematous, eczematous-like, or bullous, and may extend to large portions of the body. The forms of dermatitis venenata due to animal agents, such as ants, bugs, caterpillars, etc., have been already mentioned in Chapters XIV. and XCVI., p. 2200.

PARASITIC DISEASES.

Trichophytoses.—In tropical countries, in addition to the trichophytoses peculiar to the tropical climate, several other forms of trichophytic affections occur which are clinically identical with those met with in temperate zones, such as tinea circinata, tinea capitis, tinea barbæ. The fungi are, however, in most cases different species (see p. 2052). In our experience, tinea capitis is less common in India, Ceylon, and tropical Africa, than in Europe and America. On the other hand, it is extremely common in the American negroes. The fungi found in the tropics are generally large-spored ones. *Microsporum audouini* has never been found by us. *Favus* is rare in tropical Africa and Asia, but common in China, Egypt and in the Sudan.

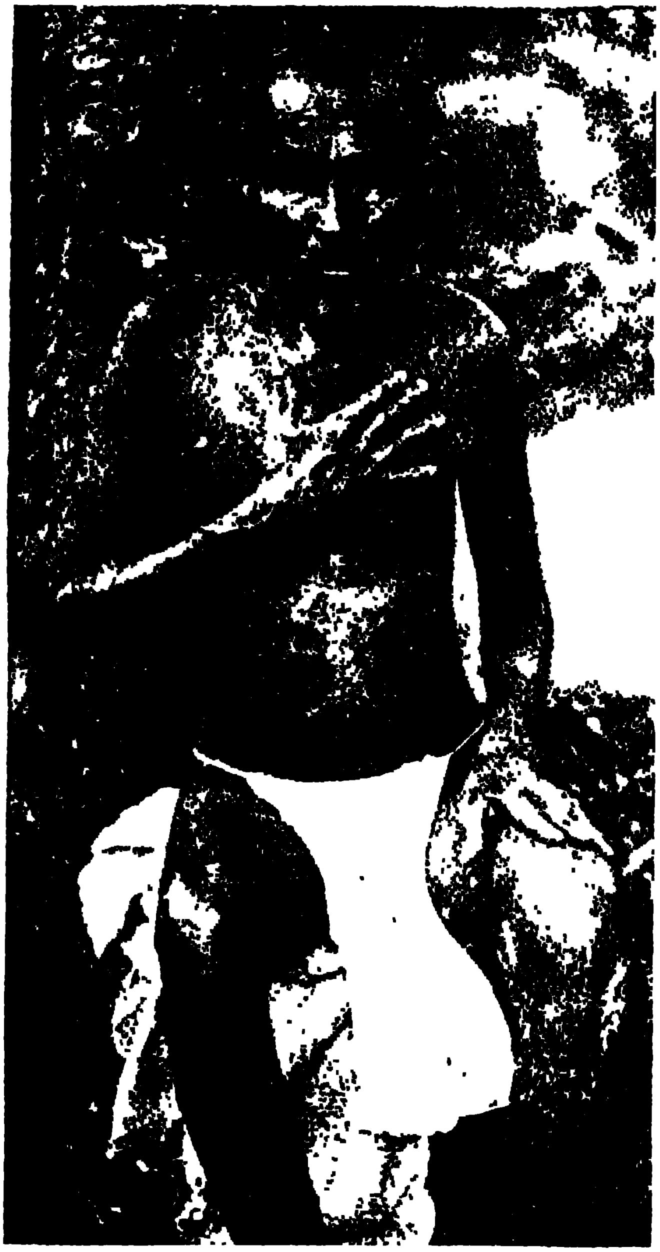

FIG. 892—SEPTIC PEMPHIGUS.

Pityriasis versicolor.—The pityriasis versicolor of temperate zones may be found in the tropics. It is to be noted, however, that several writers on tropical medicine confuse pityriasis versicolor with another dermatomycosis which is extremely common—tinea flava (see p. 2073).

Pediculosis and Scabies. *Pediculosis capitis* is extremely common, although natives generally take great care to keep their hair in good condition by regularly combing, washing, and oiling it. According to Fox, Carmichael, and Pendergast, pediculosis capitis in the Southern States of North America is much less frequent in the negroes than in the whites, as, according to them, the negroes take greater pains in the care of the scalp than do the lower-class whites. *Pediculosis corporis* and *Pediculosis pubis* are as frequent in the tropics as in temperate zones, and so is scabies. *Pediculosis pubis* may, however, be very rare or absent in races accustomed to regular shaving of the pubic hair. For description of the parasites see p. 753. Scabies is described on p. 2217.

BULLOUS ERUPTIONS.

Epidermolysis bullosa is occasionally observed.

Pemphigus vulgaris and **Septic pemphigus** cases are not rare in the tropics. In the cases of septic pemphigus we have always found virulent streptococci. The eruption is similar to what one sees in temperate zones. We have seen a case of **Pemphigus vegetans,** and we have observed a typical case of **Pemphigus foliaceus,** contracted in Ceylon, and another in Indo-China. **Dermatitis herpetiformis** is not rare.

(Of **Hydroa vacciniformis** we have seen two cases in European children.)

HERPES.

Herpes facialis febrilis is common during attacks of malarial fever and other fevers, but very rare, as is well known, in enteric.

We have seen in European children a similar condition to what some French writers call *fièvre herpétique*. The condition, as seen by us, is characterized by a sharp attack of fever lasting about twenty-four hours, and at the same time by the appearance of a few herpetic vesicles—in our cases on the thighs and buttocks.

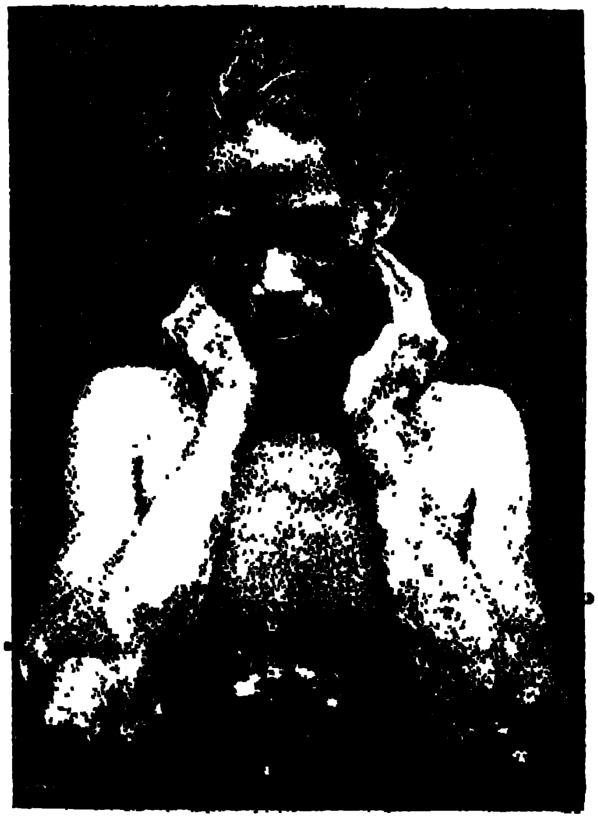

FIG. 893.—PSORIASIS.

Herpes progenitalis is very common, especially in Europeans.

Herpes zoster (zona, shingles) is frequently met with in Europeans and natives.

ECZEMA—ACRODERMATITIS PERSTANS—PSORIASIS—PARAPSORIASIS—SEBORRHŒA—DERMATITIS EXFOLIATIVA.

Eczema is extremely common, and all varieties of it are found in the tropics, as in temperate zones, both in natives and Europeans. The treatment is often very difficult. In our experience greasy preparations and even pastes are as a rule badly borne except in some chronic cases. Generally speaking, it is best to use lotions such as resorcin (½ to 1 per cent.) or liq. plumbi (2 per cent.). Some cases of eczema will improve only on the patient going to a cooler climate. Wilson's **Eczema verrucosum**, characterized by great dryness and hardness and warty appearance of the affected part, is frequently met with among natives, in whom it mostly attacks the toes.

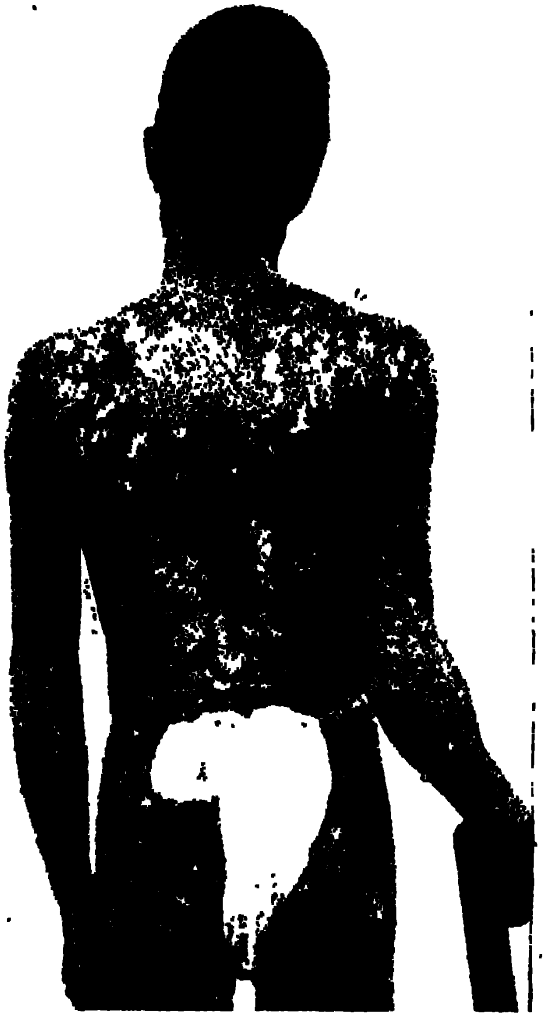

FIG. 894.—PSORIASIS IN A SINHALESE.

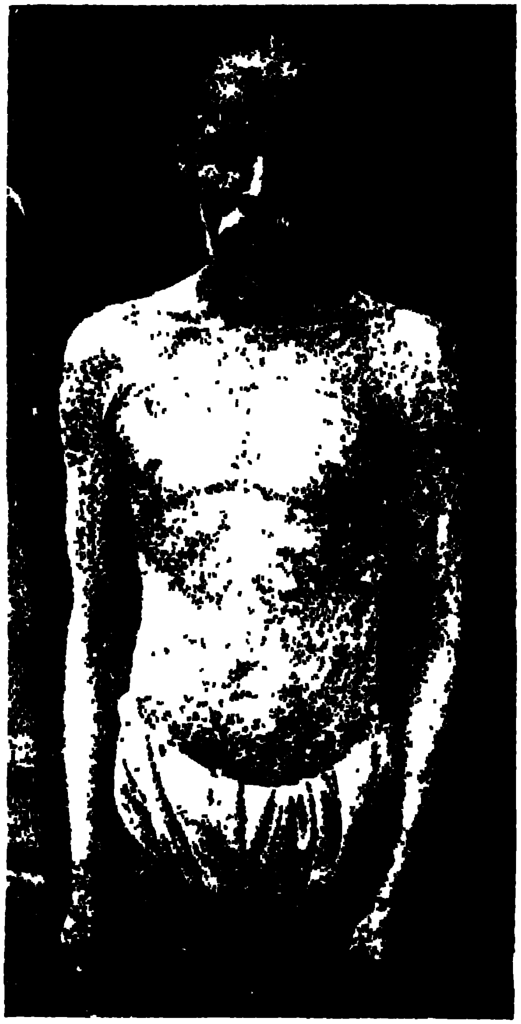

FIG. 895.—DERMATITIS EXFOLIATIVA IN A SINHALESE.

Acrodermatitis Perstans.—We have seen two cases of a very obstinate chronic dermatitis, with exfoliation, on the extremities of Sinhalese natives, apparently identical with acrodermatitis perstans of Hallopeau. They were different clinically from the acrodermatitis vesiculosa described by one of us.

Psoriasis is considered by most writers to be extremely rare or absent in native races in the tropics. Rutz states that he never saw a single case of psoriasis in a negro during his many years of practice in Martinique. Howard Fox, senior, thinks that possibly the savages of Africa are free from psoriasis on account of exposure of the skin to sunlight, and that the negroes of North America have inherited this peculiarity. In our experience, psoriasis is frequently met with in the tropics in Europeans and natives of every race.

Seborrhœic affections are common in the tropics, especially in Europeans. A *seborrhœide* of the chest is frequently met with, and often confused with ringworm. The microscopical examination will clear the diagnosis. The use of a sulphur ointment (5 per cent.) is the best treatment.

In Ceylon a peculiar form of seborrhœa capitis with yellowish scales is occasionally seen in European children between four and twelve years of age. This affection is probably due to *Pityrosporum cantliei* Castellani, 1908, and quickly disappears when the child goes to cooler climates.

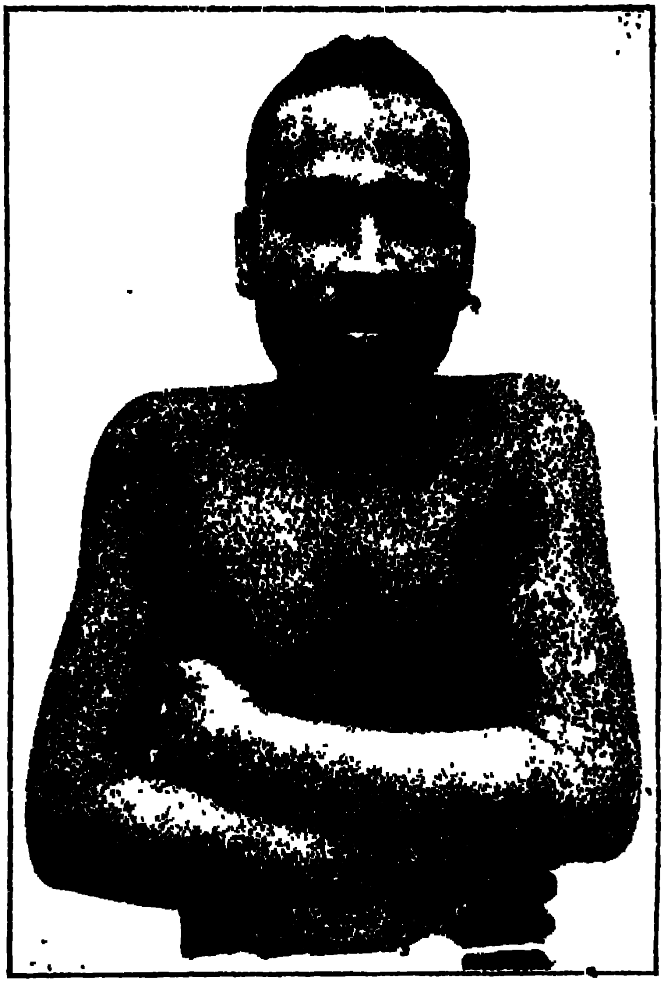

FIG. 896.—DERMATITIS EXFOLIATIVA SIMULATING TINEA IMBRICATA.

Dermatitis exfoliativa (pityriasis rubra) is not rarely met with, occasionally following on psoriasis. In Ceylon we have observed two cases in Sinhalese natives. The amount of desquamation was enormous. On removing the scales, which were white, the skin appeared of an angry red colour. At times, on superficial examination, certain cases may be mistaken for diffuse tinea imbricata.

ACNE VULGARIS—ACNE ROSACEA—ACNE VARIOLIFORMIS—ACNE CHELOID.

Acne vulgaris and **Comedos** are extremely common in all races. Both types of acne—**Acne indurata** and **Acne papulosa et pustulosa**—are observed. The treatment, which is as difficult in the tropics as in temperate zones, is based on the use of medicated soaps and sulphur or ichthyol lotions or ointments. The vaccine treatment may occasionally give good results.

Acne rosacea is, in our experience, comparatively rare in the tropics, though we have seen cases in all races. True *rhinophyma* we have also observed.

Acne Varioliformis.—This, in our experience, is as frequent in the tropics as in temperate zones, and may be found in all races. The regions of the body more commonly affected are the forehead, temples, the front of the sternum, and the interscapular region.

Acne cheloid is very common, especially among native races. The back of the neck is generally affected. Cases of *Acnitis* and *Folliclis* are occasionally seen. These are probably tuberculides.

HYPERIDROSIS AND BROMIDROSIS.

These conditions are, for climatic reasons, very common in the tropics, and have already been considered (see p. 2222). The treatment may be very difficult. Naphthol or salicylic alcoholic lotions (1 per cent.), followed by a salicylic, boric, or tannoform powder, are useful. If there is much inflammation of the skin, no alcoholic lotions should be used, but simply water solutions of boric acid (2 per cent.) carbolic acid (½ per cent.), permanganate of potassium (1 in 5,000), and occasionally hydrargyrum perchloride (1 in 2,000 or 4,000), after which a salicylic or boric powder is applied. The same powder should be sprinkled on the socks and shoes and undergarments. Internal treatment by sulphur, acid drinks, etc., is not of much use. Belladonna and atropin will stop the secretion for a time, but they must be pushed till unpleasant symptoms occur. We have seen a case of *chromidrosis* of the axilla in a native boy due to the presence of a bacillus closely allied to the *Bacillus prodigiosus*, and another due to a red-pigment-producing coccus.

Granulosis rubra nasi is occasionally seen in half-caste and European children.

LICHEN PLANUS—LICHEN SPINULOSUS—PITYRIASIS RUBRA PILARIS—PARAKERATOSIS VARIEGATA—POROKERATOSIS.

Lichen planus is common in the tropics among Europeans and natives of the various races. In very dark-skinned natives the diagnosis may be difficult to the medical man used to seeing skin diseases in Europeans only. Apart from the colour, however, the skin lesions are identical, the papules having an angular outline and a flat, occasionally umbilicated, shiny surface. When the eruption disappears, it generally leaves behind some pigmentation, which is extremely well marked in natives. *Lichen nitidus* has been seen by us on the penis of a half-caste and several Europeans.

Lichen spinulosus is occasionally met with in children.

Of **Pityriasis rubra pilaris** we have seen a case of a European.

Parakeratosis variegata was seen by us in a half-caste patient. We have come across two cases among natives of Mibelli and Resphighi's **Porokeratosis.** We have seen a case of **Granuloma annulare** in a European planter and one in a native clerk.

TUMOURS OF THE SKIN.

The tumours met with in temperate zones are met with also in the tropics in Europeans as well as natives. There is no doubt, however, that native races are more subject to some classes of tumours than to others. We would call attention to the extreme frequency among the natives of cheloid, the common occurrence of fibroma molluscum, and the comparative rarity of epithelioma of the face.

CONNECTIVE-TISSUE TUMOURS.

Benign Connective-Tissue Tumours.

Simple fibroma, Fibroma pendulum, and **Fibroma molluscum** (neuro-fibromatosis of Recklinghausen) are very frequently met with in natives. **Myomata** are occasionally observed in our cases always on the face.

Angiomata are not rare, and **multiple Telangiectases** are fairly common, and **Lymphangiomata** very frequent.

Xanthoma planum and **Xanthoma tuberosum** are frequently observed.

Xanthoma diabeticorum is very common in India and Ceylon, where the better classes suffer greatly from diabetes. An example of Balzer's **Pseudo-Xanthoma** or **Elastorrhexis** affecting the abdomen was observed by us in a half-caste woman.

Cheloid.—This is extremely frequent in native races. According to some authors, negroes suffer from it sixteen to eighteen times as much as whites. In Indian races it is not so frequent as in African natives, but still, much more frequent than in

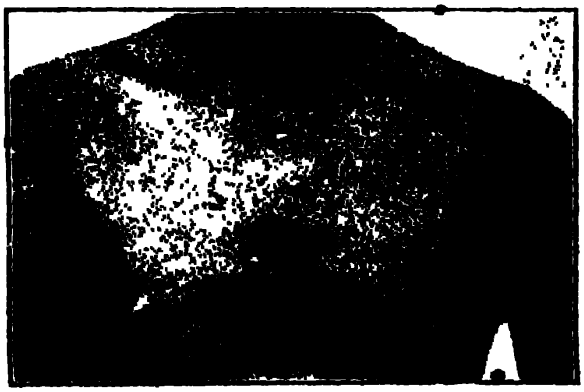

Fig. 097.—Cheloids.

Europeans. The smallest wounds, such as those made in tattooing, may be followed by cheloid. In Chinamen it often follows hypodermic injections of morphia.

Malignant Connective-Tissue Tumours.

Multiple sarcomatosis of the skin is rare. We have seen two cases, both in Sinhalese girls.

Mycosis fungoides has been observed by us once only in a half-caste man.

EPITHELIAL TUMOURS.

Benign Epithelial Tumours.

Epithelial moles are frequently observed.

Molluscum contagiosum is met with in all races.

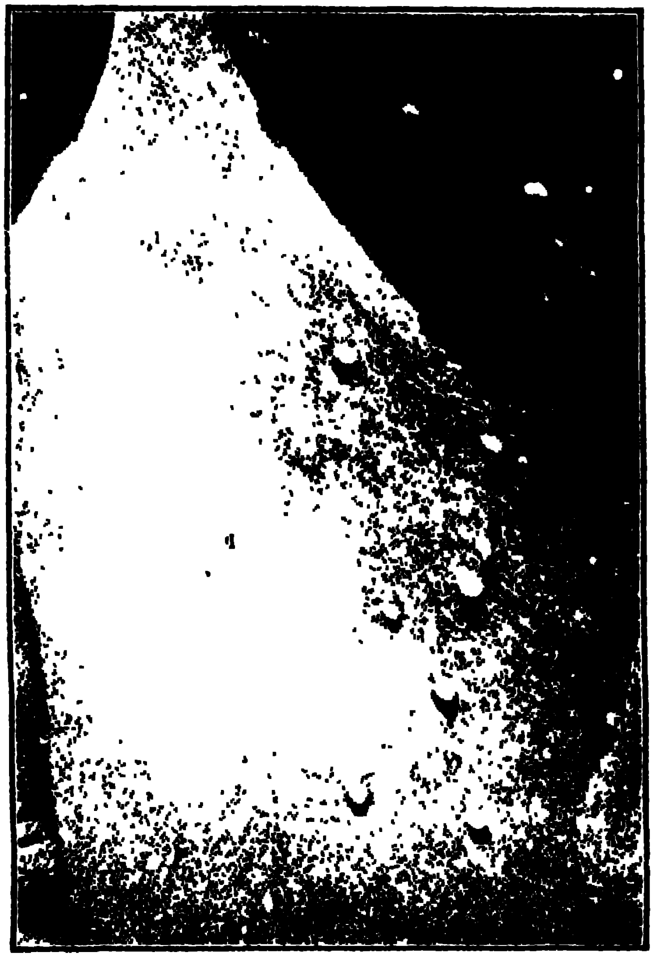

FIG. 898.—MOLLUSCUM CONTAGIOSUM.

Verrucæ and **Warts** are extremely common. In two instances we have seen Sinhalese boys covered all over the body with hundreds of warts. *Filiform warts* are met with, and *warts* on the genital organs

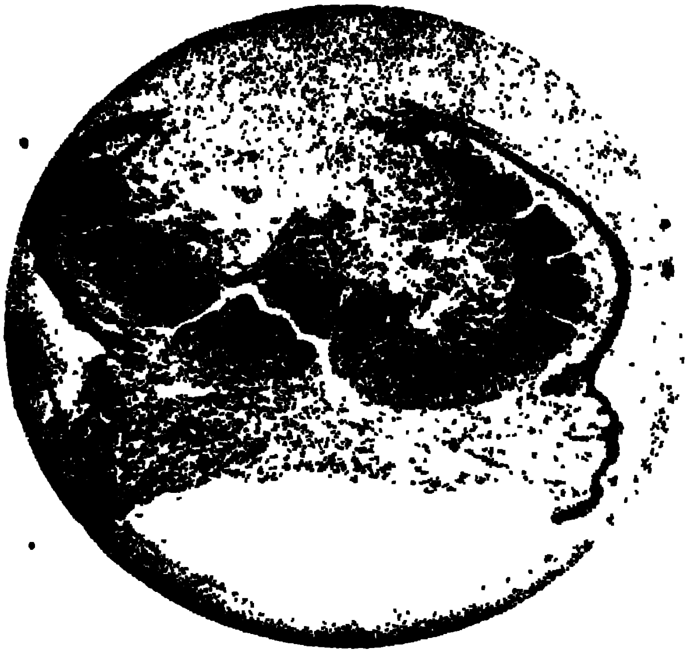

FIG. 899.—MOLLUSCUM CONTAGIOSUM: HISTOLOGICAL FEATURES.

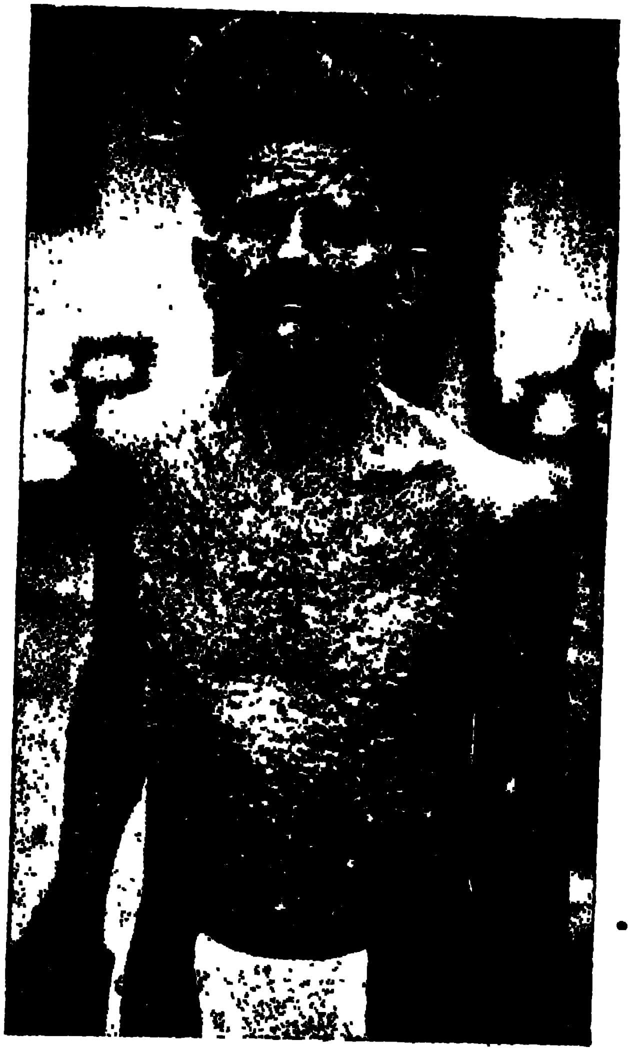

FIG. 900.—FIBROMA MOLLUSCUM IN A SINHALESE.

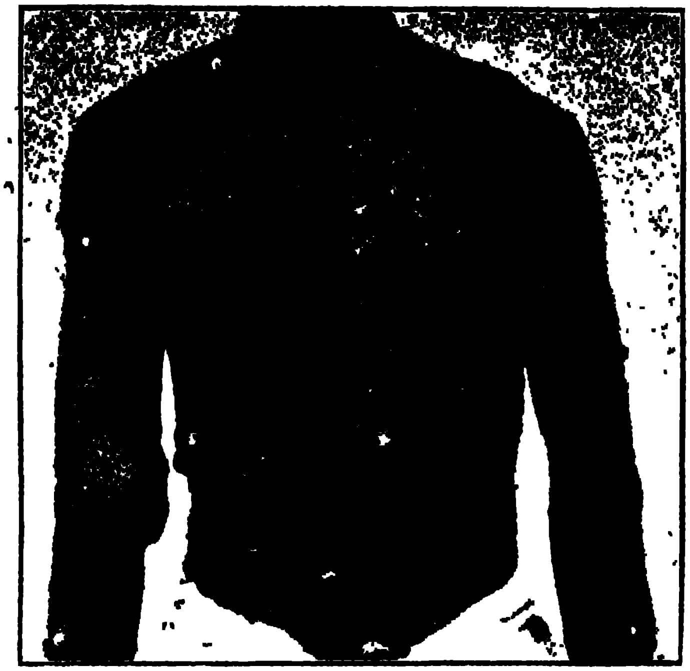

FIG. 901.—FIBROMA MOLLUSCUM: LARGER VARIETY.

FIG. 902.—FIBROMA MOLLUSCUM: LARGER VARIETY.

are very common. *Verruca senilis* and *Verruca seborrhaica* are frequent. The best treatment for ordinary warts is carbon dioxide snow.

Escomel has drawn attention to a peculiar treatment for warts in vogue among certain races in South America. These people apply the crushed body of a beetle belonging to the genus *Meloe* to the wart, the horny layer of which has been first scraped off. The wart disappears, leaving a slight whitish scar. The active principle is to be found in the beetle's blood.

Hyperkeratosis of the whole sole is often observed in natives going barefoot. We have seen several cases of *Cornu cutaneum*; the situation was generally on the hands, but in a case the condition developed at the edge of an ulcus tropicum (see Fig. 862, p. 2187).

Malignant Epithelial Tumours.

Rodent ulcer is comparatively rare among natives, but we have seen one case in a Sinhalese woman. We have observed a case of **Melanotic carcinoma** and two of **Paget's disease** of the nipple among half-castes.

MIXED TUMOURS.

Adenoma sebaceum of the face has been seen but rarely by us. We have never observed in the tropics cases of true **Angiokeratoma** on the hands, but we have seen a somewhat similar tumour on the scrotum of a European. A diffuse type of angiokeratoma of the foot somewhat resembling mycetoma has been described in South America (see p. 2147).

RHINOSCLEROMA.

A case of rhinoscleroma has been observed by us in an Indian coolie, and Gros has reported the occurrence of the disease in Algiers.

TUBERCULOSIS AND TUBERCULIDES—LUPUS ERYTHEMATOSUS.

Lupus vulgaris is met with in the tropics in all races, but, according to our observation, is far from being so common as in Europe.

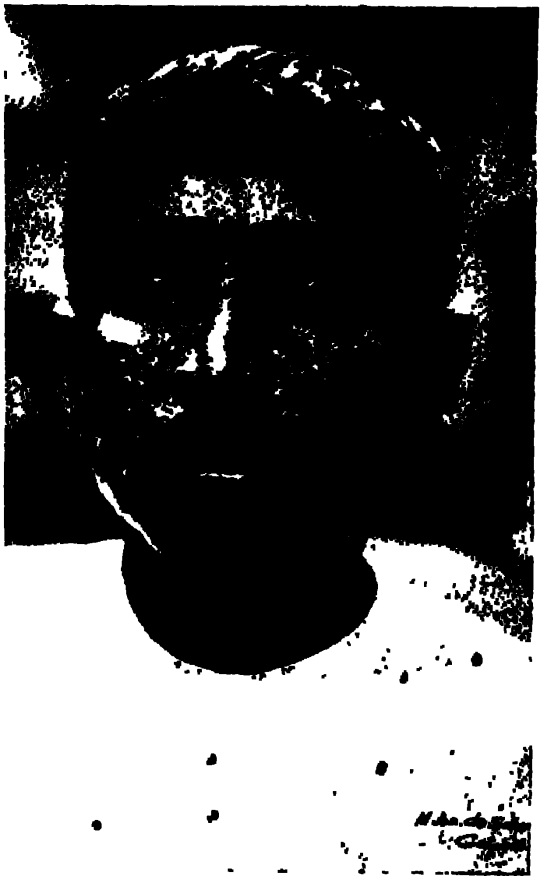

FIG. 903.—LUPUS VULGARIS IN A SINHALESE.

Tuberculosis verrucosa cutis is very rare, and **Scrofulodermia** much less common than in temperate zones. All the so-called tuberculides—**Lichen scrofulosorum, Acne scrofulosorum, Bazin's Erythema induratum, Folliclis,** and **Acnitis**—are observed but rarely in the tropics.

Lupus erythematosus, as regards which we agree with those writers who do not consider it of tubercular origin, is very rare in the tropics.

While tuberculosis of the lungs is at the present time extremely common in many parts of the tropics, skin affections of tubercular origin are, comparatively speaking, infrequently met with.

SYPHILIS—VENEREAL SORES—BALANO-POSTHITIS.

At the present date syphilis is rampant all over the tropics. In the past there is reason to believe that it was unknown in many of those tropical regions which were unopened to the cosmopolitan trade. According to Lambkin, in some parts of Uganda syphilis affects more than half of the population, and this enormous diffusion of the malady has taken place during recent years since the country

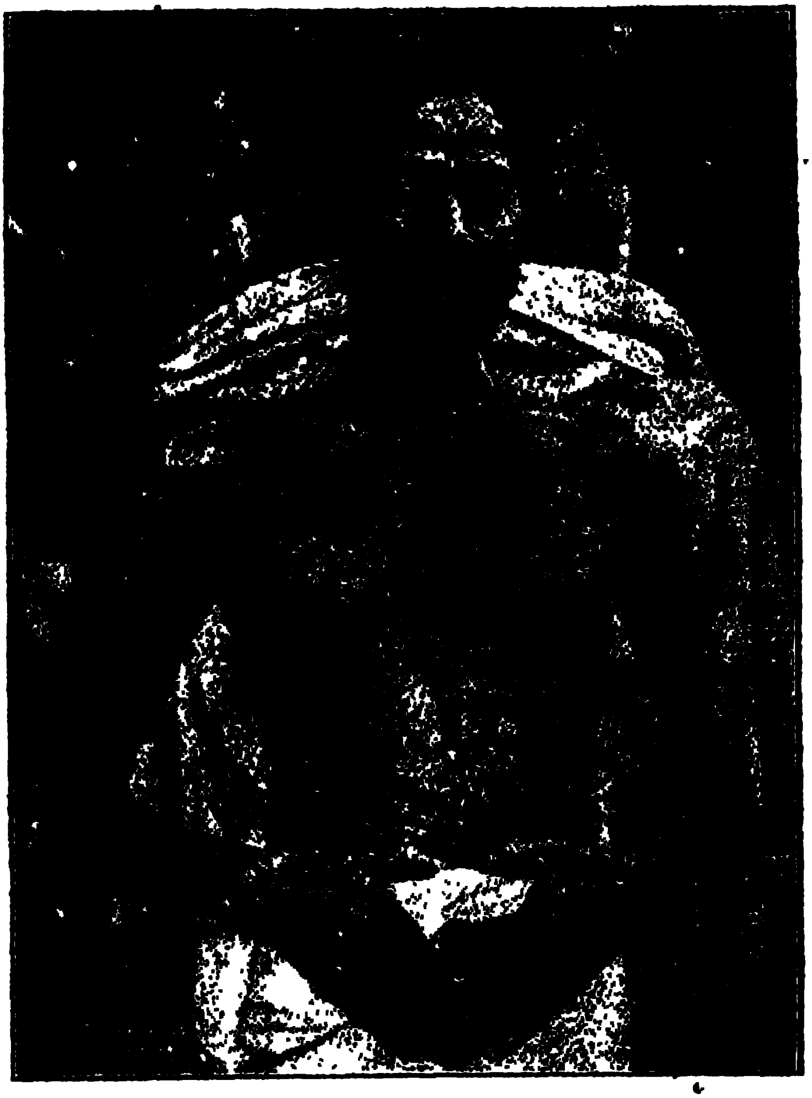

FIG. 904.—PAPULO-SQUAMOUS SYPHILIDE.

has been opened up. Syphilis is very frequently observed now also in all the other regions of Africa, and is very common in tropical Asia. It has been noted by Fox that in America it is much more frequent among negroes than among whites. In our experience, the virulence, as well as the symptoms of the disease, are not much different from what one sees in Europe. We can, however, confirm Brault's observation on the frequency of the primary sore on the supra-pubic region of natives, who regularly shave their pubis. Perhaps the general enlargement of the lymphatic glands is more marked in natives, and circinate and pustular syphilides, as observed by H. Fox, are more common. The tertiary ulcerative lesions are apt to become of enormous proportions, owing to secondary infections, and to the patient not seeking proper medical advice for a long time. Of great interest is the fact that in uncivilized native races the so-called parasyphilitic affections (progressive paralysis and tabes dorsalis) are extremely rare.

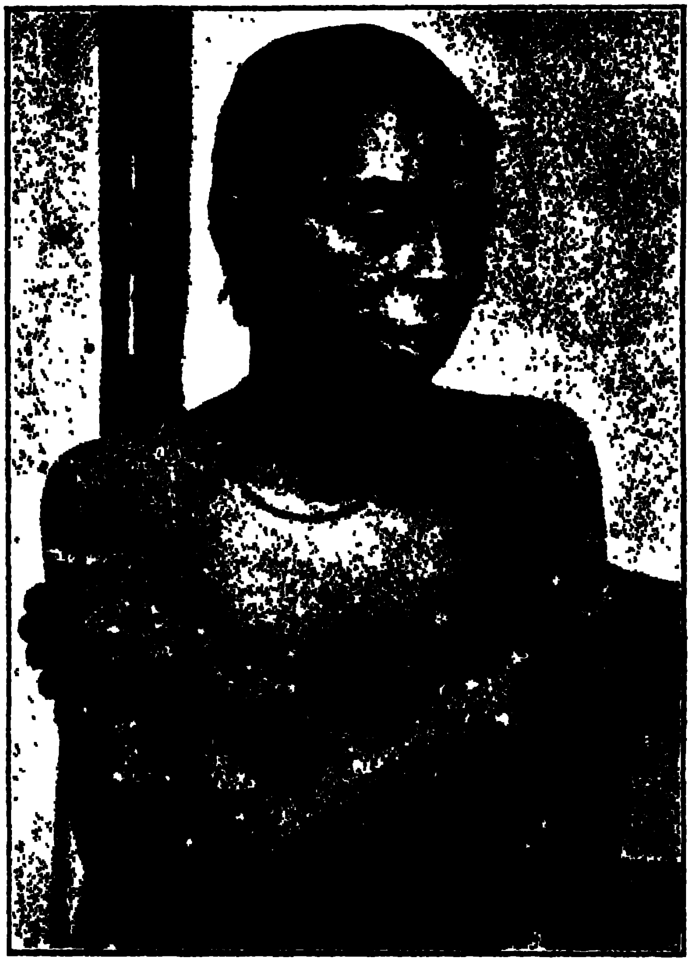

FIG. 985.—PUSTULAR SYPHILIDE

As regards the treatment of syphilis in the tropics, inunctions are very unpleasant in a hot damp climate. We generally prefer the ordinary internal treatment by hydrargyrum cum creta, gr. i., three times daily, and give also in most cases several injections of salvarsan or neosalvarsan. The technique of the salvarsan treatment has been given in the chapter on Frambœsia, p. 1560. We use also injections of various preparations of mercury. A mixed mercury and potassium iodide treatment is of advantage in some cases. Natives are said by some authors to be extremely susceptible to mercury, but in our experience this has been exaggerated. We generally give them the same doses as to Europeans. Native doctors give often mercury disguised in various ways. Decoctions of various herbs are also administered. In Abyssinia and Erythræa a decoction of a herb related to sarsaparilla and called 'usciva,' is much used, according to Annaratone.

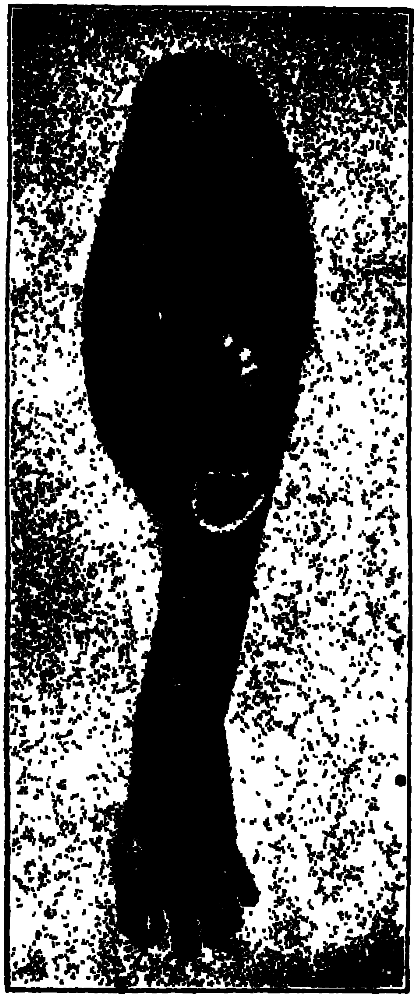

FIG. 906.—ULCER: TERTIARY SYPHILIS.

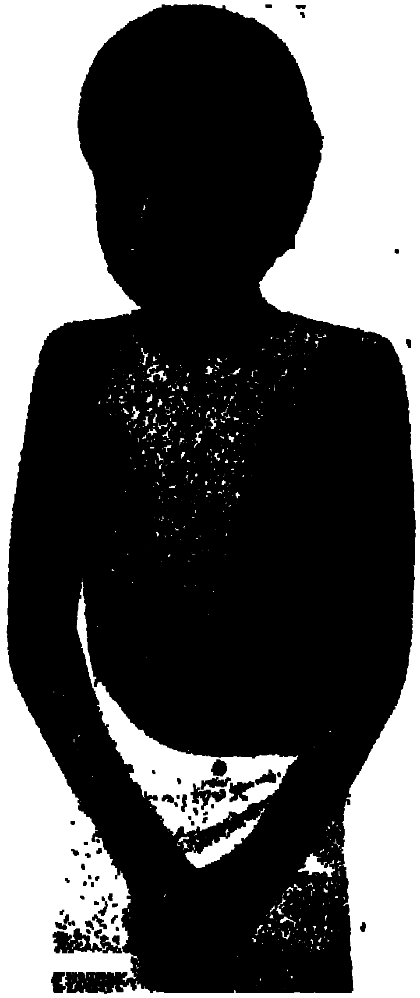

FIG. 907.—ICHTHYOSIS IN SINHALESE GIRL.

Venereal Sores.—These are common in all races, but are more apt to take a phagedænic character in the tropics.

Balano-posthitis.—Every type of balano-posthitis is met with in the tropics.

ICHTHYOSIS—SCLERODERMIA—MORPHEA.

Every type of **Ichthyosis** is met with in the tropics, from simple **Xerodermia** to **Ichthyosis hystrix.** Diffuse **Sclerodermia** is rare, but circumscribed sclerodermia (morphea) is rather frequent. We have seen a case of **Sclerema neonatorum** in a Sinhalese baby.

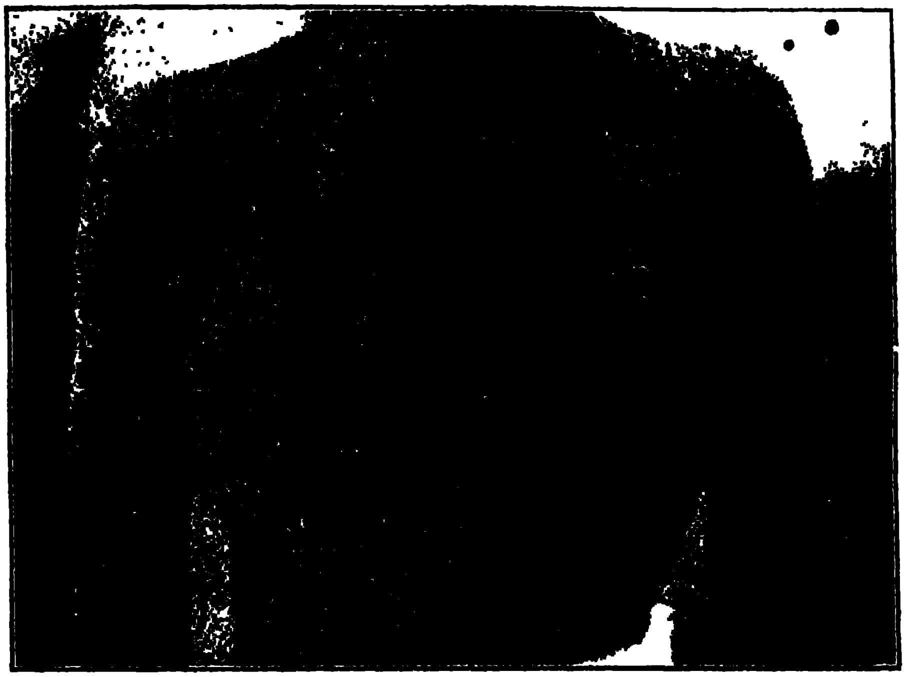

FIG. 908.—ICHTHYOSIS.

KAPOSI'S DISEASE—ACANTHOSIS NIGRICANS—DARIER'S DISEASE.

We have seen in the tropics several cases of **Kaposi's disease** (xeroderma pigmentosa) among European and half-caste children. We have come across in the tropics a case of **Acanthosis nigricans.** We have observed in Ceylon a typical case of Darier's disease in a Sinhalese beggar.

LENTIGO—CHLOASMA.

Freckling cannot be seen in very dark-skinned natives, but is easily visible in half-castes. It is very common among Europeans, especially those who live an open-air life, and are much exposed to the sun.

Chloasma is a very common affection in the tropics, and is found among Europeans as well as natives. The dark brownish or dirty yellowish patches of chloasma are plainly distinguishable in the skin of Indian and Sinhalese natives, though in African negroes they may be indistinguishable. (For more details see p. 2231.)

BIOTRIPSIS.

Cheatle has described under the name 'biotripsis,' or 'life-wear,' the trophic changes which take place in the skin of old people. In Europeans the skin, especially of the hands, may become at places shiny, smooth, inelastic, more or less pigmented than normal, and scar-like lesions may be present. Castellani has described a somewhat similar condition in old Sinhalese in whom the skin on the legs may present a peculiar appearance, becoming atrophic, and the superficial layers cracking. The condition, on superficial examination, might be taken for a mild type of ichthyosis. It is, however, probably a trophic condition due to old age. Chalmers and Drew have given an account of this condition as seen in the Sudan.

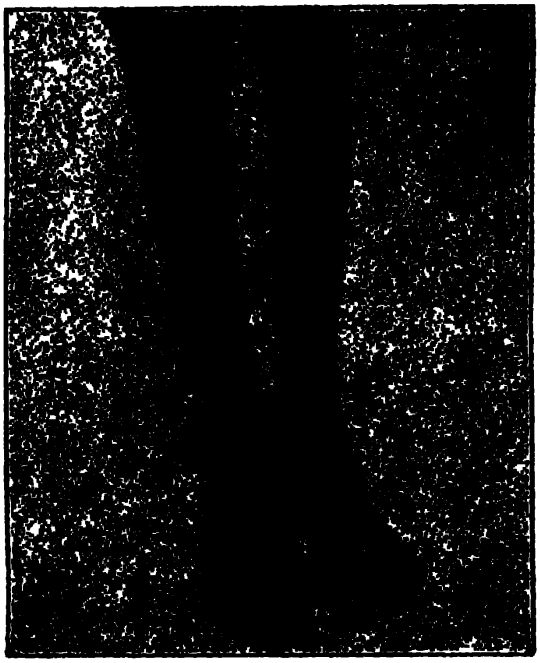

FIG. 909.—BIOTRIPSIS IN AN OLD SINHALESE MAN, SIMULATING A MILD TYPE OF ICHTHYOSIS.

DISEASES OF THE HAIR AND NAILS.

The diseases of parasitic origin are common, and have been described. Cases of **Hypertrichosis** in man and woman are occasionally met with. The so-called 'fragilitas crinium,' as well as **Trichorrhexis nodosa,** are rare in natives, this being probably due to the habit they have of frequently oiling and greasing the hair. We have seen cases of **Moniliform hair** (monilithrix) in Sinhalese and Tamils. In several Sinhalese decrepit old men, who wear their hair long, and do not take care of it, we have seen a condition of inextricable matting of the hair somewhat resembling **Plica.**

Canities is said to take place at a later age in negroes than in Europeans, but in our experience neither in negroes nor in Indian races is there any distinct difference. **Alopecia** of every origin is met with in the tropics. **Alopecia seborrhoeica** is very frequent among Europeans and educated natives. It is rare among the low classes and coolies. **Alopecia senilis** is less frequent in natives than in Europeans. **Alopecia areata** is apparently rare among natives, but recently we have come across several cases; it is fairly frequent among Europeans. We have seen a case of **pseudo-pelade** of Brocq (folliculitis decalvans) in a Sinhalese man.

All the diseases of the nails met with in temperate zones are found also in the tropics. **Brittle nails** (onychorrhexis), **ridged nails, transverse furrowing,** and **thinning of the nails, eggshell nails, shedding of the nails,** are conditions occasionally seen. **Leuconychia,** or whitening of the nails, either in spots (**leuconychia punctata**), linear (**leuconychia striata**), or affecting the whole nail (**leuconychia totalis**), is observed. We have described at p. 2236 a peculiar black pigmentation of the nails. **Onychia,** or inflammation of the nail matrix, is not rare. Ingrowing toenail is common. So-called **nail pterygium,** or outgrowth of the posterior nail fold, is occasionally seen, or the opposite condition, exposure of the root of the nail (**ficus unguium**), may be met with.

We have never observed a case of congenital atrophy, but we have seen one case of supernumerary nails. We have noted with comparative frequency a form of **onychogryphosis** affecting several members of the same family, and apparently hereditary to a certain extent. The nails are enormously thickened, and much longer than usual. All the nails may be affected, both those of the fingers and those of the toes.

Onychomycosis of various origin is a common affection, and has already been considered (p. 2059).

SOME COSMOPOLITAN DISEASES OF MUCOUS MEMBRANES.

Patches of **Leucoplakia** of the tongue are common in natives, and may be of various origin—syphilitic, framboetic, or due to irritation caused by smoking or chewing various substances. Cases of the so-called **circinate pityriasis linguæ** or **annulus migrans** are not rare. **Lingua nigra** is occasionally seen. We have already called attention to the *dark patches* found on the tongue in natives, and which by some writers have been described as a sign of ankylostomiasis. These pigmented patches are roundish or oval, and may be found also on the gums, the mucosa of the lips, on the soft and hard palate, and are apparently congenital. A condition which might be called **red or purple tongue,** and which often puzzles the newly arrived medical man, who does not know its origin, is extremely common in Ceylon among the coolies and lower-class natives, and is simply due to chewing betel. The pigmentation slowly disappears on the native discontinuing the use of betel. Cases of **furrowed tongue** (scrotal tongue) are not rare. We have seen a case of **Fordyce's disease** (pseudo-colloid of the lips) in a half-caste. A case of **cheilitis exfoliativa** in a European lady and cases of **perlèche** have been observed by us among European children. Under the term *seasonal recurrent ulceration of the lips*, Gros has described a very superficial ulceration on the lower lips in Algerian natives which is very common in the hot season, and is due, according to him, to a diplobacillus.

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